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Neurosensory function and white finger symptoms in relation to work and hand-transmitted vibration

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List of Papers

This thesis is based on the following six publications, which will be referred to by their Roman numerals.

I. Nilsson T, Burström L, Hagberg M. Risk assessment of vibration exposure and white fingers among platers. Int Arch Occup Environ Health. (1989);61: 473-481.

II. Nilsson T. Hagberg M. Burström L. Kihlberg S. Impaired nerve conduction in the carpal tunnel of platers and truck assemblers exposed to hand-arm vibration. Scand J Work Environ Health. (1994);2:189-199.

III. Nilsson T, Hagberg M, Burström L, Lundström R, Nyman I. Hand nerve function in relation to vibration and ergonomic workload. A five-year follow-up Am J Ind Med. (Conditionally accepted for publication).

IV. Toomingas A, Nilsson T, Hagberg M, Lundström R. Predictive aspects of Abduction External Rotation Test among male industrial and office workers. Am J Ind Med.(1999);35:32-42.

V. Lundström R, Nilsson T, Burström L, Hagberg M. Exposure-response relationship between hand-arm vibration and vibrotactile perception sensitivity. Am J Ind Med. (Conditionally accepted for publication).

VI. Nilsson T, Lundström R. Quantitative thermal perception thresholds in relation to vibration exposure. (Submitted for publication).

Abbrevations and acronyms

AER	Abduction external rotation test
BMI	Body mass index
CI	Confidence interval
CIR	Cumulative incidence ratio
CTS	Carpal tunnel syndrome
Cum	Cumulative
CVE	Cumulative vibration exposure
D	Dominant hand side
DPN	Diffuse peripheral neuropathy
EC1	Exposure category 1 (0<CVE≤24000 mh/s^2)
EC2	Exposure category 2 (CVE>24000 mh/s^2)
EMG	Electro myography
Exp	Exposure
HAVS	Hand-arm vibration syndrome
ISO	International Organisation for Standardization
M	Mean
M_{diff}	Difference between means
n	Number of subjects in the population
NCV	Nerve conduction velocity with reference to maximum nerve conduction velocity
ND	Non-dominant handside
NE	Non-exposed (CVE = 0 mh/s^2)
NP	Non-Pacinian
OR	Odds ratio
P	Pacinian
PPV	Positive predictive value
PR	Prevalence ratio
QST	Quantitative sensory test
RR	Rate ratio
SA	Slow adapting
SCV	Sensory conduction velocity
Sd	Standard deviation
SI	Sensitivity index
SWS	Stockholm Workshop scale
TOS	Thoracic outlet syndrome
TTS	Temporary threshold shift
vibr	Vibration
VPT	Vibrotactile perception threshold
VPT_{NP}	VPT within the frequencies (8-32Hz) most likely mediated by other than Pacinian corpuscles (Non-Pacinian)
VPT_P	VPT within the frequencies (63-500Hz) most likely mediated by the Pacinian corpuscles
VWF	Vibration white fingers

Definitions

Acceleration	A vector quantity that specifies the rate of change of velocity (m/s^2).
Acceleration level	The logarithm of the ratio of acceleration to a reference acceleration.
Allen's test	A physical examination test to show whether the radial or ulnar artery is occluded.
Antidrome	Nerve conduction stimulation causing propagation of an impulse in the direction opposite to physiological conduction.
Axon	A nerve cell process propagating electric action potentials.
Bias	Any trend in the collection, analysis, interpretation, publication, or review of data that can lead to conclusions that are systematically different from the truth.
Carpal tunnel syndrome	A disorder caused by compression on the median nerve in the carpal tunnel.
Cohort study	An investigation in which a cohort (a defined population) is studied over an extended period of time.
Confidence interval	A range of values for the effect estimate within which the true effect is thought to lie, with a specified level of confidence.
Confounder	A variable that explains a discrepancy between the desired (but unobservable) counterfactual risk (which the exposed would have had, had they been unexposed) and the unexposed risk that was its substitute.
Cross-sectional study	Comparison of disease prevalence among groups of workers or comparisons of exposures among prevalent cases and workers free of disease.
Cumulative exposure	Summation of products of exposure and the time interval during which the exposure occurred.
Distal motor latency	Interval between the onset of a stimulus and the onset of the resultant compound muscle action potential.
Exposure- effect	The biological change related to an exposure. When the numerical values for both exposure and outcome are known, the relationship can be computed.
Exposure- response	The proportion of a population having values showing an abnormal effect (fulfilling a predefined case criteria).
Frequency weighted	A term denoting that the relevant wave form has been modified according to a transfer function usually related to some human response.
Myelin	A lipid sheath around an axon produced by a Schwann cell.
Nerve conduction Velocity	Speed of propagation of an action potential along a nerve fibre. Loosely used to refer to the maximum nerve conduction velocity.
Outcome	All the possible results of an exposure.
Polyneuropathy	Neuropathy at several peripheral nerve sites.
Prevalence	Number of cases in a population at a designated time.
Raynaud's phenomenon	Intermittent blanching of fingers due to vasospasm.
Tonic vibration reflex	Reflex muscle contraction elicited by vibration applied to the muscle belly or tendon.
Vibration-induced white fingers	Intermittent episodes of secondary Raynaud's phenomenon elicited by exposure to cold.

Contents

Introduction

In manual work, muscular force is transformed to motion. Physical work is characterised by biomechanic and ergonomic work-load parameters. The muscular effort expended can be reduced by using powered machines. At any given muscular load, an increased energy can be exerted by a power machine primarily based on the principle of keeping the force low and magnifying the motion. Motion descriptors include distance traversed (displacement) by time (velocity), the change in speed of the moving object (acceleration), and when the movement distance is restricted, a repetition of the full period of motion (frequency) arises. Vibration is the description of such oscillatory motion.

In Sweden, approximately a 400 000 persons are exposed to hand-transmitted vibration in their daily work (187) and there are a total of one million powered machines.

Exposure

Hand-transmitted vibration

Vibration is a vector quantity. This means that a moving object has both magnitude (intensity) to its motion and moves in a given direction (210). A vibrating object moves to and fro over some displacement with a velocity alternately in one direction and then in the other. The measurement of vibration requires that the oscillatory movements be transduced to a measure representing the movements. The magnitude of a vibration can thus be measured by its displacement, its velocity or its acceleration. The unit of displacement is distance in meter (m). Velocity is the ratio between distance and time in meter per second (m/s). The unit of acceleration is distance/time∗time (meter/second∗second=m/s^2). Nowadays, the magnitude is usually expressed in the terms of acceleration and is measured with accelerometers (74). Vibration frequency is expressed as the number of cycles /second (Hz). The direction of the movement is expressed in three orthogonal directions designated x, y and z. For the assumed effects on the hand-arm system of vibration frequency and vibration transmission direction it is possible to report a single ”frequency-weighted” value. The evaluation standard ISO 5349 (93) uses a frequency-weighting to assess the severity of hand-transmitted vibration over the approximate frequency range of 5 to 1500 Hz. This standard uses an ”equal energy” concept so that a complex exposure pattern of any period during the day can be represented by the equivalent value for an exposure of four hours (four-hour energy equivalent frequency–weighted acceleration). Integrating the time aspects into vibration exposure can be expressed as cumulative acceleration exposure.

Table 1 Studies of temporary shifts in relation to vibration-exposure chracteristics

Exposure characteristics	Symptoms	Vascular	Nerve conduction	Vibrotactile perception	Thermal perception	2-point discrimination	Muscular function	Reflexes	Miscellaneous
Frequency aspects	(67, 101) (127)	(27) (153)	(127) (153)	(122) (67) (123) (127) (117) (151) (151) (126) (101) (190)	(86)		(127) (101)	(130)	
Intensity aspects	(127) (190)	(27) (53) (159)	(127)	(123) (127) (204) (126)	(86)		(127) (190)		
Time/ duration aspects		(53) (28)		(22) (122) (152)		(22)			
Vibration and other exposures	(161)	(26) (82) (19)		(125) (5) (152) (82)				(154) (130)	
Dose				(22) (124) (221)		(22)			
Different job titles, or single exposure		(131)	(120) (38)	(202) (172)		(80)	(185) (174)	(76)	(100) (202) (183)

Vibration is a physical stressor when transmitted to the hand-arm of the operator. The body responds characteristically to certain critical vibration frequencies. The frequencies to be considered are within the range 5 – 1500 Hz. according to the ISO 5349 (93) or 5 –5000 Hz according to the NIOSH standard (84). The amount of vibration energy absorbed increases linearly with increasing handgrip force (39). In an experiment where grip and feed forces were held constant, almost all the energy from the exposure to random vibration was absorbed distal to the knuckle of the hand at frequencies higher than 400 Hz (195). For frequencies above 60 Hz the absorption takes place in the hand. Low frequency (< 50 Hz) impact vibration is transmitted unattenuated up to the elbow and is accompanied by segment-related symptoms (102). Shock-type vibration exposure give significantly higher hand forces and absorption of energy compared with non-impulsive vibration exposure (43).

Ergonomic work load factors

There is scientific evidence available on the association between work and the development of neuro-musculoskeletal disorders in the upper extremity concerning disorders such as shoulder and hand-wrist tendinitis, epicondylitis, thoracic outlet syndrome, carpal tunnel syndrome, and hand-arm vibration syndrome (79) (14). In reviews of epidemiological studies on upper extremity disorders, several ergonomic risk factors e.g. load sustained over time (force, repetitiveness, posture), ”fit, reach and see”, task invariability, psychosocial work variables and cold, vibration and local mechanical stresses have all been identified as distinctive workplace risk factors (205) (79) (14). An association between specific occupational risk factors and repetitive motion disorders, including nerve compression at the carpal tunnel, is gaining increasing scientific support (78, 155).

Temporary shifts in relation to vibration exposure

Disturbances in sensibility, motor control and blood circulation are introduced by exposure to working with vibrating machinery (166). The responses show that the body structures respond actively to the exposure, and the detrimental effects entail interaction between worker attributes, work and vibration (11, 129). Some of the effects are temporary changes, from which recovery is generally rapid, while others have been assumed to be permanent.

Among the acute responses (Table 1) revealed in experiments with vibration exposure are: temporary threshold shift for vibrotactile, thermal perception, and two-point discrimination, vascular tone change, nerve conduction impairment, increased axon excitability experienced as post-exposure paresthesia, altered sensorimotor reflexes such as the tonic vibration reflex and γ-loop interference indicated by disillusion of limb position with deranged performance.

Vibration produces a significant reduction in finger blood flow and increases in vascular resistance when compared with pre-exposure and non-vibrated finger values. Temporary vasodilatation occurred in the vibrated finger immediately after vibration exposure, whereas a progressive finger blood flow reduction occurred in both vibrated and non-vibrated fingers after 15 – 30 minutes of exposure (28). In another investigation, the extent of the digital circulatory response was found to depend on the magnitude and frequency of the vibration exposure (27). The vibration exposure at 125 Hz had the greatest impact, which is in accordance with former studies (127). Acute vascular vasoconstriction has also been demonstrated in the lower extremities during exposure to one single finger (53).

A temporary threshold shift (TTS) for vibration perception thresholds has been shown to increase with increased acceleration and to be maximal at 125 Hz (127). The magnitude of the TTS change is also influenced by the initial vibration perception threshold (VPT) value (126).

A temporary threshold shift for thermal perception has attracted little attention. Hirosawa and co-workers (86) showed the frequency dependency, with maximal effect at 125 Hz, to be similar to that for vibrotactile perception. They found a marked effect on warmth perception but less effect on cold perception. Any interpretation of the results must take into account the finger temperature change accompanying the temporary reduction in peripheral vascular flow manifested as reduced finger temperature (180).

High frequency vibration exposure produces long-lasting hypesthesia (120). Accompanying paresthesia may be attributed to disturbances in peripheral afferent fibers (38).

Rohmert and co-workers have demonstrated that vibration increases the EMG activity in the muscles of the hand–arm system (174). Vibratory exposure reduces the endurance time of muscles (185). The tonic-vibration reflex as revealed by EMG on motor unit synchronisation, is strongest below 150Hz (130).

There is active interplay between the acute perturbations and the coupling between the hand-arm system and the machinery and it constitutes one of the determinants for the actual vibration dose transmitted (171). The acute disturbances are temporary and affect most exposed workers. In none of the studies referred to did any major effects remain after more than one hour.

Many of these acute effects are not consciously perceived (129) and so far have been underrated as potential risk factors in, e.g., accidents involving fall, dropping objects, improper use of controls, and traumatic injuries.

Major hypotheses for transforming temporary vibration effects into permanent health hazard

The major hypothesis for vibration exposure to cause a permanent health shift includes: disturbance on local and central vasoregulatory control through neural, endocrine, and shear stress factors (28). A complex causal relation is in line with the multifactorial etiology of Raynaud´s phenomenon (203). The perturbation of the microcirculatory blood supply to the nerves by work related compression and vibration represents additional factors for the neurological hazards (113) (194).

Permanent shifts in relation to vibration exposure

Extensive, long-lasting exposure to manual work involving the use of vibrating power tools has been associated in epidemiological studies with persistent health disorders. The major health hazards reported are: a disorder of the peripheral micro-circulation, cold-induced Raynaud's phenomenon or "vibration white fingers" (VWF), and neurological disorders in the peripheral nervous system, either in the form of nerve entrapment at various locations (78, 98, 144)or as a peripheral nerve affection (diffusely distributed neuropathy). These health effects are collectively summarised as the hand-arm-vibration syndrome (HAVS), classified until 1986 by one single scale (200), irrespective of the fact that the nosological components may develop either concordantly or independently. This has given rise to the preparation of two separate classification scales for hand-arm vibration symptoms, one for the vascular component (69) and one for the sensorineural symptoms (34). These grading scales have shortcomings but information which could allow for a revison is still lacking (68). The vibration-related sensorineural, muscular (146, 147) and bone and joint disorders (70) still lack validated risk prediction models (68, 73).

White finger symptoms

Workers useing hand-held vibrating machines may experience episodic finger blanching in relation to exposure to cold or vibration. The main predictors for the vasospastic response are vibration duration, magnitude, and frequency (93). Many studies support an association between vibration and HAVS (Table 2). NIOSH has recognised the bulk of scientific knowledge as ”strong evidence” for a causal relation (14). Recently the ”seriousness of these vascular symptoms” as a common trait have been questioned (75), a view which is inconceivable to the physician who has witnnessed the reduction in quality of life often resulting from HAVS.

The study of Nilsson and co-workers (148) represents the first published investigation with white finger symptoms graded according to the separate Stockholm workshop vascular scale in comparison to the Taylor-Pelmear scale.

Neurosensory function

Disturbances in hand function commonly reported as numbness, paresthesia, difficulty in performing manipulative tasks, have been reported in workers handling vibrating power-machines (Table 3) and among ordinary manual workers (78). The association between reported symptoms and vibrotactile acuity is not straightforward. In a study on this topic, it was best predicted by questions relating to hand function (51). A finding that is compatible with basic somatosensory concepts of negative and positive phenomena (111).

Table 2 Studies on the risk of permanent shifts regarding primarily vascular symptoms in relation to vibration-exposure assessment and study design

	Cohort studies	Case-control studies	Cross-sectional studies	Surveys	Case series
Quantified hand-side specific, personal measurements			(65)		
Quantified personal measurements	(24)	(23) (25)	(20) (21)	(162)	(164)
Quantified area or job-specific measurements	(63) (107)		**Paper I** (13) (219) (108) (29) (220)		
Ordinally ranked jobs or tasks			(138) (222)	(169)	(95) (167)
Duration of employment	(160) (157) (105) (61)	(62)	(223) (141) (31) (137) (136) (142) (208)	(139)	(163) (48) (193) (199)
Job title: Ever employed			(52)		

Hypesthesia (a negative manifestation) reflects failure at any level along sensory channels. The person may or may not be aware of the deficit. Negative sensory symptoms are late indicators of afferent dysfunction. Positive manifestations also reflect dysfunction but are expressed mostly as symptoms (e.g. tingling, buzzing, pricking), without signs. Positive phenomena are largely due to abnormal generation of impulses in sensory channels. Microelectrode recordings from the median nerve on human subjects exposed to vibration and to electric pulse trains, respectively, indicated that paresthesia could be attributed to disturbances in afferent sensory fibers (38). A significant category of positive sensory phenomena involves inadequate subjective response to natural stimulation of receptors. Strömberg and co-workers (193), among other findings, observed abnormal intolerance of cold in a case series of vibration-exposed patients.

The sensory units (156) (nerve fibers with their endings, cell bodies and central processes) are characterised by their type of nerve fiber, type of end organ, and their adequate stimuli. The cardinal signs of altered sensory unit function are elevated threshold as a loss of function, and lowered threshold as a sign of increased sensitivity (110) at quantitative sensory testing (QST). Symptoms of numbness have been noticed (111) without sensory loss at QST. This may be due to positive phenomena, or to sensory dysfunction confined to suprathreshold stimulus (Figure 1).

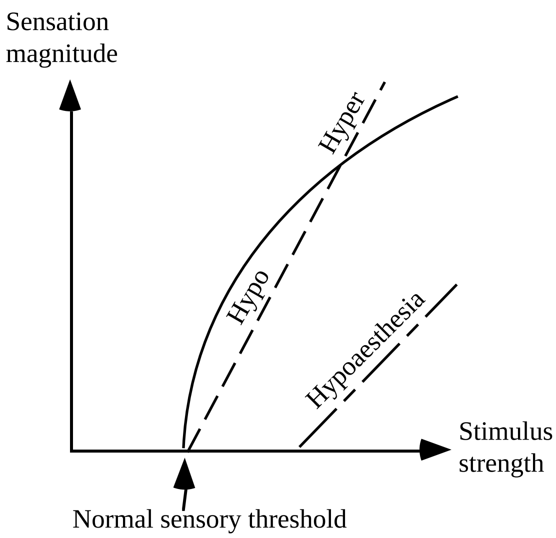

Figure 1. Disturbance in sensation could be elicited by either disturbance in normal or suprathreshold stimulation and result in hyper- or hypesthesia (15).

The discrepancy between symptoms and signs may also entail sensory impairment without subjective recognition or symptoms. This applies to for instance thermal (54) and tactile sensibility (58). Such discrepancies could be illustrated by the results from Homan and co-workers (91) (Figure 2).

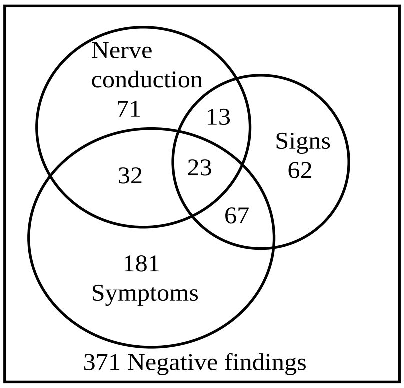

Figure 2. Prevalence of symptoms, physical findings and nerve conduction findings (. Modified from Homan and co-workers (91).

Another discrepancy between symptoms and signs arises when the subject reports symptoms of paresthesia with absence of pathological findings in physical examination, neuro-electrodiagnostic testing, and QST. Provocation test may in such cases reveal a dysfunction, but there is a lack of such studies on vibration exposed, and only few studies are published e.g. repetitive strain injuries (72).

Neurosensory symptoms in relation to hand-arm vibration exposure

So far, the vasospastic disorders have been the most thoroughly investigated of the hand-arm vibration symptoms. Recently, more interest has focused on the impact of vibration on neural structures. The wide spectrum of sensory symptoms reported subsumes both positive and negative phenomena. Negative symptoms dominate (Table 3) referring to numbness and other loss or absence of feeling, reduced proprioception and difficulty with motor skills. The positive symptoms include dysesthesia and tingling. Previously, symptoms were categorised as present or absent, while later staging is based on the Stockholm Workshop scale. The various descriptions include, for instance “Numbing of the hands was particularly common at night” or “They were forced to rub and shake their hands” (169). Strömberg and co-workers noticed the occurrence of cold intolerance expressed as pain and coldness, without blanching on exposure to a cool environment (193). Such symptoms are claimed to be a major problem following injury to digital nerves.

Many studies report that neurosensory symptoms are more prevalent (95, 108) than vascular symptoms, often in the order of 2:1 (29, 162).

A relation between sensory symptoms and signs has been claimed as e.g. subjects with more advanced sensory symptoms had a more impaired perception sensitivity for temperature and vibration (54).

The occurrence of sensorineural disturbances is reported to increase with increasing exposure to vibration, but no linear relation could be shown (20). The authors raise the question of whether the sensory scale used is fully adequate to discover a vibration exposure effect.

Table 3 Studies on the the risk of permanent shifts regarding neurological symptoms in relation to vibration-exposure assessment and study design

	Cohort studies	Case-control studies	Cross-sectional studies	Surveys	Case series
Quantified hand-side specific, personal measurements					
Quantified personal measurements	(24)		(20)sws	(162)	
Quantified area or job-specific measurements	(107)		(108)sws (220)sws (29)sws (219)sws (30)sws (207)		(54)sws
Ordinally ranked jobs or tasks			(213)	(169)	
Duration of employment		(213)sws	(58)sws	(132)sws	(193)sws (48)sws (95)sws
Job title: Ever employed		(37)	(99)sws (51)sws (32)		(48)sws (96)

SWS =Stockholm workshop scale

A symptom–sign discrepancy is extensively reported and often clinical examination fail to distinguish between symptomatic and asymptomatic workers (99), (32).

This problem was also observed by McGeoch and co-workers (132), who noticed that a number of workers reported no symptoms but had positive scores on one or more of the perception tests. Werner and co-workers performed nerve conduction examinations among symptomatic and asymptomatic persons and found that some people with verified neuropathy had symptoms and some did not (213). They reported a slowed sensory conduction velocity in the digital segment in 10% of the workers without symptoms and in 56% of those with symptoms. Nerve conduction studies by Cherniack, and co-workers (48) were neither significantly different between more or less symptomatic groups nor did they correlate with clinical and quantitative tests.

Coutu-Wakulczyk (51) investigated the association between hand symptoms and quantitative measures of hand tactile acuity and found questions on functional deficiencies (e.g. buttoning difficulties) to be the best predictor while positive symptoms like numbness only had a predictive value of 55%.

QST of thermal perception in relation to hand-arm vibration

Animal experiments indicate that exposure to vibration may induce lesions in small nonmyelinated nerve fibers close to the vibration source (115). Clinical experience and case series (54) support these findings. Only a minor number of studies have been reported on vibration and thermal perception (Table 4). The studies on the function of the thin unmyelinated and small myelinated nerve fibers with end organs reacting to heat-induced pain, warmth and cold, in relation to vibration (Table 4) have not been performed on unselected working populations with quantified personal exposure assessment. There is a lack of such studies.

QST of vibrotactile perception in relation to hand-arm vibration

The human subject’s ability to hold and control delicate objects is determined by tactile afferent input from mechanoreceptors (215). Work and motor skills might collapse if this afferent system is disturbed. Various sensory units with endorgan mechanoreceptors encode the perception of touch and vibration. The corresponding nerve fibers are larger than for thermal perception and are myelinated. According to various receptor adaptation characteristics different units handle different vibration frequencies (119). Studies on the relation between vibration exposure and remaining vibrotactile perception function have mainly been performed on case series (Table 5) and have lacked personal exposure assessment.

Table 4 Studies on the risk of permanent shifts in thermal perception in relation to vibration-exposure assessment and study design

	Cohort studies	Case-control studies	Cross-sectional studies	Surveys	Case series
Quantified hand-side specific, personal measurements					
Quantified personal measurements			**Paper VI**		
Quantified area or job-specific measurements			(30) (149)		(54)
Ordinally ranked jobs or tasks			(56)		
Duration of employment		(55) (88)	(209)	(132)	(85)
Job title: Ever employed		(158) (57)	(87)		(199)

Table 5 Studies on the risk of permanent shifts in vibrotactile perception in relation to vibration-exposure assessment and study design

	Cohort studies	Case-control studies	Cross-sectional studies	Surveys	Case series
Quantified hand-side specific, personal measurements					
Quantified personal measurements			**Paper V** (212)		
Quantified area or job-specific measurements	(4)(part of n=8)		(206) (81)	(4)	(54)
Ordinally ranked jobs or tasks			(224) (56)		
Duration of employment/exposure		(209) (88)	(58) (83) (207)	(198) (132)	
Job title: Ever employed/exposed		(182) (57) (198)	(32) (51) (35) (99)		(116) (48)

Nerve fiber dysfunction in relation to hand-arm vibration

Data supporting the view of a neurological vibration effect on the nerve fiber come from various nerve conduction studies (Table 6). Fractionated nerve conduction measurements on vibration-exposed subjects with hand symptoms have revealed a bimodal distribution, suggesting effects on both axons and peripheral sensory receptors (176). The latter effects have been termed vibration-related "diffusely distributed neuropathy" or "diffuse peripheral neuropathy" (DPN) (98). As to the effect on the axon there is the clinical observation that compression lesions usually result in relatively less effect on sensation than on motor function, indicating that large motor fibres are more susceptible than thinner sensory fibres (113).
The nerve injuries from working with power machines interact (165) with nerve injuries from compression and repetitive motion (155). Studies on nerve conduction have been performed almost exclusively on case-series of patients (Table 6). There has thus been a lack of prospective cohort studies on working populations with quantified hand-side specific exposure assessment.

Ultrastructural changes associated with vibration exposure

Takeuchi, and co-workers (196) reported histological changes such as thickening of muscular layers and fibrosis in the peripheral arteries, demyelinating neuropathy and loss of nerve fibers in the peripheral nerves of workers who had used vibrating tools.

Excessive vibration exposure of rat tail resulted in ultrastructural changes such as detachment of the myelin sheath, constriction of the axon and deranged paranodal regions accompanied by reduced nerve conduction (45). These results are compatible with earlier findings (90).

Finger biopsies from patients with vibration white fingers have a characteristic perineurial fibrosis, thickened perineurium, reduced number of nerve fibers and reduction in the size of myelinated fibers (197). The structural nerve injuries associated with vibration are dominated by myelin breakdown and interstitial perineurial fibrosis associated with incomplete regeneration or with organisation of oedema (192). Experimental evidence of disturbed microcirculation in relation to vibration exposure is revealed by the associated formation of intraneural oedema (114).

The neuromuscular effects noticed in relation to vibration exposure have mainly been studied in animal experimental models (145). Muscle response to short-term exposure to vibration induced an increase in the cross-sectional area of type 1 and 2 C fibers in a comparison with controls (147). When the vibration exposure was increased the slow-twitch type 1 fibers were significantly enlarged as were the muscle fiber nuclei more centrally positioned (146).

Table 6 Studies on the risk of permanent shifts in nerve fiber function in relation to vibration-exposure assessment and study design

	Experimental studies	Cohort studies	Case-control studies	Cross-sectional studies	Surveys	Case series
Quantified hand-side specific, personal measurements		**Paper III**				
Quantified personal measurements	(115) (128) (184)	**Paper IV**		**Paper II**		
Quantified area or job-specific measurements		(188)	(46) (89)			
Ordinally ranked jobs or tasks		(144)	(97)	(213)		
Duration of employment			(7) (140) (88) (216)* (181) (9) (10) (182)	(6)	(64)*	(50)* (98)* (135)*
Job title: Ever employed			(37) (184) (182) (176)*			(96) (48) (36) (186)*

Focus of the thesis

The existence of a crude association between work involving exposure to vibrating tools and upper extremity disorders is supported in numerous epidemiological investigations and critical reviews e.g. (79) (14). Vibration exposure, specifically, is also repeatedly reported as a separate risk factor for long-lasting health effects on the vascular and neurosensory system (Table 2-6). Though many studies have been performed, few convincing exposure-response relations have been derived. One reason for this might be the sparsity of longitudinal etiological studies (see Tables 2-6) with good assessment of exposure (see exposure assessment classification according to Checkoway (47) in Tables 2-6) together with well-defined measures (with or without consideration of the dilemma of discrepancies between symptoms, signs, and test results) of disease.

Epidemiological studies addressing the quantitative relation between work and upper-extremity neuropathy have variously indicated an association with both the occupational hand-arm vibration and the manual load aspects e.g., force, repetition, and posture sustained over time (71). The evaluation of the consistency and strength of the association has, however, been controversial (12) and the risk factors cannot be distinguished from each other. In vibration-associated neuropathy, conceivable target structures are the peripheral sensory receptors, the large myelinated, the thinly myelinated, and the small-calibre non-myelinated nerve fibres. Diagnostic tests that attempt to identify which of these structures are involved have so far produced inconclusive results (33). The focus of this thesis is predominantly on exploring the effects of exposure on nerve fibres of different dimensions but also to assess the vascular symptoms.

This thesis comprises six studies (I-VI) of neurological and vascular functions in subjects exposed to vibration and ergonomic work-load factors. The first of these studies focuses on the risk of self-reported signs of VWF. The second study addresses risk assessment of nerve conduction in relation to work with vibration exposure while the third study focuses on the effect of hand-specific cumulative vibration exposure and manual workload on the nerve fiber of both motor and sensory nerves in a cohort-based design. The fourth study explores the abduction external rotation provocation test as a longitudinal predictor of nerve dysfunction as manifested in symptoms, signs, and nerve conduction. The fifth and sixth studies cover the association between vibration exposure and negative neurosensory manifestations revealed by quantitative sensory testing of vibrotactile and thermal perception respectively.

Aim

The overall aim of the present studies was to assess the quantitative relation between cumulative vibration exposure and self-reported signs of "white fingers", quantitative sensory test findings and electro-neurophysiological indices of impaired nerve function.

The investigation of vascular aspects (Study I) had a twofold aim:
To assess the prevalence and odds ratio for vascular disorders in the hands in relation to vibration exposure and to compare the actual occurrence of vibration white fingers with the occurrence predicted according to the ISO 5349 (94) schedules.

The relation between work with vibrating tools and nerve function was investigated with the specific aims of:
Assessing the relative risks of contracting impaired nerve conduction among vibration-exposed as opposed to non-exposed referents (Study II), and assessing the possible deterioration in nerve conduction for motor and sensory nerves over the carpal tunnel segment in relation to vibration exposure after a 5-year follow-up. The aims also included assessing such deterioration in relation to physical workload and to compare the effect on the sensory nerves between the hand-finger segment and the carpal tunnel segment in the hands of platers and office workers respectively (Study III).

The relation between vibration exposure and nerve provocability was studied (Study IV) with the specific aims of:
Quantifying the association between a physical examination nerve provocation (Abduction External Rotation) test outcome and nerve conduction in the wrist/hand regions and investigating the exposure factors predictive of AER signs that appeared 5 years later .

The relation between vibration exposure and neurosensory function was investigated with the specific aims of:
Quantifying the association between cumulative use of vibrating hand-held tools and somatosensory perception for the modalities vibration (Study V), and cold, warmth and pain induced by heat (Study VI) and examining whether the different populations of mechanoreceptive afferent units were equally affected and whether cold and warmth receptors were equally affected.

Methods

Study design and study population

From the entry of a dynamic cohort comprising male platers, truck assemblers and office workers, two cross-sectional studies were completed which investigated the effect of vibration exposure on finger blood flow (Study I) and neurological functions in the hands (Study II). At end of the 5-year follow-up, two cross-sectional studies (Studies V, and VI) on sensory perception, and two prospective cohort studies on nerve conduction (Study III) and the AER-provocation test (Study IV) respectively were completed. In the five-year follow-up study on nerve conduction (III) the temperature-adjusted (34°C) measurements at follow-up were compared with those at entry for the cohort. The follow-up of the physical examination provocation test (AER test) included symptoms, signs, and a nerve conduction test. The cross-sectional studies focused on vibrotactile sense (Study V) and thermal perception of warmth, cold, and heat-induced pain (Study VI).

At entry, the criteria for inclusion in either the exposure or reference category respectively were as follows: 1. job title criterium (plater, assembler, or office worker); 2. male gender; 3. age (≤ 54 years); 4. currently at work (work criterium).

The source population entailed 500 office workers and 112 male steel platers listed on the employee rosters. When the study began, 100 platers were employed. All subjects were employed full-time on monthly salaries. From the source population, 61 randomly admitted male office workers and 90 of the 93 accessible (2 studying, 2 long-term sick-listed, 3 excluded due to age-above 55 years) male platers were enumerated in the prospective cohort (participation rate 97%). Among the truck assemblers, 70 persons were randomly admitted from a source population of 114.

All subjects worked in a factory that constructs and produces paper and pulp-mill machinery. The work tasks of those 67 platers, who had been occupationally exposed to vibration during their lifetime working period until follow-up (“ever-exposed”), consisted mainly of welding, plating and grinding on iron and stainless steel. The work tasks also included the finishing of the product by grinding. The number of persons extensively exposed to vibration during the follow-up period (1987 - 1992) was 45. The truck assemblers were engaged in the mechanical assembly of trucks, using both manual tools and vibrating power tools. The work of the non-vibration-exposed group included various job categories within office work, such as manager, construction engineers, instructors, and postal clerks. The work content for the reference group varied from engineering construction at a desk to supervision and selling. The main task was office work at a desk.

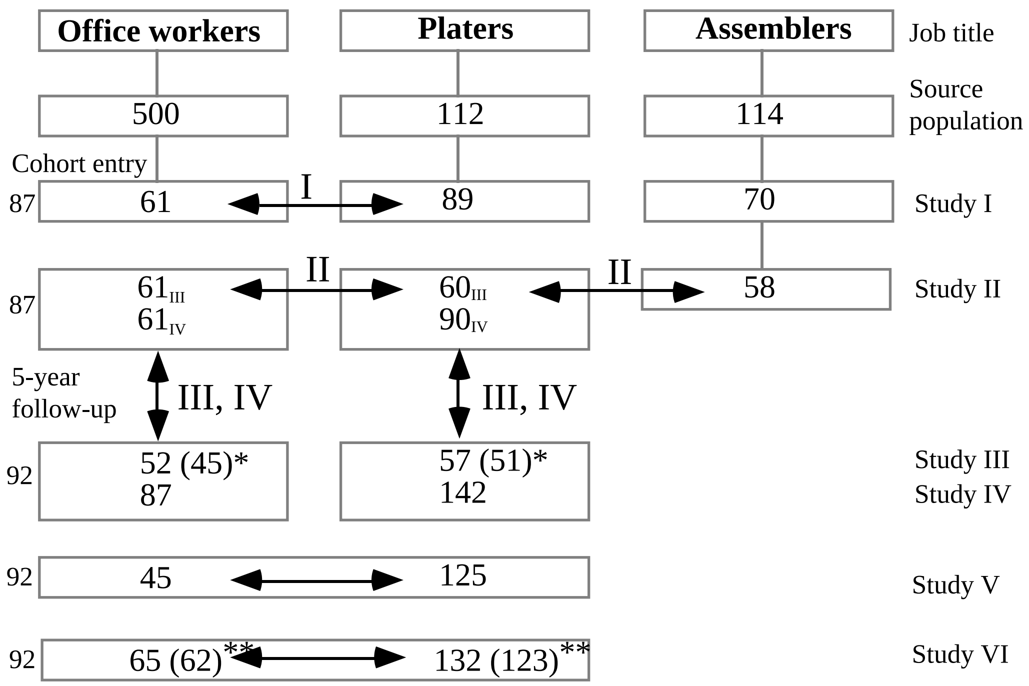

Figure 3. Job titles and numbers of subjects in the source population of the study groups in the cross-sectional studies I and II (1987), V and VI (1992), and at the follow-up studies III and IV (1992). The numbers within parentheses indicate the sizes of the final study groups after exclusions.

The cross-sectional Study I comprised 89 workers employed as platers and 61 office workers from the same company (Figure 3). Study II was a cross-sectional investigation of a cohort (n=179) of platers, truck assemblers and office workers (Figure 3). In Study II, the neurophysiological parameters were measured for all 61 office workers and for the first 60 platers and 58 assemblers consecutively examined. Study III was a prospective five-year follow-up study based on the study population of platers and office workers in Study II. A total of 121 workers were followed from 1987 to 1992. The actual study group in Paper III comprised 96 workers. The neurophysiological parameters were measured for all 61 office workers and the first 60 consecutively examined platers, in 1987. A total of 121, workers were thus followed from 1987 to 1992. Eight subjects were lost (follow-up rate 93%) at follow-up and 17 were not included. For the nerve conduction study the actual follow-up group comprised 96 workers after exclusions.

Eight workers did not attend the follow-up (4 working abroad, 1 in another part of Sweden, 1 dead. One worker had changed employer, and two executive managers did not attend). Three subjects did not complete the follow-up (1 injured after a car accident, 1 suffering acute illness, 1 with deafness which caused instruction difficulties). Three subjects were physically examined but could not complete the electroneurography in time. Eleven subjects were excluded due to polyneuropathy (2 with diabetes, 2 for reasons related to alcohol, 3 with signs of polyneuropathy related to alcohol or other disease) or earlier hand surgery (4 carpal tunnel releases after entry examination). The AER test (Study IV) was conducted on 137 workers both at entry and at follow-up.

The cross-sectional studies on vibrotactile sensitivity (V) and thermal perception (VI) were performed on 170 and 197 subjects respectively. In the latter study twelve subjects were eventually excluded, mainly on the grounds of earlier hand surgery or electroneurographic test results indicating carpal tunnel syndrome (n=8), polyneuropathy related to diabetes (n=2) or unclassified (n=2).

Procedures

Each subject was interviewed and examined by a physician (T.N.), both on entry and at the follow-up. A standard procedure was followed for physical examination of the upper extremities regarding the neuromuscular and skeletal systems. The examination was complemented with chemical laboratory screening and, at the follow-up, additional lower extremity nerve conduction measurements. These investigations were performed in order to check for and identify other diseases, primarily polyneuropathy, which might interfere with the outcome. The ensuing results formed the basis for possible exclusion. The criteria for rejection were previous hand surgery or clinical signs of polyneuropathy together with abnormal sural nerve conduction. The subjects provided supplementary basic data through a questionnaire. The questions covered e.g. age, work, years at work, exposure, and use of nicotine.

Exposure assessment

Vibration exposure

The vibration exposure data included exposure characterisation ranging from "ever employed in a job involving use of vibrating tools" to estimated, quantitative, individual measures of the cumulative frequency-weighted vibration exposure for each hand (Tables 7 and 8).

Quantified personal energy-equivalent vibration exposure was assessed for all subjects with vibration intensity measured (1987 and 1992) and classified on a job-task basis together with exposure times. The tool vibration intensity was measured for all types of tools and at all relevant job stations. The vibration was measured in accordance with ISO 5349 (93) in three mutually orthogonal directions. The daily vibration-exposure time was assessed both by subjective assessments and by an objective measurement of the time spent using each type of hand-held tool. The objective measurements were carried out by observation where the observer noted the kind of tool the operator was handling, whether the machine was working, and which hand was exposed, for each minute during an observation time of 150 minutes. Each subject´s vibration exposure value was calculated on the basis of individual exposure time assessments from observation, questionnaires, and diaries, combined with the mean measured vibration intensity for the dominant direction of the tools used. Furthermore, all platers were interviewed to obtain information about their entire lifetimes, the number of years in different jobs, types of exposure, and duration of exposure per day. On this basis, the cumulative lifetime equivalent frequency-weighted vibration exposure was estimated. A detailed measurement description is given in a separate report (42). One- and two-handheld grinders were the most frequent source of hand-transmitted vibration (65%). They were used for grinding, polishing, and cutting. Hammers used for finishing welding seams accounted for 25% of the tools in the company´s assembly of machinery, while other tools, such as die grinders, drills, and nut wrenches, together accounted for about 10%.

Based on the results obtained from work analyses in 1987 and 1992, diary results from 1992, and vibration measurements both when the cohort was enumerated and at the follow-up, a separate quantified job-title estimate of the vibration exposure for the left and the right hand could be calculated. The cumulative vibration exposure (CVE) for each individual's hands was then estimated using the formula,

$$CVE = <a_{h,w}> \cdot t_d \cdot k \cdot t_y \ (mh/s^2)$$

where $<a_{h,w}>$ is the individual frequency weighted acceleration level (mh/s^2), t_d is the individually graded daily exposure (hours/day), k equals 200 working days in a year (days/year), t_y is the individual's number of years of vibration exposure (years).

Cumulative vibration exposure was classified into three different categories. NE (Non-Exposed; CVE = 0 mh/s^2), EC1 (Exposure Category 1; $0 < CVE \leq 24000$ mh/s^2) and EC2 (Exposure Category 2; CVE >24000 mh/s^2). The upper limit of EC1 corresponds, according ISO 5349 (94), to a 10% prevalence of vascular disorders after 10 years of exposure to a 4h-equivalent frequency weighted acceleration $(a_{h,w})_{4h}$ level of 2.9 m/s^2.

The intra-worker variance for the vibration-exposed group regarding daily exposure time (diary information) revealed a daily mean exposure time of 54 minutes (median 33.5) and a standard deviation of 76 minutes. Within the vibration-exposed group half of the subjects reported daily exposure times that varied less than 22 minutes from their mean.

Table 7. Hand-held machine acceleration exposure intensity. The mean acceleration magnitude and standard deviation (Sd) according to ISO 5349 is presented for cohort entry in 1987 and for the follow-up in 1992. Number of tools examined is given within parentheses.

	1987		1992	
	Mean (m/s^2)	Sd (m/s^2)	Mean (m/s^2)	Sd (m/s^2)
Angle grinders	5.9 (n=13)	1.9	5.2 (n=24)	2.9
Straight grinders	4.4 (n=4)	1.3	4.7 (n=12)	2.8
Chisel hammers	10.3 (n=16)	2.9	12.0 (n=16)	3.7
Others	1.5 (n=3)	0.3	3.5 (n=5)	2.0

Table 8. Cumulative vibration exposure (CVE), cumulative time with power grip (Cum. grip time), and equivalent vibration exposure for the dominant (D) and the non-dominant (ND) hands in the study groups.

	Vibration exposed		Vibration exp 87-92		Unexposed 87-92		Never exposed	
	Mean	Sd	Mean	Sd	Mean	Sd	Mean	Sd
Number	67	..	45	..	51	..	29	..
CVE. D (mh/s^2)	26787	17126	8211	4206	..	..	..	..
CVE. ND(mh/s^2)	21724	13589	6569	3365	..	..	..	..
Equivalent vibr. exp. (m/s^2)	3.4	1.4	3.9	1.3	..	..	..	..
Cum. griptime D (h/5 y)	2605	2272	3690	2013	348	141	320	0
Cum. griptime ND (h/5 y)	1367	1019	1857	893	338	94	320	0

Ergonomic work load

The particular aspect of exposure to ergonomic factors investigated was the duration of time a power grip (flexion of dig. 2-5 opposed to dig. 1) was used. Repetitive and forced grips were measured for the two hands separately (Table 8). In Study II, the mean daily time spent using different grips was measured from observation of a subset of 12 subjects. The mean percentage of the total working time spent using forced grips by the left and right hands was calculated. For the assemblers, the time spent using different grips was measured for each subject over a period of 18 minutes with sampling every second minute. These 18 minutes represented a balance on the assembly line, which the worker repeated throughout the whole day. The mean percentage of the total working time spent with the left and right hands in a forceful grip was calculated. Light, repetitive manual tasks occurred in the referent group, but no forceful grips were anticipated and thus were not measured.

In the follow-up study (III), quantified individual ergonomic exposure for the left and right hand was measured separately on a subset of subjects. The ergonomic exposure was assessed by rating hand position and grip from ten-minute extracts of video recordings on a sample of vibration-exposed (n=25) and workers without vibration exposure (n=22). Quantified job-title specific estimates of the percentage of time that power hand grips were used for both the right-hand

and the left-hand side were assessed from information obtained from two weeks of daily diaries (n=137) and the work analysis from 1987 and 1992 (Table 9).

Table 9. Power grip duration. Mean percentage of power grip time for each hand estimated from work analysis with additional information from a diary and from the rating of video-recorded work tasks. Standard deviation given within parentheses.

	Work analysis*				Video analysis**	
	1987		1992		1992	
	Right	Left	Right	Left	Right	Left
Plater group	69 (16)	26 (18)	62 (30)	30 (28)	44 (30)	33 (28)
Office worker group	..	..	4	4	4 (6)	6 (11)
Welder group	..	..	62	30	..	..
Cutter group	..	..	13	10	..	..
Carpenter group	..	..	50	25	..	..
Assemblers	22	17	..	..	..	..

*Work analysis combined (n=24) with diary information (n=137)

**Video analysis of platers (n=25) and office workers (n=22)

Outcome assessment

Symptoms of white fingers

The staging according to the Taylor-Pelmear Scale (201) was based on questionnaire data concerning white finger symptoms, information about the occurrence of the symptoms in summer and winter and ensuing social and work impairment. The staging according to the Stockholm Workshop Scale (69) was based on a symptom questionnaire (Table 10) and drawings of the distribution of white fingers on the hand. Interview data were used to clarify details.

Table 10. The Stockholm Workshop scale for the classification of cold-induced Raynauds phenomenon in the hand-arm vibration syndrome*.

Stage	**Grade**	**Description**
0	-	No attacks.
1	Mild	Occasional attacks affecting only the tip of one or more fingers
2	Moderate	Occasional attacks affecting distal and middle (rarely also proximal) phalanges of one or more fingers
3	Severe	Frequent attacks affecting all phalanges of most fingers.
4	Very severe	As in stage 3, with trophic skin changes in the finger tips.

*The staging is made separately for each hand. In the evaluation of the subject, the grade of the disorder is indicated by the stages of both hands and the number of affected fingers on each hand.

Symptoms of paresthesia

The subjects also provided supplementary data in a questionnaire. The questions concerned e.g. age, work, years at work, exposure, use of nicotine, and symptoms. Information about symptoms of nocturnal paresthesia was sought in the question, “Numbness in hand or fingers at night?” Answers were given on a four-grade scale; ”no”, ”insignificant”, ”some” and ”rather much”.

Timed Allen´s test
Peripheral circulation in the hands was tested by means of an extended Allen's test (92). This test measures the time lapse until resumption of blood flow in the ulnar and radial arteries is resumed after obstruction. The subject first clenched his fist for 20 seconds, while the physician kept the ulnar and radial arteries compressed, and was then asked to open his hand while the physician simultaneously released the compression in one of the two vessels. The time was measured from the release of the compression until circulation was re-established, as evidenced by the change in skin colour in the hand from pale to normal. This test was performed on the radial and ulnar arteries on both sides. The test was terminated after a maximum measurement time of 35 seconds.

Nerve conduction
The median nerve conduction measurements were performed with a Neuromatic® 2000 C (two-channel neurograph). The stimulation and recording electrodes were bipolar saline-soaked felt surface electrodes (diameter 7 mm, spacing 23 mm). Nerve distances from the centre of the cathode to the active recording electrode were measured with a tape measure. The skin temperature was controlled and kept above 28 °C. Both in 1987 and 1992, all nerve conduction measurements were taken by the same neuro-physiological technician using the same technical set-up.

The distal latency time for the median motor nerve was measured after stimulation at the cubital fossa and the wrist with the recording electrode placed on the abductor pollicis brevis muscle. A grounding electrode was positioned between the stimulation and the recording electrodes. The distal latency time measurements from 1987 and 1992 were temperature adjusted (-0.3 ms/°C) relative to 34°C (104).

The median sensory nerve conduction velocity was measured after antidrome percutaneous stimulation. The recordings were fractionated for the carpal tunnel segment and the segment distal to the palm. The stimulation electrode was placed 2 cm proximal to the distal wrist crease and in the palm. The recording electrode was attached to the ulnar side of the third digit. The recording electrodes were placed with one of the two felt electrodes proximal and the other distal to the proximal interphalangeal joint. The conduction velocity measurements from 1987 and 1992 were temperature adjusted (1.4 m/s/°C) relative to 34°C (109).

The Abduction External Rotation test
The AER test was carried out as described by Roos - 90° abduction and external rotation and elbow flexion (“hands-up position“) together with simultaneous intermittent closing and relaxing of the hands during 3 minutes(175). Criteria for positive neurological signs at the AER test were: pain, tingling or numbness in ulnar side of the hands (ulnar), anywhere distal to elbow (distal) or neck-shoulder and arm proximal to elbow (proximal). “AER signs“, as reported in this study, means “positive neurological proximal or distal sensations either in the right or left upper extremity during the AER test“, unless otherwise stated. Vascular

(cyanosis) and other signs (tiredness, stiffness) were recorded separately, but are not reported here.

Vibrotactile perception threshold measurement

The vibrotactile perception threshold (VPT) was measured using a method of limits on the pulp of the right and left index finger using a modified version of a von Békésy audiometer (Brüel & Kjear 1800/WH 1763). The equipment provided a sinusoidal vibration at seven different frequencies from 8 to 500 Hz with an amplitude regulated remotely through a button on a hand switch. When the button was pressed the stimulus amplitude gradually declined, to be subsequently increased as soon as the button was released. The rate of the amplitude change was 3 dB/s. The vibration was delivered perpendicularly to the pulp from above through a cylindrical Perspex probe with a flat contact surface (diameter: 6 mm). The vibration exciter was mounted in accordance with a beam balance in order to provide a constant static pressure of 3.5 N/cm^2 to the skin.

The subjects were asked to sit on a chair with the forearm and the dorsum of the hand resting extended and relaxed on a test fixture. If the subject’s skin temperature was lower than 28° C the hand was warmed with the help of an infrared lamp. The position of the stimulator probe was carefully adjusted to cover the pulp of the index finger. The subject was instructed to press the button on the hand switch with his contralateral hand as soon as the vibrations could be perceived and to keep it depressed as long as the vibrations were felt. In this way the subject's vibrotactile perception threshold was continuously tracked between the perception and non-perception levels. The increasing and decreasing level of vibration was recorded as a zigzag pattern, a tactilogram. This psychophysical threshold tracking method (the “von Békésy method”) has long been used in the field of audiometry. The threshold at each frequency was defined as the average midpoint between the upper and lower limits, expressed in dB relative to 10^{-6} m/s^2_{rms}.

The frequency of the vibration stimuli was automatically changed by the instrument itself in an ascending order: 8, 16, 32, 63, 125, 250, and 500 Hz. At each frequency, the threshold was tracked for about 30 seconds with no pauses between frequencies. The whole test took an average of 20 minutes to perform, including a period for installation, familiarisation, and training in order to obtain stable and reproducible threshold levels.

Ageing is reported to have a negative influence on, for instance, tactile sensitivity (118). To be able to compare vibrotactile perception threshold data both within and between exposure categories when there is a broad distribution of age it is necessary to take this effect into account. All threshold data for each individual in our study were normalised to a predefined reference age of 30 years. It is possible to do this separately for each test frequency on the basis of our current knowledge about sensory reduction due to ageing (118) .

For each exposure category an average VPT was calculated for all seven test frequencies separately and for the three lowest (8-32 Hz) and the four highest (63-500 Hz) test frequencies together. As tactile perception within the frequency region of 63-500 Hz is most probably mediated by activity from Pacinian corpuscles, this average threshold is denoted VPT_P. Lower frequencies are mediated by other, non-Pacinian, types of mechanoreceptive afferents and are therefore denoted VPT_{NP}.

Assessment of thermal perception thresholds
Thermal perception was determined by a Somedic modification of the "Marstock" method (60) with computer assisted automatic exposure and response recording (Thermotest; Somedic, Sales AB, Sweden). A thermostimulator was applied to the skin through a Peltier contact thermode. When measuring cold and warmth perception, the probe (25 mm x 50 mm) was gently applied to the volar surface of the two distal phalanges of the second digit (lengthways along the finger) and to the thenar eminence on each hand respectively. Heat pain perception was only measured from the right and left thenar eminences. The perception thresholds of cold, warmth, and pain induced by contact heat were assessed by the method of limits. The rate of the temperature change was linear and approximately 1°C/s. Prior to the quantitative evaluation of thermal sensibility, the skin temperature at each body site was measured by contact thermometry. A baseline starting temperature was accomplished by using the skin temperature perceived by the subject as “indifferent”. The subject was instructed to press a switch whenever he experienced the onset of a change in temperature sensation (cold, warmth, and heat pain sensation). The operating temperature range was set at 10-52°C. After each response, the temperature of the thermostimulator changed direction and returned to the baseline temperature. The measurements of warmth and cold were performed ten times. The mean of the measurements was taken as the threshold. The ”neutral zone” was defined as the temperature difference between the warm and cold perception levels. When assessing heat pain sensation, the thermode temperature returned to a predetermined subjective baseline level, from where five consecutive stimulation trials were made. The interstimulus interval for all threshold measurements was randomly distributed within 2 seconds.

Statistical methods

In Study I, frequency measures were computed as prevalence rates and in Studies II, III, and V, point prevalence rates were given as percentages. The unpaired t-test was used for testing group mean differences, and the paired t-test for the difference between left and right hands (II, VI), and between exposure categories (V) with 95% confidence intervals. Correlations between nerve conduction measures and anthropometric values were evaluated with the Pearson correlation coefficient.

Case definitions: The dependent variables in Study I were symptoms of white fingers and the timed Allen´s test result. A value exceeding the upper 95% confidence limit of the means (Allen´s test and nerve conduction) of the non-exposed office-workers was considered case-criterion (Studies I and II). In the follow-up study (III) on nerve conduction the case definition for impaired median nerve function was a prolonged latency time, or a reduced conduction velocity at the follow-up as compared with the values at entry. In the follow-up study on the AER test a multiple logistic regression analysis was made using the AER test outcome in 1992 as dependent variable. Case definitions for “seniority at current work“ (more than the group median, 7 years),“exposure to vibrations“ (more than the group median, 15 min/day), “shoulder asymmetry“, “asthma“ and “neck trauma“ as independent variables. The case definitions in the QST –studies on vibrotactile perception (study V) and thermal perception (Study VI) was based on the mean and the standard deviations. The case definition of impaired vibrotactile sensitivity was a VPT of more than 1 standard deviation above the mean for the non-exposed category, while the corresponding thermal criterion was the mean threshold (for all subjects) value for each test site plus (warmth and heatpain) respectively minus (cold) one standard deviation. In Study VI, the criterion for beeing classified as suffering from nocturnal paresthesia was the answer alternatives ”some” and ”rather much” symptoms on the four-grade questionnaire scale.

Association: Rate ratios were used as the measure of association between effect and exposure in Studies II and III, and odds ratios standardised for age according to the Mantel-Haenszel techniques in Study I. Multiple logistic regression was used for the analysis of interaction effects. The predictors in the multiple logistic regression models were chosen from among the variables considered to be of biological importance. The regression coefficients were used to calculate odds ratios. The association between vibration and exposure to ergonomic factors in relation to distal motor latency time measurements over the carpal tunnel was tested with multiple linear regression models (106). The predictors in these models were chosen from among variables considered to be of biological importance. They were screened by stepwise selection and condensed to age, cumulative vibration exposure during the follow-up period and during lifetime, exposure to power grip (percentage of workday spent using power grip) and individual with use of power grip in percent of a working day (%), weight, height and body mass index (BMI= weight in kg/ squared height in meters). Age, BMI, height, weight, vibration exposure, and the two ergonomic exposure indices were all treated as continuous variables. In the analysis of linear regression each hand was treated as an independent measurement. Positive predictive values (PPV) and unadjusted prevalence ratios (PR) or cumulative incidence rates (CIR) with 95% confidence intervals (95% ci) have been calculated as measures of association in Study IV. The risk of having reduced vibrotactile perception was given as an odds ratio in Study V. Correlation coefficients were obtained by linear regression modelling. The bivariate association between vibration exposure and contact thermal perception measurements was given as a rate ratio, while the multivariable association was tested with multiple logistic regression models. The relation between accumulated vibration exposure and the thermo-neutral zone was estimated by linear regression.

Follow-up analysis The difference in distal motor latency between the examination on entry (1987) and the follow-up (1992) is given as a mean paired difference ($M_{T87-T92}$) with 95% confidence intervals. Improvement in nerve function is represented by a motor latency difference ($M_{T87-T92}$) greater than zero, over the interim period and a conduction velocity difference (less than zero over the interim period, or by a conduction velocity difference less than zero btween entry and follow-up. The power to detect a population mean difference between entry and follow-up was tested with the one-sample t-test (SPSS). The risk of having contracted a deterioration of nerve conduction during the follow-up interim for vibration-exposed versus unexposed subjects was expressed as a rate ratio. Positive predictive values (PPV) and unadjusted prevalence ratios (PR) were used in Study IV. PR and PPV of symptoms and signs at the 1992 examination are reported separately for the whole group of subjects (prevalent, all cases) and CIR and PPV among subgroups who, at the 1987 examination, were free from the respective symptom or sign being analysed (incident, new cases). A multiple logistic regression analysis was made using the AER test outcome 1992 as dependent variable.

Results

White finger symptoms and signs

The white finger point prevalence rates for the job entitled "platers" and for that entitled "office workers" were .45 and .08 respectively and the odds ratio was 14 (95% CI 5.1-38). When those exposed to vibration (platers + office workers with previous vibration exposure) were compared to non-exposed office workers the point prevalence rates were .40 for the former and .02 for the latter while the odds ratio was 56 (95% CI 12-269). For the platers currently exposed to active vibration the point prevalence rate was .42 and with the non-exposed office workers as reference group the odds ratio was 85 (95% CI 15-487).

A successive increase, related to years of vibration-exposed work, was observed in the number of hands staged as 1-3 according to the Stockholm Workshop scale. A total cumulative prevalence of 29% for the left hand and 25% for the right hand was found when all affected fingers were included.

The number of fingers showing symptoms of cold-induced Raynaud's phenomenon increased with the number of years of work involving vibration exposure (Figure 4). During the first 10 years it was more common to find Raynaud´s phenomenon on one to three fingers than on all five fingers. Raynaud's phenomenon involving all 5 fingers was, however, also found within the first 10 years of vibration exposure.

There was a exposure-response relation between years of exposure and symptoms of white fingers. In a multiple logistic regression model of VWF with the variables age and vibration exposure years, the odds ratio for the vibration exposure years was 1.11 (95 CI 1.05 - 1.17) and age 1.05 (95 CI 1.01 - 1.09).

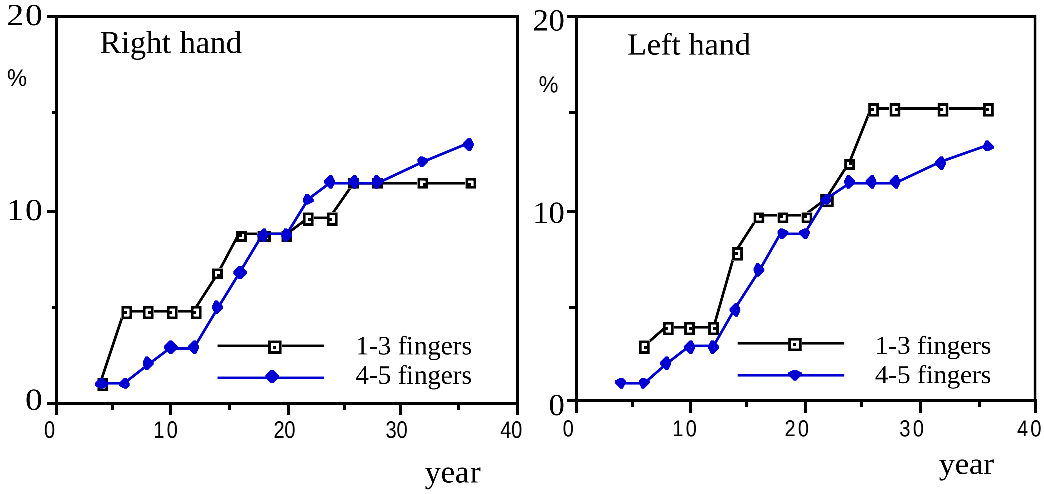

Figure 4. The cumulative percentage of persons with symptoms of white fingers in 1-3 fingers and 4-5 fingers respectively for the left and right hand according to the Stockholm Workshop Scale (SWS), in relation to the number of years exposed to vibration.

In the Allen´s test, the time of delay between the release of compression on the artery and blushing of the palm varied widely, and in some subjects very slow to no perfusion was found. When the upper 95% confidence interval limit for the non-exposed office workers was used as a cut-off criterion (left ulnar artery = 6.0, right ulnar artery = 5.8, left radial artery = 4.6, and right radial artery = 6.0 seconds), a longer refill time was found for platers than for office workers with odds ratios 1.2 - 3.4. Higher odds ratios were found for the right hand than for the left hand.

A multiple logistic regression model of pathological timed Allen´s test for the right radial artery with the variables vibration exposure, use of nicotine, white fingers, and age, gave the odds ratio of 3.9 for white fingers (95% CI 1.47 - 10.55). The odds ratio for pathological Allen´s test for the right ulnar artery and age was 1.04 (95% CI 1.00 - 1.08) and for vibration years 1.06 (95% CI 1.01 - 1.11). For the left ulnar artery the odds ratio for vibration years was 1.07 (95% CI 1.02 -1.13).

Nerve function (Studies II and III)

Cross-sectional study on nerve function (Study II)

The highest prevalences for impaired nerve conduction were found for the platers (Table 5). The prevalence for prolonged distal latency was higher for the vibration-exposed categories than for the office-worker group. A long latency time was more prevalent among the platers than among the assemblers. In the plater group, a long latency time was more prevalent for the left hand than for the right hand. In the group of assemblers, a slightly higher prevalence of long distal latency time was found for the right hand than for the left. In the plater and assembler groups, the prevalences of reduced amplitude and impaired nerve conduction over the carpal tunnel were higher than among the referens. In the plater group, this applied to both hands, in the assembler group, however, only to the right.

Impaired nerve conduction over the carpal tunnel segment was evidenced by rate ratios of 1.2-2.0 for distal latency and 0.9-1.6 for nerve conduction velocity. The rates were generally higher in the left hand than in the right. For the arm and for the palm-to-finger segments, the risks of impaired nerve conduction were not increased. The highest rate ratios were found for the distal latency time measurements.

Increased risks of prolonged distal latency time, reduced nerve conduction velocity and decreased amplitude were found among the platers and the assemblers when contrasted to office workers (Table 11). An increased risk was also found when the vibration-exposed workers, irrespective of job title, were contrasted to non-vibration-exposed office workers. The corresponding magnitudes of the risk were higher when the comparison was based on job title than on exposure to vibration only. The rate ratios were generally higher in the left than in the right hand and the they were generally higher for the platers than for the assemblers.

Table 11. Prevalence rates (%) of nerve conduction impairment in relation to the 95% confidence interval (95% CI) in the reference group, among the plater group, assembler group and referent group office workers. The rate ratio is given with its 95% CI.

	Hand	Platers (n=56)	Assemblers (n=58)	Office workers (n=61)	Rate ratio	95% CI
Distal latency time	Right	55	..	33	1.69	1.10-2.59
		..	40	33	1.21	0.75-1.95
	Left	50	..	25	2.03	1.22-3.39
		..	38	25	1.54	0.89-2.67
Conduction velocity	Right	54		34	1.56	1.02-2.38
			43	34	1.25	0.79-1.97
	Left	61		46	1.32	0.94-1.87
			43	46	0.94	0.63-1.40

In a logistic regression model controlling for age, nicotine use, and years of vibration exposure, it was found that the duration of vibration exposure was a predictor of prolonged distal latency. The derived odds ratios were 1.12 (95% CI 1.02-1.23) for the right hand; and 1.09, (95% CI 1.00-1.20) for the left hand. The risk for prolonged distal latency and vibration-exposure remained when the model was expanded to control for assembling and plating.

Cohort study on nerve function (Study III)

The mean paired difference in temperature-adjusted nerve conduction between the cohort at entry and follow-up revealed a shorter latency time (0.12 ms and 0.40 ms for the right and left hands respectively).

In both hands the conduction velocity showed an insignificant increase in velocity in the wrist-to-hand segment and in the right hand in the hand-to-finger segment.

Considering the undecided and wide confidence intervals, the latency times were marginally reduced at followup as compared with at entry (Table 12). This tendency was revealed both in the analyses of the cumulative lifetime vibration exposure and the follow-up period exposure.

The conduction velocities at follow-up were, with the above reservation concerning confidence intervals generally faster than at entry except for the distal segment of the left hand. In the lifetime vibration-exposed group the conduction velocity over the carpal tunnel was increased less than in the unexposed group.

Table 12. Change in nerve conduction (temperature-adjusted relative to 34 °C) between the measurements in 1987 and 1992 for "vibration exposed" and "vibration unexposed". The difference values are the means of unpaired measurements.

	Hand	Exposed	Un-exposed	Mean Difference	95% CI
Distal latency time (ms)	Right	0.06	0.17	-0.11	-0.31 - 0.09
	Left	0.39	0.41	-0.02	-0.24 - 0.20
Conduction velocity wrist-palm (m/s)	Right	-1.44	-1.88	0.44	-3.58 - 4.46
	Left	-2.43	-0.80	-1.63	-5.90 - 2.65
Conduction velocity palm-digit (m/s)	Right	-1.18	-1.07	-0.11	-4.03 - 3.81
	Left	2.20	-0.31	2.51	-0.84 - 5.87

Nerve provocability (Study IV)

The prevalences of AER signs in 1987 and 1992 were 24% (n=151) and 15% (n=219), respectively. Distal signs (1987: 20%; 1992: 12%) were more common than proximal signs (1987: 5%; 1992: 6%). Few ulnar signs were noted (1987=4%; 1992=2%). Right and left side signs were about equally common.

Results from the AER tests both in 1987 and 1992, were available for 137 subjects. The PR of AER signs in 1992 among those with signs in 1987 versus those without, was 6.2 (95% ci=3.3-12). The corresponding values were 6.6 (1.8-24) for proximal signs, 7.8 (3.8-16) for distal, and 26.4 (7.3-95) for ulnar signs. Assuming a steady state condition and no transient cases during the five-year period we found that the cumulative incidence of AER signs between 1987 and 1992 were approximately 1.7/100 person-years and the recovery rate could be estimated at approximately 9.4/100 case-years. The mean duration for the persistence of AER signs was calculated at roughly 17.7 years.

Numbness in the hands in 1987 was strongly predictive of AER signs in 1992, both prevalent and incidental. Other symptoms from the neck and upper extremity regions in 1987 were mainly associated with prevalent signs at the AER test in 1992. Positive signs in 1987 during any of the other nerve compression tests, or of decreased vibration and touch sensitivity on the finger tips, were also strongly predictive of prevalent and incident signs at the 1992 AER test.

Seniority at current work and exposure to vibration from hand-held tools reported in 1987 were predictive of both prevalent and incident AER-signs 5 years later. Among medical conditions, asthma was associated with prevalent AER signs in 1992, as was previous trauma to the neck or shoulder regions. Reports of triggering factors for neck or upper extremity compression symptoms were strongly associated with AER signs. The PPV for prevalent AER signs varied mainly between 0.2-0.6, being highest for medical examination signs, asthma, or reports of previous trauma to neck/shoulders or of triggering factors. The PPV values for incident AER signs was much lower.

The risk factors from 1987 (seniority at work, vibration exposure, shoulder asymmetry, asthma, and neck trauma), that were entered in the regression model for prevalent AER signs in 1992 had OR above 2, but with wide confidence intervals.

Symptoms in 1992, both prevalent and incidental, in the shoulder, upper arm and elbow-forearm regions as well as numbness in the hands were predicted by signs during the 1987 AER test. AER signs in 1987 also predicted prevalent and incident nerve compression signs 5 years later. The PPV varied between 0-0.6, being highest when the frequency of the symptom or sign was high in 1992.

The cumulated incidence of AER signs between 1987-92 was about 1.7/100 person-years. Seventeen (53%) of subjects with signs in 1987 had persisting signs five years later while the other 15 (47%) had lost their signs. The recovery rate could thus be estimated at about 9.4/100 case-years. The mean duration of the persistence of AER signs was calculated to approximately 17.7 years.

The sensory nerve conduction velocity in the median nerve on both hands was lower, indicating reduced nerve function, among subjects with signs at the 1992 AER test, seen most clearly between palm-wrist. The motor conduction velocity in the median nerve between the wrist and the thenar muscles was only slightly lower among those with AER signs, as reflected by somewhat longer motor latencies. A small decrease in the sensory nerve conduction velocity between the palm and the wrist in the right hand ooccurred in the follow-up interim among subjects who became AER positive during that period (Table 13). The reverse was found for the left hand. A decrease was also recorded among subjects with persisting signs on both occasions. Those who lost the signs present in 1987 or did not react with signs either in 1987 or in 1992 had less substantial changes.

Table 13. Temperature-corrected sensory nerve conduction velocities palm-to-wrist and their intra-subject differences between 1987and 1992 among subjects with new, persistent or absent signs at AER test in 1992 compared to AER test in 1987. Positive difference = increase and negative = decrease in nerve conduction velocity between 1987 and 1992

Hand side	AER test outcome 1992 vs. 1987	Nerve conduction m/s n	1992	1987	Difference 1992-1987 M/s	95% CI
Right hand	New signs	9	51.4	55.8	-4.41	-12.8 - 3.97
	Persistent signs	7	50.6	57.6	-6.93	-19.3 - 5.48
	Lost signs	8	61.5	57.1	4.43	-3.44 - 12.3
	Never had signs	80	56.4	55.0	1.43	-0.86 - 3.72
Left hand	New signs	3	54.7	50.9	3.87	-28.1 - 35.8
	Persistent signs	9	52.6	56.2	-3.53	-9.06 - 2.00
	Lost signs	10	58.0	59.7	-1.63	-8.44 - 5.18
	Never had signs	80	57.9	56.0	1.92	-0.52 - 4.35

Neurosensory perception (Studies V and VI)

Vibrotactile perception (Study V)

Individual VPT_{NP}, VPT_P and SI, for both left and right hands together in relation to CVE indicate a decreasing tactile sensitivity with increasing vibration exposure ($VPT_{NP} \approx 57 \cdot 10^{-6} \cdot CVE + 103.2$, $r \approx 0.19$; $VPT_P \approx 85 \cdot 10^{-6} \cdot CVE + 104.4$, $r \approx 0.20$; $SI \approx -1.9 \cdot 10^{-6} \cdot CVE + 1.06$, $r \approx 0.21$). Correlation coefficients of about 0.2 indicate a weak positive linear exposure-effect relation.

Regardless of exposure category, the curve shape of the thresholds for the seven test frequencies can be considered typical and normal (Figure 5). The differences between the NE and EC1 groups for all threshold measures are relatively small and uncertain. A comparison between NE and EC2 indicated, however, a clear tendency towards elevated VPT (1-4 dB), especially in the Pacinian-mediated area where the differences were substantial.

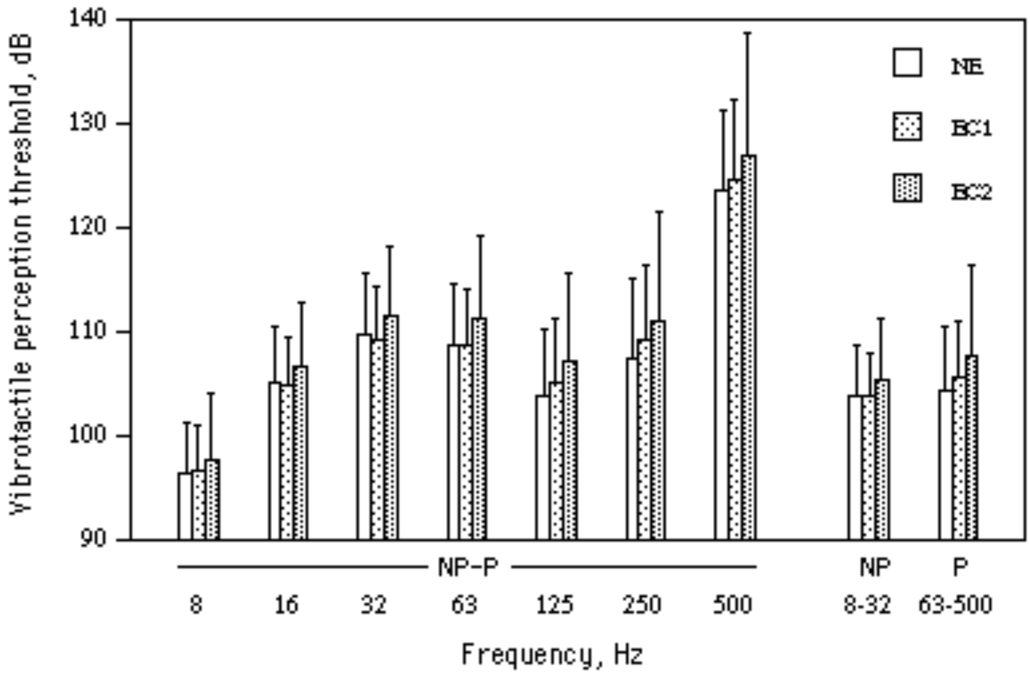

Figure 5. Mean VPT for discrete frequencies in non-Pacinian (NP) and Pacinian-mediated areas (P), and their corresponding standard deviation (vertical bars) for individuals in three exposure categories. (Pooled data from both hands, dB relative to 10^6 m/s^2).

The criterion for “impairment” of vibrotactile sensitivity was met by some individuals also in the non-exposed group, but in the EC1 and EC2 groups the tendency was more outspoken. Reduced and seriously reduced vibrotactile sensitivity were found predominantly for the right hand in EC2. For the right hand SI, about 4% of the vibrotactile sensitivity values were found to be abnormal among the non-exposed but as much as about 14% in the EC2 group. The percentages were somewhat lower for the left hand.

Considering all test frequencies together, i.e. VPT_{NP-P} and SI, the results reveal an elevated risk of impaired vibrotactile sensitivity when EC2 is entered The odds ratios of impaired vibrotactile sensitivity was close to unity between the two lowest exposure categories for all VPT measures. For the mechanoreceptors in the areas without Pacinian receptors (NP), the odds ratio of impaired vibrotactile sensitivity was between 1.2 and 2.0 with wide confidence intervals. For the Pacinian area, the odds ratios were between 2.6 and 4.3.

Thermal perception

The total mean perception threshold in the thenar region, calculated over all groups and both hands, was 27.2°C for the sensation of cold(lower row of markers in figure **6**, left diagram, 31.0°C for warmth (middle row), and 46°C for contact heat pain (upper row). The corresponding values for cold and warmth on the second finger were 25.1°C and 34.2°C, respectively. Figure 6 shows the separate values for each exposure category and the two hands for the thenar and digit test sites.

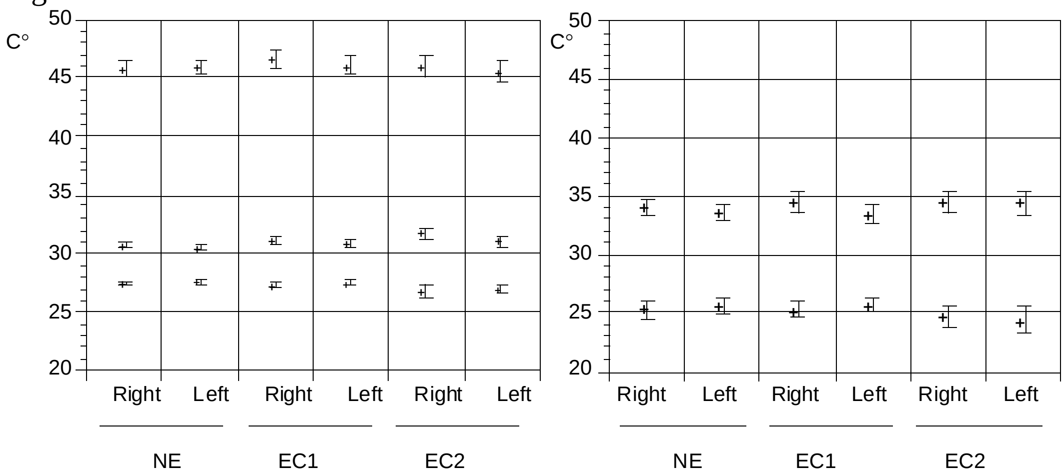

Figure 6. Mean and 95% CI of cold, warmth, and heat pain perception thresholds at the thenar eminence (left diagram) and on the second digit of the right and left hands (right diagram) in the different exposure categories (NE = 0 mh/s^2, EC1; 0< CVE < 24000 mh/s^2, EC2; CVE >24 000 mh/s^2).

The thermal sensibility of the right-hand side was slightly impaired compared to the left. The magnitude of the difference between left- and right-hand sides was approximately twice as large for warmth as for cold. Measurements from the distal phalanges of the second digit revealed lower perceptual sensibility both to cold and warmth than on the thenar eminence, resulting in a “neutral zone width twice that on the thenar (Figure 1).

Reduced sensibility was found for warmth and cold thermal perception thresholds within the vibration-exposure categories (Figure 6) for the thenar measurements. Changes in warmth and cold perception contributed about equally much to the width of the neutral zone. Cold perception changes alone resulted in a wider gap only in the right hand fingers. The exposure-effect trend over the vibration exposure categories was significant for the neutral zone at the thenar test site both for the left- (0,01) and the right-hand (0,00) side. The trends for the underlying warmth and cold thresholds were all significant except for the perception of warmth on the left hand.

The risk of having sustained reduced thermal sensibility was increased for all test sites. The risk was higher for the thenar measurements than the finger measurements.

In logistic regression modelling a 4000 mh/s^2 change in cumulative exposure increases the risk of sustaining a wider neutral zone by 18% for both right and left-hand side, controlling for age and skin temperature. In a linear regression model exposure predicts 7% of the individual value (right hand). One unit change (4000 mh/s^2) in exposure increases the neutral zone gap by 0.14°C.
Subjects with symptoms of nocturnal numbness run an increased risk of having wider neutral zones than subjects without these symptoms. The rate ratio for an increased neutral zone at the thenar eminence was 2.80 (95% CI 1.17 - 6.67) for the right hand and 2.72 (95% CI 1.12 - 6.63) for the left hand.

Discussion

Vascular symptoms and signs

Work and vascular symptoms
High prevalences of white fingers were found in the plater group together with high risk-estimates. When the upper 95% confidence interval limit for the non-exposed office workers was used as a cut-off criterion in the timed Allen's test, a longer refill time was found for platers than for office workers with odds ratios 1.2 - 3.4.

Hand-transmitted vibration as a specific risk factor for vascular symptoms
The occurrence of white finger symptoms in Study I was strongly associated with vibration exposure. As a crude measure, it was found that fewer fingers were affected after short than after long vibration exposure times, but there were large interindividual variation. The numerical risk estimate of developing white finger symptoms (odds ratio) increased, although with wide confidence intervals, when the contrast was made with data based on stricter vibration exposure criteria. When the symptoms of white fingers were defined more strictly according to the stages of the Taylor-Pelmear scale (200), the prevalence of VWF (= Taylor-Pelmear stages 1-4) was 31 %. The prevalence of white fingers (= stage 1-4) according to the Stockholm Workshop scale was a little lower even than that figure. This discrepancy is due to the separation of the two hands in the Stockholm Workshop scale. Vibration exposure constitutes the dominant source for VWF and corresponded to an attributable fraction of approximately 8% for those contracting white fingers within 4 years, 84% for 5-9 years, 94% for 10-19 years and 92% for 20 - 40 years of vibration exposure. Each year of vibration exposure raises the odds ratio for VWF by 11%.

In addition to the symptom questionnaire, hand circulation was assessed by a timed Allen's test. The odds ratio for a positive Allen's test was higher for the vibration-exposed category than for the group with no vibration exposure. There was a higher prevalence of pathological Allen´s tests for the right hand than for the left and a higher prevalence for those exposed to vibration than for controls. For persons with VWF, the odds ratio for a positive Allen´s test on the right radial artery was four times higher than that of the controls. For the ulnar artery the odds ratio increases 6% for the right hand and 7% for the left hand per vibration exposure year even when age and nicotine were controlled for. The diagnostic value of the timed Allen´s test when properly (66) performed is mainly to suggest further investigation of the circulation. The timed Allen´s test showed a relation to vibration exposure time and was more often positive with longer vibration exposure. A strong relation between white fingers and vibration exposure was found, but there was no correlation between vibration exposure time and the stage reached on either of the two symptom grading scales. This emphasises the importance of the individual exposure-effect relation, where individual susceptibility and individual exposure patterns matter.

Ergonomic exposure as a specific risk factor for vascular symptoms
In plating work, physical exposure may not be to vibration alone but also to other traumatic elements such as hammering and pressure on the vessels. This may lead to lesions of the vessels such as ulnar artery thrombosis (hypothenar hammer syndrome) (121). For the right hand, we found an odds ratio of 2.8 (95% CI 1.3 – 6.2) for positive Allen´s test, indicating ulnar artery dysfunction, when we contrasted platers with office workers. Cumulative exposure was also related to number of years of work with hand-held vibrating tools, but the ergonomic component was not separated from vibration.

Target structure and vascular symptoms
In our study, white finger symptoms were assessed by questionnaire in which the subject marked the extent of finger blanching on a map drawing of the hand together with examination and interview by a physician. This examination was performed to separate the vascular symptoms from neurosensory manifestations. Cold intolerance, without vascular features, as an additional alternative (193) was not asked for.

Guiding standards and vascular symptoms
Our theoretically predicted exposure duration for contracting a 10% prevalence of VWF according to the ISO 5349 (93) was 6 to 7 years, but the observed latency was shorter. Thus the present study supports the view that the ISO 5349 standard applied to the investigated platers did not represent an overestimation but rather an underestimation of the VWF risk at current exposure. Lately it has been emphasised that ISO 5349 greatly overestimates the risk for VWF (75). In the very same review it was recognised that exposure intensity varies greatly and that duration is important for the exposure-response relation. Most studies are based on self-rating of exposure time. If exposure time or intensity is overestimated, which is often the case (217) it follows that there will be an underestimation of the true risk for VWF. In our study (I) thorough, individual exposure assessment, could be one of several possible reasons to explain our finding that ISO 5349 underestimates the risk. The factors to consider is amply presented in the evaluation of ISO 5349 prediction model by Gemne and co-workers (68).

A quantitative relation between vibration exposure and health is given only for the prevalence of vibration white fingers (93). It should be noted that the equation does not predict the risk for vibration-induced white fingers occurring in any particular individual within a group. Factors likely to influence the effect pertain to climatic conditions, diseases, and agents affecting peripheral circulation, such as use tobacco and certain medicines. In our studies tobacco was not a major factor.

Vascular symptoms and the HAVS staging classification
Contrary to the Stockholm Workshop scale the Taylor Pelmear scale does not distinguish between the hands and does not separate vascular and neurosensory symptoms. This may partly explain the higher cumulative prevalence found for the latter.

Nerve conduction

Work and nerve conduction
The neurological data from the cross-sectional investigation of platers, assemblers and office workers (II), revealed a job title difference related to job title between the exposure and referent groups. For the plater and assembler categories, the distal latencies over the carpal tunnel segment of the arm were prolonged compared with the latencies for the office worker group. In the same study the nerve conduction velocity was found to be lower in the right hand than in the left. A rate ratio of 1.17 (95% CI. 0.77 – 1.79) for prolonged latency time for the right hand was found in Study III in the vibration-exposed plater group when compared with the office workers.

Hand-transmitted vibration as a specific risk factor for nerve conduction
The neurological outcome was assessed in a cross-sectional (II) and a follow-up study (III). In the cross-sectional investigation of platers, assemblers and office workers (II) a slower nerve velocity was observed in the right hand than in the left. An increased risk (rate ratio) of prolonged latency time was found for the vibration-exposed plater group when contrasted to the office workers. There were higher rate ratios for the thicker myelinated motor fibers than for the sensory nerve fibres. The results of the follow-up study (III), focusing on the change in nerve conduction during the five-year follow-up period, did not support the findings of the cross-sectional study (II). The nerve conduction parameters of the cohort at entry and at follow-up did not indicate any deterioration of nerve function attributable to work involving vibration exposure. Although no major effects were found, the results were more consistent for the wrist segment, than for the distal segment and for the motor nerve measurements than for the sensory measurements. The results revealed no apparent exposure-effect relation between the nerve conduction parameters and the cumulative vibration exposure. This indicates that vibration exposure at the intensity level currently investigated was not a major risk factor when considering the outcome over the time span of a five-year interval. In contrast, an indicated association with the individually assessed ergonomic exposure was observed. The magnitude of the outcome data was influenced by the temperature adjustment factor chosen and by the standardised temperature level adjusted to.

The tendency to improved motor distal latency times at follow-up for the lifetime vibration-exposed group compared to the never-exposed group was consistent with more improvement in nerve conduction velocity at the follow-up for those never exposed than for the exposed group. When the comparison considered interim exposure, a similar tendency was found. Although these findings were consistent, none were statistically significant.

The majority of those studies, which claim to show evidence of an association between vibration exposure and nerve conduction impairment, come from case-control studies. The cases have been selected either from a population of patients (7, 176), from subjects with suspected hand-arm vibration syndrome disorders, or from job categories entailing a well-recognised exposure to vibration (8). The results in the present, prospective study of nerve conduction over the carpal tunnel, performed on a working population, show no exposure-effect relation between quantified job-specific cumulative vibration exposure and impaired nerve conduction.

Ergonomic exposure as a specific risk factor for nerve conduction

Only for the individually assessed ergonomic exposure was an association with the nerve conduction measurements indicated (III). But, interaction suggests that the effect from vibration and ergonomic factors can not be interpreted separately. Such an interaction could be expected in the work studied here: the two exposures are correlated ("take place simultaneously"), the vibration exposure in our study was in the range where vibration has effects on motor units (130), and the coupling between the hand and the handle is influenced by vibration (152).

Our reported increment in risk (Study II) for the left hand in comparison with the right cannot be explained by vibration exposure alone. A lateralisation of increased risk measures to the non-dominant hand has also been shown for other effect measures. In office work, as well as in plating and assembling, the highest ergonomic work load (occupational and non-occupational) is predominantly directed towards the dominant hand, most often the right hand. The relative impact of some other specific exposure, for instance vibration, may thus be greater for the non-dominant hand, due to a smaller total work load, compared with the dominant hand.

In the literature there is strong evidence that repetitive work, alone or in combination with force and straining postures may cause nerve compression in the carpal tunnel (14).

Target structure and nerve conduction

When platers were contrasted to non-vibration-exposed office workers the rate ratios were somewhat higher for motor nerve measurements than for sensory measurements. From the observed distinguishing clinical features of conduction block (194) large myelinated nerve fibers were found to be the most susceptible and unmyelinated the most resistant. Clinical findings would indicate that motor fibers are more susceptible than sensory fibers. In our study we observed only minor effects. In those cases where vibration does not cause conduction block, only minor changes could be expected. Manual work, however, entailing compression on nerves or hindering the blood flow might interfere with conduction. The rate of appearance and degree of conduction failure may also be modified by coexisting pathological states, so that the person with HAVS becomes resistant to ischaemic conduction failure. Nerves that are subjected to chronic endoneurial hypoxia become resistent to ishemia (44) and will continue to conduct for longer at reduced blood flow compared to referents (133). Vascular interference could thus possibly be modified.

Guiding standards and nerve conduction
Annex A in ISO 5349 contains information on health effects and, in the current draft (3) also recognises neurological hazards. The staging scales referred to in the draft are mainly symptomatological. The positive neurosensory manifestation dealt with is tingling and the negative is symptoms of numbness. A quantitative relation is suggested but only between vibration exposure and white finger prevalence and not for neurosensory health hazards.

Nerve conduction and the HAVS staging classification
The relation between the decreased conduction velocity characteristic of demyelinated nerve and the clinical manifestations of peripheral nerve disease is open to question (179). Patients who have completely recovered from peripheral neuropathy may have persistently reduced nerve conduction velocities without clinical symptoms. Reduced nerve conduction correlates best with degree of weakness (103). A symptom not asked for in the present staging classification. Slowing of conduction by itself leads to little, if any, clinical symptoms, as long as all the impulses arrive at the target organ. Adaptive systems compensating for decreased peripheral conduction velocity, particularly in sensory systems, make positive symptom staging ineffective for screening nerve conduction disorder in hand-arm vibration syndrome.

Nerve provocability test

Work and nerve provocability
Work-related factors such as seniority at work remained an independent risk factor in the multiple regression analyses of prevalent positive AER test. The analysis of the incident cases also revealed seniority at work to be the most prominent risk factor.

Hand-transmitted vibration as a specific risk factor for nerve provocability
Seniority at current work and exposure to vibrating hand-held tools reported in 1987 were predictive of both prevalent and incident AER signs five years later. Results from multiple logistic regression analysis of prevalent AER signs in 1992 gave high odds ratios 3.3 (95%CI 1.07-10.3), although with wide confidence intervals. The association between exposure to vibration from hand-held tools and neurological AER signs is still not straightforward. One possibility is that low frequency components are transmitted to the brachial plexus or surrounding tissues, while high frequency components are attenuated at the wrist and elbow. The frequency spectra in the present study impose that vibration-induced damage to the nerves mainly restricts its effect to the distal parts of the upper extremities.

Another explanation is the possible traumatisation due to the combined effects of jerks, power grips, unhealthy working postures, or movements associated with the use of vibrating hand-held tools. According to the double crush (or “multiple crush“) theory, distal traumatisation may affect the brachial plexus through disruption of the endo-neural axonal flow.

Ergonomic exposure as a specific risk factor for nerve provocability
Clinically, work-related musculoskeletal disorders, such as carpal tunnel syndrome have long been associated with increased susceptibility to provocation (signs of Tinel, Phalen, Spurling) (177). Determination of vibrotactile thresholds combined with provocation by means of wrist flexion, showed an increase in vibration threshold at least twice the unprovoced value (17).

Target structure and nerve provocability
The AER test was assumed to assess increased mechanosensitivity from the brachial plexus. Positive neurological manifestation from the brachial plexus often accompanied by a symptom–sign discrepancy, has been referred to by some authors as disputed neurogenic TOS (218). Ectopic impulse generation resulting from peripheral nerve hyperexcitability has been shown to underlie paresthesias provoked by arm elevation in the thoracic outlet syndrome (77). Abnormal modes of impulse conduction involve “cross-talk”, impulse reflection and ectopic impulse generation (211), which can all be related to the “double crush” concept. This hypothesis suggests that serial impingement on a peripheral nerve can act cumulatively to cause entrapment neuropathy. Although the hypothesis of double crush mainly entails axonal transport interference this could on its part be due to injury, compression, oedema or blood supply deficiency (113). Our results demonstrated that the outcome of the AER test is associated with occupational exposure, vibration, and other biologically plausible conditions. It also predicts future disorders in the neck and upper extremities. Almost every other subject with an AER sign in 1987 had new symptoms in the neck or upper-extremities and other new signs of nerve compression five years later (PPV=0.4-0.6). In addition, almost half of the subjects with numbness in the hands in 1992 had had a positive AER test five years earlier, all indicating an increased susceptibility or increased mechanosensitivity. Nerve provocation tests, such as the test for vibration tolerance , have revealed an association between the test results and repetitive strain as well as minor polyneuropathy in patients with repetitive strain injury (72).

Guiding standards and nerve provocability
Increased mechanosensitivity is not included in the present guiding standard.

Nerve provocability and the HAVS staging classification
The currently recommended HAVS neurosensory staging scale (34), is vague concerning the question whether the defined symptom and signs criteria are to be looked upon as sufficient or necessary components. The first and second stages are based on symptoms only, disregarding the possible symptom-sign discrepancy

and the possible existence of provocative symptoms other than tingling. The positive manifestation of increased nerve mechanosensitivity could be categorised into the concept of a ”tingling” sensation.

Neurosensory perception tests

Work and neurosensory perception

The results from the cross-sectional Study V revealed a clear association between groups who work with vibrating hand-held tools and the outcome from quantitative sensory tests of vibrotactile perception thresholds. A significantly increased VPT was found for the Pacinian mediated frequency range (63-500 Hz) among the vibration-exposed as compared to the non-vibration-exposed workers.

Hand-intensive work including vibration exposure, in the cross-sectional Study (VI), was associated with an increased risk of developing impaired thermal perception for the modalities of warmth and cold.

Hand-transmitted vibration as a specific risk factor for neurosensory perception

Vibrotactile perception - A four-fold increase in relative risk for elevated vibrotactile perception thresholds was observed for the category with the highest exposure (EC2) as compared with the non-exposed group (NE). The relative risks increased when the contrast was based on wider exposure gaps. The prevalences of abnormal VPT_P (both hands pooled) were 1.1%, 1.8%, and 10.7% for the NE, EC1, and EC2 exposure categories respectively. This may be considered an indication that there is a exposure-response relation between vibration exposure and sensorineural disorders of the mechanoreceptive system.

An exposure-response relation with increased impact from vibration on the high frequency measurements was also the result of Virokannas and co-workers (206) in a case-control study. These authors based their dose-assessment on the median length of time during which vibrating tools had been used, thus dividing the subjects into “high” and “low” exposure groups. Their findings support the view that frequency weighted vibration exposure is associated with vibrotactile sensory disturbances. Our association between exposure and outcome as expressed in the linear regression model was much weaker than the corresponding (r^2=0.58) presented by Virokannas (206). The only non-positive study on exposure-response between vibration exposure and vibrotactile perception is presented by Flodmark et. al, (58) who found no exposure-response relation between years of vibration exposure and vibrotactile sensitivity in a cross-sectional study.

Thermal perception - In Study VI, we found a exposure-response relation between cumulative vibration and impairment in thermal perception. Vibration exposure lower then the recommended EU threshold level showed signs of being a health hazard. To our knowledge only one additional study, that by Ekenvall and co-workers (54) has focused on the exposure-response relation. In their study temperature thresholds were not related to exposure dose, in contrast to our findings. Investigators addressing vibration and thermal perception have noticed a reduced sensibility in the right hand compared to the left (56, 57) but no study so far has separated the vibration exposure for each hand. The 0.80 exposure coefficient between the non-dominant (mainly left) and the dominant (mainly right) hand was possible recognised in the outcome result difference. Studies on non-vibration exposed subjects have found that perception thresholds values are normally symmetrical for the left and right hands (112, 134).

Risk assessment for thermal perception impairment based on vibration exposure during the last five years preceding the investigation revealed lower risk estimates with higher precision than those based on lifetime exposure.

The risk of developing impaired thermal sensibility increases by 18 % for each year of work entailing vibration corresponding to a dose at the recommended standard level (93), indicating that neurosensori effects can appear at lower exposure levels than for white fingers.

Ergonomic exposure as a specific risk factor for neurosensory perception
Entrapment neuropathies has iteratively been reported associated with reduced vibrotactile perception e.g. (16). Experiments where subjects performed 5 minutes keyboard typing followed by vibrotactile perception measurement revealed elevated vibrotactile thresholds (72). Cross-sectional studies on construction trade painters, exposed to both manual work, paint and solvents revealed that painters had significantly more temperature sensitivity thresholds classified as “high” than the reference group (18). Calluses caused by heavy manual work have been suggested as one possible explanation for the right- and left-hand discrepancy in vibrotactile perception (57).

Target structure and neurosensory perception
Among the sensory modalities vibrotactile sensation would be more susceptible than thermal perception and nociception when considering nerve fiber type. As regards thermal perception, our results did not support the hypothesis that the large warmth-mediating sensory units were more susceptible. The data we obtained showed that vibration exposure influenced warmth and cold sensory units equally much.

Guiding standards and neurosensory perception
Our results on vibrotactile perception (V) demonstrated a statistically more stable association between vibration exposure and disturbance in the Pacinian mediated mechanoreceptors than in the non-Pacinian receptors. In the current ISO draft for measurement of vibrotactile perception thresholds two of three recommended test frequencies are in the non-Pacinian area (4 Hz and 25 Hz) (2).

Our cross-sectional study (VI) of vibration-exposed mechanical and office workers, focusing specifically on thermal sensory units with thin fibre afferents, revealed a relation between cumulative vibration exposure and sensory function. The results of the study indicated sensory impairment, as assessed by increased perception thresholds, for warmth and heat pain and lowered thresholds for cold.

The effect appeared at vibration levels currently suggested as safe and below the upper limits of the standard guidelines.

Neurosensory perception and the HAVS staging classification
For vibrotactile perception we found abnormality according to SI-diagnostics in approximately 7% of our working population of office workers and platers. The case-criteria for impairment chosen in vibrotactile and thermal perception analysis were based on the mean $\pm$ 1 Sd. The neutral zone case criterion used was almost twice the normative value given elsewhere (54) yet still gave a prevalence of almost 10% of impaired thermal perception in a working population of both office workers and platers.

Slightly reduced vibrotactile perception also occurred in the non-vibration exposed office-worker category, a finding in accordance with the results of a study by Greening and co-workers (72) who found increased vibrotactile thresholds in their office-worker group.

For thermal perception measurements, the majority of those with increased neutral zone width did not report symptoms of paresthesia (nocturnal).

Exposure

Vibration exposure
The underlying model for the development of vibration-related disorders was restricted to the effect of vibration as a cumulated measure. Our studies of metal workers with job tasks involving exposure to vibration, revealed a fairly low mean acceleration level and cumulated interim vibration exposure when compared with studies that investigated models for risk prediction (68). The mean 4-hour, frequency-weighted, equivalent vibration exposure for the plater group was 3.9 m/s^2. Based on the results from Study III, the vibration intensity level was approximately 10% higher for the left hand than for the right. The exposure duration time was longer for the right hand than for the left resulting in the cumulated vibration exposure in the current studies, where the cumulated vibration exposure was 80% for the left hand compared with the right. Although the mean exposure levels were low, all the vibration exposure measurements, both at entry and at follow-up, showed wide ranges, indicating a large inter-individual variation.

During the follow-up time, the company invested in new machinery, introduced shorter exposure times, and reorganised the work in order to meet the demands of a preventive policy for health. The net result was an approximately 30% reduction in vibration exposure time and a corresponding 20 % reduction in cumulative vibration load between 1987 and 1992.

Ergonomic exposure
In the studies included in this thesis, we analysed only the duration of power grip as an approximation of the manual ergonomic load. Other risk factors associated

with upper extremity disorders e.g. location, intensity, and repetitiveness of the workload (79) were omitted from the analysis. The hypothetical basis for using manual hand grip as a significant index for ergonomic exposure was that the power grip might be related to increased intra-canalicular pressure, and thus contribute to the pathogenesis of work-related neural disorders (11).

In this investigation we only measured one of these factors, the portion of the working time when the forced grip was used. The outcome showed that the duration of forced grip was twice as long for the assembler group than for the plater group. This result is in agreement with the more pronounced manual aspects of the assembly work compared to plating. There was a predominance of forced grip for the right hand among the assemblers, which was not found for the platers. This outcome is interpreted as further evidence of the manual character of the assembly work.

The power-grip duration time obtained for the plater group was slightly longer (right hand: 44% from video recording) in our study compared to the corresponding percentage of time with "whole hand grip" among platers as measured by Fransson-Hall and co-workers. (38% -36%) (59). The left-to-right hand coefficient for manual use of power grip was approximately 50% in our study. This can be compared to approximately 70% reported for assembly line workers (59). The asymmetry between left and right hand was larger when the estimate was based on work analysis and diary information than on observation of individual video recordings.

Ergonomic and hand-arm vibration exposure interrelation

Hand–arm vibration exposure is inherently linked to ergonomic exposure, as the manual work is performed while gripping an oscillating power tool. Increasing grip and feed forces increases the vibration energy transmission to the hand (41). Temporary threshold shifts (Table I) reduce sensibility and are over-compensated for by increased grip force while simultanously increasing the grip force increases the temporary shift (152). Grip force is increased by the tonic vibration reflex and by increased vibration amplitudes (170). Vibration affects how tools are held and may result in the use of more force than is necessary. Increased grip force exerts contact pressure on the blood vessels and reduces the regional blood flow. Increased grip force also exerts compression on the nerves. Working posture influences the transmission of vibration to the upper extremities (174).

In addition to concomitant exposures the health hazards of vibration and ergonomic stress factors might share common elements in the pathogenesis. The oedema hypothesis for carpal tunnel syndrome and vibration exposure might be one such example (113).

The acute effects of vibration are thus to be regarded both as intermediate elements in the exposure (11) as well as outcome.

Time-effect relation between exposure and outcome

The unknown time-related aspect of the exposure makes it difficult to draw conclusions about whether it is the cumulative life-time exposure, the interim period exposure, the exposure during the last preceding week or the preceding hours that is crucial for the outcome. Our exposure measures were relevant for the lifetime- and interim period exposures but did not characterise the short-term effects. There is a documented variability in influence of injury to the nerves that varies within day and night such as early damage to the nerves, e.g. early carpal tunnel syndrome, giving nocturnal symptoms that revert during the daytime. If our results mirror the last day or part of the last day effects our study would not reveal the significant exposure factor. Support for the hypothesis of short-term effects is provided by experimental studies (113) which demonstrate that increased intracarpal tunnel pressure can lead to impaired conduction and sensory function of the median nerve in less than 1 hour.

Our outcome in the longitudinal study (III) reflects the difference in nerve function between the entry and the follow-up study. The exposure level was considerably lower at follow-up than at entry. If the nerve function measurements reflect the effects of momentary exposure levels rather than of cumulative exposure, the 20% interim exposure reduction might explain why no effects were observed. It is plausible that the effect might influence the results from the sensoryneural system more than from the vascular system.

In cross-sectional studies there is the problem of length-biased sampling, so that the cases might overrepresent cases with long duration and underrepresent cases with short duration of illness (178). Hence white finger symptoms could be positively associated with exposure duration in cross-sectional studies and thus produce an exposure time relation. Length-biased sampling effects would possibly differentiate between vascular and neurological disturbances, as the outcome alternatives are greater for the latter. Results indicate that most subjects claim improvement or sustained VWF symptoms with interrupted exposure but there is also a small number of subjects who complain of worse problems (225). The same authors claim that for vibration-induced neuropathy there may only be limited or even no reversibility of impairment after cessation of exposure. Thus we could also expect negative neurosensory findings among the former vibration-exposed subjects in the referent group.

The rate of reversibility of HAVS symptoms on removal from exposure to vibration is a controversial matter. For some occupational groups (e.g. chain saw workers) there is evidence of recovery of VWF after reduced exposure (189) but there are few studies on VWF reversibility among other occupational groups exposed to power-tools (24). Some longitudinal studies have shown that sensorineural symptoms might be more resistant to improvement or recovery than the vascular disorders (24).

Outcome in relation to guiding standards

The guidance proposed in the current draft of ISO 5349-1 (3) is derived from limited quantitative data from practical experience and laboratory experimentation concerning human response to hand-transmitted vibration as well as limited information regarding current exposure conditions (68). The use of the information proposed in the ISO 5349 should protect the majority of workers from serious health impairment associated with hand-transmitted vibration. Our results, however indicated that work with hand-held vibrating tools may have resulted in neurosensory impairment in a significant proportion of workers demonstrating different types of neurosensory impairment. The different aspects of the neurosensory system should be attended in the guidelines so that the physicians, who assesses sensation in order to detect abnormality, which, if present, may investigate disordered function of the different sensory end organs, afferent neurons, central tracts, nuclei or cerebral region.

Our result indicate that the risk for white fingers predicted by the model in the ISO 5349 annex underestimates the true risk for white fingers. They also indicate that neurosensory disturbances may occur with short latency. This is more in line with the European recommendation of an eight-hour action level of 2.5 m/s^2 (1) then with the 2.9 m/s^2 suggested by ISO (3). Although the recommendations include general advice about incorporating ergonomic principles in the work task design, this occurs only in the context of vibration exposure. No present standard for work with hand-transmitted vibration give guidelines for the concomitant ergonomic aspects of the work.

Based on the multiple crush hypothesis, suggesting that cumulative injury to the nerve is accumulative irrespective of its origin beeing from vibration exposure, compression entrapment or reduced vascular suply, justifies consideration of not only vibration but also other ergonomic factors.

There is reason to support the medical guidelines of NIOSH (150) until exposure assessment has learnt to encompass both vibration and other ergonomic aspects by combining them in an “internal” energy uptake dose. Even with the development of highly sophisticated energy uptake measures will they still fall short in representing the hazardous aspects of posture, the exposure over-time relation, the effect of rest (40), and the different resting time demands for the different structures of the body.

A cornerstone in the NIOSH criteria for a recommended standard is the requirement for medical monitoring of *all* vibration exposed workers to identify the first signs and symptoms of HAVS and to remove workers who have developed stage 2 on the Stockholm Workshop scale from vibration-exposure until they are free of vibration related symptoms. Our finding of a significant prevalence of signs in an asymptomatic work population supports the recommendation for a census approach in medical monitoring. The great importance of the staging of neurological symptoms calls for strict criteria in the assessment of sensory unit dysfunction. In our cohort there was a substantial number of workers with susceptibility, a condition not dealt with in the guidelines.

Assessment of sensory unit function in HAVS

Sensory perception assessment is suggested to include the thermal perception measurements of cold and warmth thresholds and vibrotactile perception at least in the areas of Pacinian sensory units. After clinical evaluation of adequate subjective response of receptors to stimulation, warmth and cold thresholds can be combined in a single measure of thermoneutral zone width (neutral zone). The value of heat induced pain was limited in our population and this test is not recommended. Cold induced pain can be considered more useful, both for threshold assessment and for the diagnostics of allodynia or symptoms of abnormal cold intolerance. If several assessments of neurosensory function are performed, the cold pain test must be the last one, as all neurosensory functions are temperature dependent.

Nerve conduction was examined by motor and sensory nerve conduction velocities, amplitudes and motor latencies. In follow-up settings, F-wave latency may be preferable to our measurements, due to superior intertrail stability and reliablity (103). For cases with positive nerve findings electromyography should be recommended for discriminating between axonal and demyelinating neuropathy.

The observed predictive value of the nerve provocation test justifies its use, at different locations of the upper extremity, in the clinical evaluation of patients with suspected hand-arm vibration syndrome.

Methodological considerations

Matters of precision

Sampling and selection of study population

The overall design was cohort-based with census admission of vibration-exposed platers and random admission of office workers. The underlying sampling aim was to find subjects that varied in respect to vibration exposure and manual load aspects.

All the office workers admitted were examined. The office workers worked mainly at worldwide maintenance and selling. As travelling attracts the young and healthy among the office workers the mean age of those who remain in Sweden and were accessible to the study was high. Office workers with less vigour may therefore have been selected, perhaps resulting in an underestimation of the true risk. The possible health hazards (carpal tunnel stress or syndrome) associated with keyboard typing was not recognised at entry but subjects contracting carpal tunnel syndrome were excluded from our analysis.

The effect of selection bias (healthy worker effect) in the study population was regarded as small.

Study size

The cross-sectional studies comprised 150, 179, 170, and 197 subjects respectively. In the follow-up studies AER outcome was assessed both at entry and at follow-up for 137 workers and nerve conduction for 121. The small number of subjects restricts the precision of measurements, but most analyses were made on both hands. The number of measurements performed, therefore is twice that of included subjects.

Study efficiency

The contrast ratio between vibration-exposed subjects and referents was influenced by previous exposures. An analysis of those listed on employment rosters as office workers revealed that every fourth worker had previous experience of work with vibrating power machines, thus reducing the number of non-exposed referents. During the follow-up period, a significant number of platers reduced their vibration exposure so that 45 workers in the nerve conduction measurements, were continuously vibration-exposed during the follow-up period. The power of the nerve conduction follow-up study to detect a 0.1 ms difference in e.g. motor distal latency time between entry and follow-up was still fairly high (0.7). In the study on vibration white fingers the number of cases was 41. The AER test results gave 32 prevalent cases in 1987 and 26 in 1992 and 9 incident cases during the follow-up interim period. In the nerve conduction studies and QST studies, subjects with signs of polyneuropathy, carpal tunnel syndrome or former handsurgery were excluded. After exclusion 19 subjects remained who fulfilled the criteria for increased neutral zone width and 13 for impaired vibrotactile perception. The restricted number of cases limits the modelling possibilities (49).

Matters of validity

Possible confounding

Age and use of nicotine were controlled for because of their biological and theoretical importance for the outcomes. The use of nicotine (current or former use of snuff or tobacco) was more common among platers than office workers. The prevalence rates of nicotine consumption for vibration-exposed workers (1987) were 0.72 and 0.53 for office workers. In the cross-sectional study of 1992 the corresponding numbers were 0.59 and 0.40 respectively. Tobacco was also associated both with exposure and outcome but we found no significant contribution to the prevalence of VWF. The etiological role of tobacco for VWF is still beeing debated but prognosis studies show a significant decrease in the frequency of white finger attacks among non-smokers, and an increased frequency among smokers (168).

Pay incentive is one aspect of the job that influences individual work methods and thus the ergonomic and vibration exposure. Incentive work has been associated with a higher prevalence of vibration syndrome among chippers and grinders when compared with hourly work (170). In our study, the pay incentive was a 100% piecework for the assemblers, 15-25% for the platers in 1987 and monthly salary for the office workers in 1987 and 1992. During the follow-up period, the piecework payment for platers was replaced by a monthly salary.

Exposure characteristics correlated with age comprise several life-style factors, including sports activity, leisure-time use of vehicles with vibrating handlebars and recurrent episodes of excessive alcohol consumption. By definition, age is correlated with cumulative exposure. The mean age of the referent group was approximately 3 years higher than that of the vibration exposed group.

We found no nerve impairment association to either height, weight, or body mass index.

Information bias

Nerve conduction tests are influenced by several measurement and host factor parameters among which the most important is temperature (109). Other covariates are height (173), weight (143), body mass index (214), age, sex (191) and examiner effect (109). The follow-up study design with the same subjects being retested by the same examiner using the same apparatus set-up makes temperature adjustment the primary methodological concern. In our nerve conduction studies the 1.4 m/s°C temperature correction slope given by Letz and co-worker. (109) was used for conduction velocity. For distal motor latency we used -0.3 ms/°C, a value that is also recommended in major textbooks e.g. (104). The mean skin temperature in 1987 was 31.1°C for the vibration-exposed group and 31.3°C for the non-vibration-exposed. The corresponding values in 1992 were 1°C lower.

In the studies on nerve conduction, anatomic landmarks were used for the distal motor nerve measurements, while nerve conduction velocities were calculated according to measured distances. This might have given the nerve conduction velocity outcomes greater measurement precision.

In the study focused on white fingers (I), the interpretation of the defined symptom criteria may have varied among persons. The potential risk involved in choosing less strict criteria was balanced by the use of hand drawings commented on in the physical examination.

In the nerve conduction studies, the case definition for impaired nerve conduction was not equivalent to the medical criterion for disease. Thus the prevalences of impaired nerve conduction were not directly comparable to those found in studies of neuropathy associated with carpal tunnel syndrome. With the present criteria, high point prevalences of neurological impairment is to be expected by definition.

Polyneuropathy and other diseases have been controlled for in only a few studies on nerve conduction (e.g. 46, 96). Nerve conduction findings indicating neuropathy cannot distinguish between diffuse general distal neuropathy, a disorder caused by specific disease, local entrapment, or neuropathy of any other origin. A small fraction of the subjects in Study II can be expected to have had some unidentified disease or polyneuropathy. Reduced finger temperature is found in some subjects with vibration-induced white fingers (37). This finding may explain the difference found in nerve conduction studies between vibration-exposed and unexposed workers. No temperature difference was found in Study

III between vibration-exposed and non-exposed subjects, although there was a 1 °C difference between entry and follow-up.

The possible misclassification with respect to exposure is influenced by several factors. The most important of those are: (1) transfer within the cohort (from vibration-exposed to unexposed categories) (2) interpolation of job-specific exposures into individual estimates and (3) the cumulative lifetime exposure versus short-term exposure.

The outcome of vibration assessment shows a high concordance between the reported time of exposure to vibrating tools during the investigated day and the corresponding objectively measured exposure time. This is interpreted as indicating a good knowledge of the content of the work.

Detailed analyses of exposure to vibration revealed that job title was a crude measure of exposure to vibration. In the reference group, 25% of the office workers had had substantial exposure to vibration in their previous work and a small fraction of platers worked with tasks where there was no current vibration exposure.

In these analyses, only occupational vibration exposure has been controlled for. A substantial exposure might come from leisure-time activities such as driving snow-scooters or other vehicles with vibrating handlebars or from using powered hand tools. The assumption of an even distribution of this in the exposure and reference groups has to be questioned because of the to different age distributions. Information about exposure to ergonomic factors other than vibration in former activities, occupations, and leisure-time has neither been asked for nor analysed. The influence of sports, former work and free time activity could not therefore be controlled for.

Conclusions

From the study of vascular symptoms (I) the following main conclusions could be drawn:

- Vibration exposure constitutes the dominant source for VWF and corresponds to the largest attributable fraction for those contracting white finger symptoms.

- Application of the risk prediction model for white fingers in Annex A of ISO 5349 somewhat underestimated the VWF risk.

- There was no correlation on an individual basis between vibration exposure time and the stage reached on either of the two existing symptom classification scales.

- The timed Allen´s test was related to work with vibrating machines.

From the studies on nerve conduction (II and III) the following main conclusions could be drawn:

- The nerve conduction results indicated a relation to work, but the specific contributions from vibration and manual workload could not be separated.

- Vibration and biomechanical aspects of work are important for nerve conduction impairment in the wrist.

- The study of assembly workers showed clear neural effects despite low vibration exposure intensity, as measured by ISO 5349, and short employment times. This emphasizes the importance of considering, in addition to vibration, the manual workload aspects, and indicates that the ISO 5349 standard may not adequately take into account those aspects of vibration that are relevant for adverse health effects on nerves.

- The follow-up study did not indicate an exposure-effect relation between quantified job-specific cumulative vibration exposure and impaired nerve conduction at the vibration level currently found.

- An indicated association was observed between distal latency time in the median nerve and individually assessed time with power grip.

- Although no major effects were found, the results were more consistent for the wrist segment of the median nerve than for the distal segment and more consistent for the motor nerve measurements than for the sensory measurements.

- The wide ranges in inter-individual exposure measurements indicated that, for both vibration and ergonomic load factors, mean job-specific exposure is a poor approximation to true exposure.

From the study on nerve provocability (IV) the conclusions were:

- Factors related to work, vibration exposure, constitution, and disease were associated with neurological AER signs.

- The estimated duration for positive neurological AER signs is extended (12-18 years) and should be considered in the prognosis. The occurrence of neurological AER signs should alert the clinician to the possibility of an unfavorable exposure from work or an ongoing disease process.

- Neurological AER signs predict future upper-extremity symptoms and signs of nerve compression which are compatible with the suggestions given in the "double crush hypothesis" of cumulative trauma and nerve function interference.

From the studies on somatosensory function (V and VI) it was concluded that:

- Cumulative vibration exposure is a separate risk factor for disturbing the normal function of the sensory units of thermal and vibrotactile perception.

- The impact from cumulative vibration was most clearly demonstrated in the sensory units localised in the region with Pacinian receptors (frequency range 63-500 Hz).

- Sensory impairment, as assessed by reduced vibrotactile perception, and in the form of increased perception thresholds for warmth and lowered thresholds for cold appeared at vibration levels currently suggested as safe and below the standard guidelines. This indicates a need for a review of the current recommendations.

- Quantitative sensory testing offers a possibility of assessing the specific hazard to thermal sensory units associated with hand-intensive work involving vibration and should be included in addition to vibrotactile perception measurements in the diagnostics of the hand-arm-vibration syndrome.

Summary

Nilsson T. Neurosensory function and white finger symptoms in relation to work and hand-transmitted vibration. Arbete och Hälsa 1998:29

The present thesis, which is based on six studies, focuses on the vascular and the neurological outcomes in relation to work and hand-transmitted vibration. The overall aim was to assess the quantitative relation between cumulative vibration exposure and self-reported signs of "white fingers”, nerve conduction, nerve provocation test, and quantitative sensory testing of vibrotactile and thermal perception. Vibration exposure data was characterised from "ever employed" in a job involving use of vibrating tools to quantitative, individual estimates of cumulative frequency-weighted vibration exposure for each hand. The manual load aspect of the exposure was measured as time with a forced grip.

The cross-sectional study on the vascular component of the hand-arm vibration syndrome revealed a high prevalence of white fingers in the plater group together with high risk estimates. Hand circulation was assessed by a symptom questionnaire and a timed Allen's test. The odds ratio for a positive Allen's test was higher for the vibration-exposed category than for the non-exposed.

The neurological outcome was assessed in a cross-sectional and a follow-up study. In the cross-sectional study, a lower nerve velocity was found in the right hand than in the left. An increased risk of prolonged latency time was found for the vibration exposed plater group when contrasted to the office workers. The follow-up study, focusing on the change in nerve conduction during the five-year follow-up period, did not support the findings from the cross-sectional study. This indicates that vibration exposure per se, at the intensity level that we investigated was not a major specific risk factor over a five-year interval time span. In contrast an exposure-effect relation was indicated when ergonomic exposure was individually assessed.

The prospective cohort study on nerve provocation revealed that work factors, including vibration exposure, were associated with AER signs. Subjects with AER signs showed lower nerve conduction velocities in the wrist.

The study on vibrotactile function demonstrated elevated thresholds -primarily for the Pacinian mediated sensation - related to vibration. In the study on thermal perception the risk for the vibration exposed group of having contracted reduced thermal sensibility was found to be increased at all test sites. The risk was higher for the thenar measurements than the finger measurements. Application of the risk prediction model for white fingers in Annex A of ISO 5349 rather underestimated the VWF risk among the currently exposed platers. The results indicate a relation between sensory impairment and cumulative vibration exposure. This effect appeared at vibration levels below the limits suggested in the current standard.
Key words: Vibration, ergonomics, hand-arm vibration, white fingers, nerve conduction, Allen´s test, AER test, thermal, vibrotactile, perception, QST.

Sammanfattning (summary in Swedish)

Nilsson T. Neurosensory function and white finger symptoms in relation to work and hand-transmitted vibration. Arbete och Hälsa 1998:29

Föreliggande avhandling bygger på sex undersökningar av sambandet mellan arbete med vibrerande verktyg och vasospastiska samt neurosensoriska störningar. Syftet innefattade det kvantitativa sambandet mellan kumulerad exponering för vibrationer och rapporterade tecken på ”vita fingrar”, nervledningsfunktion, retbarhet vid nervprovokation (”Abduction External Rotation Test”= AER) samt tröskelbestämning av perceptionen för värme, kyla och värmeutlöst smärta. Vibrationsexponeringen definierades utifrån yrke och som indivdiuellt, kumulerat, frekvensvägt 4-timmarsvärde för var hand. Tid med kraftgrepp fick karaktärisera den kraftergonomiska exponeringen.

Vibrationsskadesyndromets vaskulära komponent undersöktes i en tvärsnitts-studie. Undersökningen visade på hög förekomst av vita fingrar i plåtslagargruppen, vilket återspeglades som höga odds kvoter. Den distala cirkulationen undersöktes med frågeformulär och med Allens test. Den vibrationsexponerade gruppen uppvisade högre odds kvot för ett positivt Allens test jämfört med den icke vibrationsexponerade gruppen.

Vibrationsskadesyndromets neurologiska komponent bestämdes i en tvärsnitts- och en uppföljningsstudie. I tvärsnittsstudien visade resultaten på lägre nervledningshastighet för höger hand jämfört med vänster. När de vibrationsexponerade plåtslagarna jämfördes med tjänstemän erhölls en ökad risk för förlängd distal latenstid. Uppföljningsstudien, som inriktades på att undersöka förändringar i nervledning mellan mätvärden från kohortens början och dess uppföljning, kunde inte stödja de fynd som framkommit i tvärsnittsstudien.

Den prospektiva kohortstudien med nervprovokation visade att faktorer i arbetet, vibrationsexponering, var relaterat till AER fynd. För de som uppvisade AER tecken påvisades en försömrad nervledning över handleden.

Undersökningen av det vibrotaktila känselsinnet visade på högre känseltrösklar, främst för Pacini medierat känselsinne. Den kvantitativa känsel tröskel-bestämningen av temperatursinne och smärta visade att de som exponerats för vibrationer hade försämrad känselförmåga. Effekten var tydligare för mätningarna thenart jämfört med distalt på fingret.

Resultaten tyder på att vita fingrar och känselstörning är relaterat till ackumulerad vibrationsexponering medan sambandet till nervledning är oklart. Påverkan uppkommer vid vibrationsnivåer lägre än nuvarande riktlinjer. Vibrationsexponeringen samvarierar med ergonomiska faktorer.

Nyckelord: Vibration, ergonomi, Hand-arm vibration, Vita fingrar, nervledning, Allens test, AER test, Temperaturtröskel, Vibrationströskel

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