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Role of physical load factors in carpal tunnel syndrome

by Eira Viikari-Juntura, DMedSci,[1] Barbara Silverstein, PhD[2]

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Epidemiologic and experimental studies were reviewed to assess the role of postural factors, high handgrip and pinch forces, repetitive hand and wrist movements, external pressure, and vibration in the occurrence of carpal tunnel syndrome (CTS). Forceful repetitive work, vibration, and extreme wrist postures have been associated with CTS in several epidemiologic studies. Experimental studies have shown that certain forearm, wrist, and finger postures, even moderate hand loads and external pressure on the palm, can increase carpal tunnel pressure (CTP) at least temporarily to levels at which nerve viability is threatened. It is concluded that while more research is needed, there is sufficient information to suggest that reducing the duration, frequency or intensity of exposure to forceful repetitive work, extreme wrist postures and vibration is likely to result in a reduction of the incidence or severity of CTS in working populations.

Key terms epidemiology, experimental studies, external pressure, force, postural load, repetitive work, risk factor, vibration.

Carpal tunnel syndrome (CTS) is a fairly common nerve entrapment in the upper limb. In the Dutch general population between 25 and 74 years of age, the prevalence of CTS based on typical symptoms and abnormal nerve conduction in the median nerve at the carpal tunnel was 9.2% among the women (5.8% had undetected CTS and 3.4% had the disorder diagnosed earlier) and 0.6% among the men (1). In a North-American general population study, the incidence of first occurrence of CTS, based on visits to a doctor, was estimated as 3.5 cases per 1000 person-years (2). The diagnosis of the International Classification of Diseases (9th revision) appearing in the medical files was accepted as the basis for case definition, and 45% of the cases had positive nerve conduction studies. For the Washington State working population, workers' compensation claims show an incidence rate of 2.7 per 1000 workers per year with some industries having almost 8 times the industry-wide rate (3). Electrodiagnostic studies were conducted in approximately 77% of the cases.

According to a recent consensus document, the diagnosis of CTS in epidemiologic studies should be based on typical symptoms and electrodiagnostic findings, and in the absence of electrodiagnostic examinations specific combinations of symptoms and signs can be useful, but they are likely to result in greater misclassification of the disease status (4). Using the Delphi method, another group developed consensus criteria for CTS in surveillance and etiologic studies. Typical symptoms combined with 1 clinical finding or 1 abnormal nerve conduction time were considered sufficient for the diagnosis of CTS (5). In clinical practice, fairly similar criteria are used, with the exclusion of other diseases as the source for the symptoms as an important element of differential diagnosis.

Of the soft-tissue disorders of the upper limb, CTS is probably the one whose etiology and pathomechanisms have been most extensively studied. In the 1990s, several reviews have appeared in the literature, especially on epidemiologic studies (6—11). Because of the high number of epidemiologic reviews, and only a few reviews on experimental studies, especially reviews with any attempt to link the physical loads to possible pathomechanisms (12), we chose to approach the role of physical load factors in CTS with a broad spectrum of studies. We wanted to identify the possible mechanisms associated with modifiable workplace physical factors that have been associated with CTS. An understanding of

1 Finnish Institute of Occupational Health, Helsinki, Finland.
2 Washington State Department of Labour & Industries, Olympia, Washington, United States.

Reprint requests to: Dr Eira Viikari-Juntura, Musculoskeletal Research Unit, Department of Physiology, Finnish Institute of Occupational Health, Topeliuksenkatu 41 a A, FIN-00250 Helsinki, Finland. [eira.viikari-juntura@occuphealth.fi]

mechanisms may lead to research that can identify optimal safe limits of exposure that can be incorporated into the design of work.

Epidemiologic studies have identified several associations of work factors, individual factors, and psychosocial factors with CTS. Of these, many of the individual factors are less modifiable than the workplace factors. The physical factors most frequently associated with CTS include forceful, repetitive work, often in combination with extreme postures, and vibration. However, exposure assessment in these studies lacks the precision necessary to develop job and tool design parameters to prevent work-related CTS in the future.

Laboratory studies of humans generally include intermediate outcomes such as increased carpal tunnel pressure (CTP), maximum acceptable limits, and temporary physiological changes prior to the expression of frank disease. In these studies, the measures of exposure are usually much more precise and controllable than in epidemiologic studies. They have included repetitive loading, postures, frequency, force, and vibration.

Laboratory studies of animals have evaluated the effect of repetitive loading on nerve, tendon, and muscle function. In some cases, this information can be extrapolated to human exposures and responses. Primarily, rabbit and rat models have been used.

In clinical studies of patients, CTP values have been measured in a resting situation and in different postures of the wrist and loadings of the fingers. Comparisons have been made between patients with CTS and healthy subjects, and also between the pre- and postoperative status of patients.

Our aim was to review the evidence of the role of postural factors, the use of high hand grip and pinch forces, repetitive hand and wrist movements, external pressure, and vibration in CTS. Epidemiologic studies, experimental studies on healthy humans, cadaver studies, and animal studies were included along with the clinical studies on patients. The results of especially experimental studies were associated with current knowledge on pathomechanisms and weighted with an emphasis on whether the loads under study were comparable with those in work situations.

Search of studies

We performed a literature search in Medline from 1966 to 24 November 1998. We used the following terms as MESH terms and terms in the text: "carpal tunnel syndrome" OR "median nerve" AND the following 5 physical load factors: "posture OR postural OR position"; "force OR forceful"; "repetition OR repetitive"; "external pressure OR pressure with adverse effects"; "vibration OR vibrating".

This search produced 780 citations. Some references cited in these articles were also checked with regard to useful information. Recent reviews on nerve pathology with their references were scrutinized. Several researchers in the field were contacted. Additional Medline searches were made to look for prospective epidemiologic studies of CTS, and none was found dealing with the physical load factors of interest.

Due to the broad spectrum of our review, consisting of very different types of studies, a systematic approach was not feasible. In epidemiologic studies study design aspects and the quality of assessment of outcome and exposure were considered in the review process, although no explicit inclusion and exclusion criteria were defined. Experimental and cadaveric studies were selected on the basis of their relevance and richness of information with regard to the risk factors of interest and an understanding of the pathomechanisms of CTS.

Functional anatomy

Carpal tunnel syndrome (CTS) is an entrapment of the median nerve in the carpal tunnel, an open-ended fibro-osseus canal in the wrist. The floor of the tunnel is formed by the carpal bones and the roof by the ligamentous flexor retinaculum. Besides the median nerve, 9 flexor tendons of the fingers pass via the carpal tunnel to the hand. Using gross anatomic, radiographic, and histologic examinations of cadavers, Cobb et al (13) redefined the flexor retinaculum to include 3 continuous segments: the thin proximal segment composed of the thickened deep investing fascia of the forearm, the transverse carpal ligament, and the distal portion of the flexor retinaculum, composed of an aponeurosis between the thenar and hypothenar muscles (figure 1). In earlier literature, the transverse carpal ligament had been considered to play a central role in CTS, and the proximal and distal portions of the flexor retinaculum had not been well described.

The flexor retinaculum is covered superficially by the antebrachial fascia proximally and by the palmar fascia distally. The antebrachial fascia encloses all the structures of the flexor compartment of the forearm (ie, the flexor carpi radialis and ulnaris in addition to the contents of the carpal tunnel) and the deep investing fascia encases only the contents of the carpal tunnel. These 2 fascial layers merge medially in the distal forearm area but are separated radially and ulnarly. The deep investing fascia is continuous with the transverse carpal ligament. The transverse carpal ligament passes from the pisiform to the tubercle of the scaphoid proximally and from the hook of the hamate to the tubercle of the trapezium distally. This part of the flexor retinaculum is the thickest (mean 1.5 mm). The thenar muscles attach to the

radial half of the transverse carpal ligament. At the distal portion of the flexor retinaculum, the thenar muscles overlay the palmar radial aspect and the hypothenar muscles overlay the ulnar aspect of the tunnel, the central part forming a broad aponeurosis between the thenar and hypothenar muscles. In this region, small fibrous septa fuse the palmar fascia to the flexor retinaculum.

Using contrast materials in cadavers, Cobb et al (14) showed that, while the carpal tunnel may appear to be an open compartment anatomically, it functions as a relatively closed compartment with respect to the transfer of pressure from the flexor compartment of the forearm into the carpal tunnel.

Nerve trunks consist of nerve fibers enclosed in endoneural sheaths. The sheaths are bundled together into fascicles by a perineurium. The fascicles are embedded in a loose connective tissue framework called the epineurium. There is probably a lymphatic capillary network in the epineurium, while there are no true lymphatics in the fascicles. There is an extrinsic blood supply system which reinforces the intraneural vascular bed at varying intervessel plexuses in different layers of nerve. The intraneural vessels form an anastomosing network that is continuous throughout the length of the nerve (15). The intraneural vascular system has a great reserve capacity. It has sympathetic innervation.

Biomechanics

Armstrong & Chaffin (16) estimated loads on adjacent wrist structures as a function of flexor tendon curvature and load. The total force exerted by a tendon on adjacent wrist structures increases almost linearly with increasing wrist flexion or extension.

Biomechanical calculations based on measurements of cadaver hands have shown the loads of the second and third flexor digitorum profundus tendons to be 4.3 and 3.7 times the pinch force and 2.8 and 3.1 times the grasp force (17). The difference is due to the fact that, in pinch grip, external force is exerted only on the distal phalange and, in grasp, loads are exerted on all 3 phalanges.

Dennerlein et al (18) measured flexor digitorum superficialis tensions of the long finger in vivo during a pinching task with 0—9 N of force in CTS patients during surgery. The average ratio of the tendon tension to the fingertip contact force ranged from 1.7 to 5.8 (mean 3.3, SD 1.4) for the 9 patients, and it was higher than predicted by current isometric tendon force models. An even higher ratio was measured during a rapid loading task (19).

Goldstein et al (20) subjected male and female cadaver flexor profundus tendons to step stress tests with load levels corresponding to those of industrial tasks. The stress-elastic strain curves were nonlinear, and they differed for men and women, the strain in men being higher. There was a strain difference over the carpal tunnel area, the strain in the distal part of the tendons being 0% to 40% less than that in the proximal part. The difference was dependent on applied load and wrist deviation and was higher for flexion than for extension. These results indicate that significant stresses exist at the tendon, tendon sheath, and flexor retinaculum interface. Other evidence of such stresses was seen in histologic specimens of cadavers, demonstrating increased density of fibrous, synovial and connective tissue, and median nerve epineurium (21). These changes were maximal in sections at the transverse carpal ligament, and they diminished proximally and distally.

A study on cadaver specimens showed that, during active finger flexion, the flexor tendons and the median nerve glide within the carpal tunnel, the relationship between the median nerve and flexor digitorum superficialis excursion being about 0.3—0.4 and higher with the wrist in extension than in flexion (22). Median nerve strains during various degrees of finger flexion were compressive proximal to the carpal tunnel area and tensile within the carpal tunnel, and highest with the fingers in

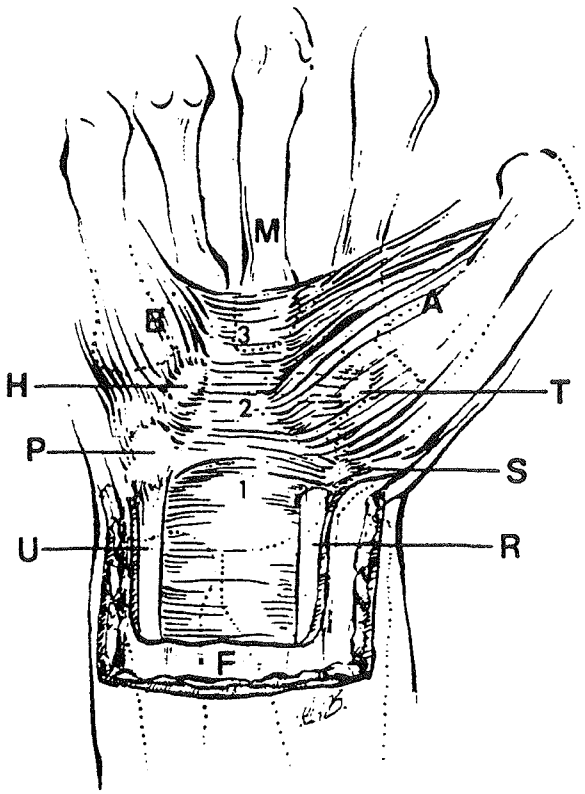

Figure 1. The flexor retinaculum. (1 = proximal portion, 2 = transverse carpal ligament, 3 = distal portion of the flexor retinaculum; A = thenar, B = hypohtenar muscles, T = tubercle of trapezium, H = hamate, S = tubercle of scaphoid, P = pisiform, R = flexor carpi radialis, U = flexor carpi ulnaris)[Published with permission of the *Journal of Hand Surgery*, American volume]

extension. The strain showed high interindividual variability.

Pathophysiology

There is some literature relevant to the pathomechanisms of peripheral nerve entrapment. In animal studies it has been possible to produce a range from mild to severe pathological changes and then follow blood circulation, nerve function, and histologic changes over time after the injury. In studies among humans, only temporary changes can be experimentally induced, but these studies enable the recording of associated symptoms and findings of nerve function. In table 1, a selection of animal and human studies is reviewed. It demonstrates the effects of experimentally induced acute and more long-term nerve compression, repetitive contractions, and vibration (23—38).

The major pathways of injury to the median nerve are (i) ischemic effects on the nerve due to increased pressure in the carpal tunnel, (ii) effects of vibration from hand-held tools, and (iii) mechanical injury due to contact stresses on the nerve (figure 2). The extent and reversibility of events depend on the level and duration of median nerve compression and contact stress. The sequence of events can be best studied in vivo, but only few such investigations have been carried out. Due to such studies, the microcirculation of the nerve is currently best understood.

In externally applied compression, the first sign is the retardation of venular flow in the epineurium. In a rabbit model (26), such retardation was almost immediately seen after the application of 20—30 mm Hg (2.7—4.0 kPa) of pressure. At higher levels of compression, endoneurial capillary flow and arteriolar flow in the epineurium were reduced. Complete ischemia was seen at 60 to 80 mm Hg (8.0—10.6 kPa).

In a rat model, Schwann cell degeneration and later demyelination was seen after 30 mm Hg (4.0 kPa) of pressure for 2 hours, whereas axonal degeneration was infrequent at this pressure level (29). At 80 mm Hg (10.7 kPa), the nerve was edematous, axons were swollen, and there was disintegration of myelin. Later, axonal degeneration was seen; it persisted until the end of the 28-day follow-up. All the changes were the most pronounced subperineurially and less marked in the endoneurial interstitium.

In a rabbit vagus nerve model (30), compression of the nerve with 20 mm Hg (2.7 kPa) for 8 hours induced a decrease in the fast axonal transport of proteins, and compression of 30 mm Hg for 8 hours led to a decrease in the slow axonal transport of proteins. This process results in an impaired transmitter function of the nerve and, if prolonged, in a lack of structural proteins needed for the distal axon.

Nerve function in association with elevated intracompartmental or intratunnel pressures has been studied with dogs and healthy human volunteers. Measurements of intracompartmental pressures of the anterolateral muscle compartments of the hind limbs of dogs have shown that the time to produce conduction block is inversely related to intracompartmental fluid pressure (25). A pressure of 50 mm Hg (6.7 kPa) has been enough to cause complete block, and lower pressures of 30 and 40 mm Hg (4.0 and 5.3 kPa) have caused incomplete conduction block after 6—8 hours of pressurization. Pressure of 20 mm Hg (2.7 kPa) for 8 hours did not have any effect on nerve conduction. In healthy volunteers, 40 mm Hg (5.3

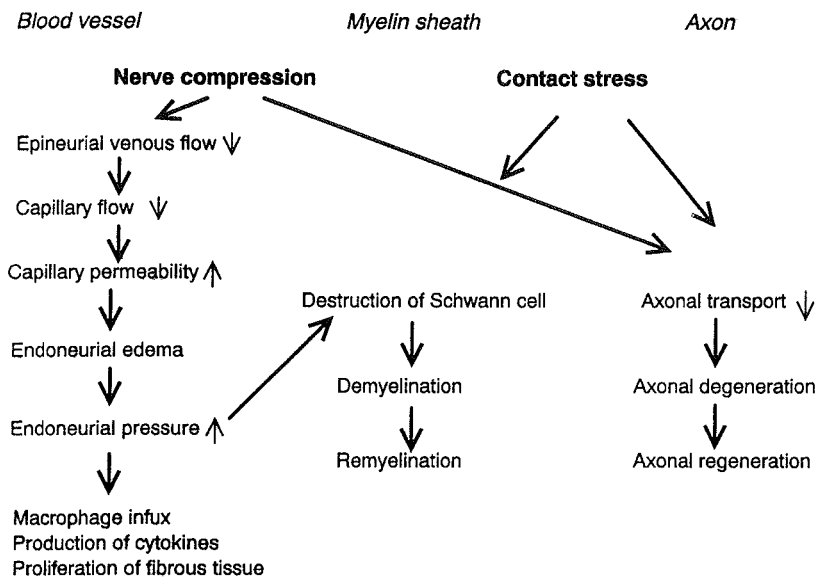

Figure 2. Pathomechanical pathways of carpal tunnel syndrome.

Table 1. Summary of selected studies on the pathomechanisms of nerve injury. (AMP = action potential amplitude, NCV = nerve conduction velocity, CTP = carpal tunnel pressure, DL = distal latency, SH = Schmidt-Lanterman incisure, MCV = motor conduction velocity, MDL = motor distal latency, ↑= increase, ↓ = decrease, → = leading to, 1 mm Hg ≈ 0.133 kPa)

Study	Species or subjects	Exposures	Measures of effect	Results	Comments
Nerve compression studies					
Lundborg (15)	218 rabbits (tibial and sciatic nerve)	Ischemia, ischemia + compression induced by a pneumatic cuff (mean intraneural pressure 141 mm Hg) for 2, 4, 6, 8, 10, 12 hours	Permeability of intraneural vessels, deterioration of nerve function (AMP, maximal NCV), histological findings immediately and hours and days postinjury	Ischemia: 6 hours → permeability ↑ in peri- and epineurium, 8 hours → permeability ↑ also in endoneurium, 10—12 hours → more intensive findings; release of cuff after ischemia: ischemia for 2 to 4 hours → AMP and NCV normalized within minutes, ischemia for 6 hours → almost full recovery, ischemia for 8 hours → poor recovery, ischemia for 10 hours → no recovery. Ischemia+compression: 2 hours → permeability ↑ slightly in peri- and epineurium, 4 hours → permeability ↑ also in endoneurium; release of the cuff: compression for 2 hours → minimal return of nerve function, compression for 4 and 6 hours → no recovery; long-term follow-up: compression for 4—6 hours → degeneration of distal nerve segment	Compression from pneumatic cuff of great significance for the occurrence of neuromuscular injury. Restitution of blood flow after only ischemia provides a wide margin of safety. Endothelial cells of endoneurial microvessels resistant to ischemia. Development of endoneurial edema might interfere with postischemic recovery of nerve function
Ochoa et al (23)	16 female baboons (medial popliteal nerve)	Compression induced by a 5.5 cm broad pneumatic cuff around the knee using 500 and 1000 mm Hg pressure for 1—3 hours	Ultrastructural changes in nerve fibers 2—3 minutes to 6 months after compression	Primary lesion displacement of the node of Ranvier from its usual place under the Schwann cell junction, accompanied by stretching of the paranodal myelin on one side of the node and invagination of the paranodal myelin on the other; changes were maximal under the edges of the cuff and seen only in larger myelinated fibers. Paranodal demyelination seen after 1 and 2 weeks and, for longer durations of 1000 mm Hg compression, Wallerian degeneration. Remyelination after several weeks.	Pressure gradient between the compressed and non-compressed part of the nerve may account for the nodal displacement. Intramyelin and periaxonal edema may account for delayed recovery
Rydevik & Lundborg (24)	78 rabbits (tibial nerve)	Local compression of 50, 200, 400, 600 mm Hg for 15 minutes to 6 hours by compression chamber	Intraneural edema shortly after pressurization and after 3 to 7 days	Results shortly after pressurization: 50 mm Hg for 2 hours → epineurial edema, 50 mm Hg for 4—6 hours → endoneurial edema at edges of compressed zone, 200 mm Hg for <4 hours → marked epineurial edema and endoneurial edema at edges of compression segment, 200 mm Hg for 4—6 hours → endoneurial edema throughout compressed segment, 400 mm Hg for 15 minutes → endoneurial edema at edges of cuff, 400 mm Hg for 2 hours → more marked endoneurial edema at edges of cuff; no changes in perineurium at any of the pressure levels; results 3—7 days after pressurization: swelling of compressed nerves, incomplete perfusion of endoneurial microvessels, epineurial and endoneurial edema, intact perineurium	Vascular findings beneath edges of cuff more sensitive to pressure level, and vascular injury at the center of the compressed segment more sensitive to the duration of compression. Maximization of injury beneath the edges of the cuff probably a result of special physical forces acting on the nerve, resulting in intraneural shear stresses

(continued)

Table 1. Contiunued.

Study	Species or subjects	Exposures	Measures of effect	Results	Comments
Hargens et al (25)	Anterolateral muscle compartment of hind limb of 22 dogs	Elevation of intra-compartmental pressure by autologous plasma infusion to 10, 20, 30, 40, 50, 60, 80, 100, 120 mm Hg for 8 hours (except 40 mm Hg for 14 hours)	Peroneal nerve function (NCV and AMP) from extensor digitorum brevis muscle); histology of peroneal nerve by light and electron microscopy	NCV: 10—20 mm Hg → no effect, 30—40 mm Hg → NCV ↓, 50—120 mm Hg → complete conduction block; time required inversely related to pressure level (for 80—120 mm Hg <2 hours); AMP: 10—20 mm Hg → no effect, 30—120 mm Hg → amplitude ↓; time required depending on pressure level (with 120 mm Hg no amplitude after 70 minutes); recovery of impulse transmission possible after pressure of 120 mm Hg for 55—60 minutes, but not if kept for 8 hours; histology: ≥60 mm Hg → severe loss of large myelinated fibers within nerve fascicles 3 weeks after pressurization ≥100 mm Hg → various stages of axonal degeneration and demyelination	Lack of immediate recovery suggests high intermittent pressures over prolonged periods (days, weeks, months, years) may lead to nerve damage
Rydevik et al (26)	22 rabbit tibial nerves	Local compression of 10, 20, 30, 40, 50, 60, 70, 80 mm Hg until cessation of circulation (last pressure kept for 2 hours): few exposed to 400 mm Hg for 2 hours and examined after 3 to 7 days	Intraneural blood flow in vivo (vital microscopic technique)	20—30 mm Hg → retardation of venular flow, 40—50 mm Hg → impaired arteriolar and intrafascicular capillary flow, 60—80 mm Hg → complete ischemia; upon release of compression after 2 hours, return of circulation within first minute, intra-neural edema, 400 mm Hg → persistent impairment of intraneural circulation	That complete ischemia did not occur before 60—80 mm Hg of pressure was applied may be due to 2 reasons: (i) slightly elevated pressure within the edno-neurium and negative pressure in the muscle or subcutaneus tissue, resulting in outwardly directed net pressure gradient and (ii) possible capacity of large epineurial arterioles to supply blood with high pressures
Lundborg et al (27)	12 rat sciatic nerves	Local compression of 30 and 80 mm Hg for 2, 4, 6, and 8 hours by compression chamber	Endoneurial fluid pressure by micro-pipette techniques 1 or 24 hours post-operatively, histo-logical analysis	30 mm Hg 4 hours → endoneurial pressure ↑, 30 mm Hg 8 hours → maximal endoneurial pressure, 80 mm Hg 2 hours → endoneurial pressure ↑, 80 mm Hg 4 hours → maximal endoneurial pressure, severity of endoneurial edema in correlation with endoneurial pressure	Blood-nerve barrier in the endothelium of the endoneurial vessels and perineurium protect endoneurium from edema
Gelberman et al (28)	10 healthy human volunteers	Elevated CTP of 40, 50, 60, and 70 mm Hg for 30—240 minutes by external com-pression (measured by wick catheter)	Median sensory and motor AMP, sensory and motor DL during compression and at 2- to 5-minute intervals after compression; symptoms at 10-minute intervals; neurological examination at 5-minute intervals	40 mm Hg → sensory and motor AMP ↓, sensory and motor DL ↑, numbness, after 240 minutes altered vibratory perception; upon release of compression immediate return of nerve function, 50 mm Hg → sensory and motor AMP ↓ and disappeared within 15—40 minutes for most subjects, sensory and motor DL ↑ following sensory and motor AMP ↓, paresthesia, altered vibratory sensation, 2-point and moving 2-point discrimination, and Semmes-Weinstein monofilament test abnormal (paresthesia first symptom in 15 minutes), strength of abductor pollicis brevis muscle ↓ later, 60—70 mm Hg → similar findings to those above	50 mm Hg threshold pressure at which nerve viability is acutely jeopardized in normotensive persons

(contiuned)

Table 1. Continued.

Study	Species or subjects	Exposures	Measures of effect	Results	Comments
Powell & Myers (29)	91 rat sciatic nerves	External compression of 10, 30, and 80 mm Hg for 2 hours	Histology by light and electron microscopy at 4 and 24 hours, and at 2, 5, 6, 7, 10, 14, and 28 days (10 and 30 mm Hg analyzed only at days 5, 6, and 7)	30 mm Hg → demyelination primarily subperineurially, axonal degeneration infrequent, 10 mm Hg → as above, but occasionally, 80 mm Hg → edema within 4 hours and throughout study period, most pronounced in the subperineurial space, severity in correlation with axonal damage. Proliferation of fibrous tissue in days, marked epineurial fibrosis at 28 days. Swelling of axons at 24 hours and 2 days, axonal degeneration at 10,14, and 28 days. Macrophages in endoneurium at 28 days, disintegration of myelin at 5 to 7 days, demyelination at 7 to 10 days, remyelination at 14 to 28 days	Schwann cell degeneration and disintegration of myelin sheath considered as mechanism for demyelination. Fewer degrees of compression sufficient to cause demyelination and higher level needed for axonal degeneration
Dahlin & McLean (30)	26 rabbit vagus nerves	External compression of 20 and 30 mm Hg for 8 hours	Electrophoretic analysis of transported axonal proteins at the end of experiment	20 mm Hg → fast axonal transport partially inhibited in some nerves, no effect on slow axonal transport, 30 mm Hg → slow axonal markedly inhibited transport	Both slow and fast axonal transportation inhibited at relatively low levels of compression. Impaired provision of cytoskeletal elements to distal axon may be of significance in nerve entrapment syndromes
Sommer et al (31)	50 rat sciatic nerves	Local compression by 4 slightly constrictive ligatures 1 mm apart from each other	Thermal hyperesthesia every second day up to two weeks and then weekly, guarding of hindfoot, histology of nerve at day 1, 3, 5, 7, 9, 11, 28, 42, and 84 (light and electron microscopy)	Hyperesthesia present from day 1—3 onwards, maximal between 7—15 days, gone by 6 weeks; guarding of the foot similar time course; light microscopy findings: day 1: marked edema, axons of myelinated fibers swollen, myelin sheaths disintergrated, unmyelinated fibers normal, granulocytes and mononuclear cells in epineurial vessels, day 3 and 5: as above but more marked findings, perineurial layer separated by edema. Under ligature all large myelinated fibers damaged, and some distal to ligatures, subperineurial layer more severely affected than center of fascicle, 1 week: number of fibroblasts increased, macrophages throughout the endoneurium, sprouting axons without myelin subperineurially, Wallerian degeneration in the center of fascicles, 2 weeks: edema reduced, sub-perineurial nerve fibers under ligatures thinly remyelinated, 6 weeks: proximal portions close to ligatures returned to normal, 12 weeks: remyelination reached distal nerve segments; electron microscopic findings confirmed those obtained by light microscopy	Sequence of pathophysiological events: venous stasis, edema, acute fiber degeneration, macrophage influx and cytokine production, disruption of perineurium, nerve fiber regeneration
Szabo & Sharkey (32)	49 rat tibial nerves	Constant and cyclic local compression by compression chamber for 6 hours or until conduction block: constant compression of 0, 30, 60, and 90 mm Hg; cyclic compression between 0—30, 20—50, and 30—60 mm Hg, sawtooth waveform at 1 Hz	AMP and NVC every 15 minutes	Constant compression: 60 and 90 mm Hg → conduction block after 150 min, 30 mm Hg → AMP 18% of initial value, NVC 90% of initial value after 6 hours of compression; cyclic compression: 0—30 mm Hg → AMP ↓ gradually and the decrease was less than for 30 mm Hg constant compression, NVC 88% of initial after 6 hours, 20—50 mm Hg → similar effects as for 30 mm Hg of constant compression, 30—60 mm Hg → AMP ↓ more than for 30 mm Hg but less than for 60 mm Hg of constant compression, NCV similar to that for 20—50 mm Hg	The effects of cyclic compression on nerve conduction seem to be equivalent to the effects of constant compression at the average applied pressure. Cyclic loading does not appear to be an important pathogenetic factor in the development of nerve conduction block

(continued)

Table 1. Continued.

Study	Species or subjects	Exposures	Measures of effect	Results	Comments
Repetitive contraction studies					
Andersson (33)	235 rabbit carpal tunnels	10 hours of electrically induced flexion-extension contractions at the radiocarpal joint with a rate of 80/min (with intact and cut transverse carpal ligament)	Water content and morphological examination immediately and 18, 48, 72, and 96 hours postexercise, motor latency over the radiocarpal joint at 18, 72 and 96 hours postexercise	Water content of carpal tunnel tissues: maximal immediately after experiment until 18 hours postexercise, gone by 96 hours postexercise (intact and cut transverse carpal-ligament); morphological examination showed a reduction in the number of large nerve fibers; motor latency ↓ at 18 and 72 hours, but not at 96 hours; decreased motor latency found only with intact transverse carpal ligament	Changes in median nerve function considered an effect of increased CTP resulting from repeated muscular contractions. Intact transverse carpal ligament required to bring about changes in nerve conduction
Vibration studies					
Lundborg et al (34)	10 rats	Vibration (82 Hz, peak to peak amplitude 0.21 mm) induced in 1 hind limb during 4 hours/day for 4 days	Permeability of intraneural microvessels by light microscopy and fluorescence microscopy	Increased permeability and edema in the epineurium but not in the endoneurium	Epineurial edema an early stage change after vibration exposure. The blood-brain barrier of the endothelial cells of the endoneurial capillaries and the diffusion barrier of the perineurium protect the nerve fascicles in the endoneurium
Ho & Yu (35)	20 rabbits, saphenous and median nerves	Vibration (60 Hz, 0.35 mm amplitude, 51 m/s^2) induced during 2 hours daily for 6 days per week to all legs. Total vibration dose 150, 250, 450, and 600 hours	Changes in electron microscopy, diameters of nerve fibers, myelin disruption	Disruption of myelin sheath and constriction of the axon, accumulation of vacuoles in the nodal gap and paranodal region, disorganization of the paranodal end loops and detachment of the end loops from the axolemma, dilation and increased density of SLIs, disappearance of neurotubules and neurofilaments in axons; the extent of myelin disruption proportional to vibration dose; disrupted fibers 2—12 μm in diameter, corresponding to many types of sensory and A α and A γ motor fibers	Destruction of myelin an early finding and precedes that of axon; dilation and increased density of SLI and disruption of peri-incisural myelin represent early phase of Wallerian degeneration
Lundborg et al (36)	34 rats, plantar and sciatic nerves	Vibration (82 Hz, 0.21 mm amplitude) for 4 hours on 5 days	Changes in light and electron microscopy, immediately and 2 and 4 weeks postexposure	No changes seen in light microscopy; immediately after exposure: electron microscopy of nonmyelinated fibers in the plantar nerves showed deranged axoplasmic structure or accumulation of smooth axoplasmic reticulum; at 2 weeks: slight changes; at 4 weeks: no changes; no changes in the sciatic nerve	Since the injury was seen primarily in nonmyelinated fibers, and since sympathetic activity is mediated by thin nonmyelinated fibers, disturbed sympathetic function (eg, instability in the regulation of microvascular flow) may be induced as a result of vibration
Chang et al (37)	36 rat tails	Vibration (60 Hz, amplitude 0.4 mm, 56.9 m/s^2) induced in rat tail for 2 or 4 hours/day, 6 days/week. Total vibration dose 200, 500, and 800 hours	Maximum MCV, AMP of evoked response, and MDL of the tail nerve every 2 months, histological findings by electron microscopy	MCV ↓ after 4 (4 h/day) and 8 (2h/day) months; no clear change in AMP of evoked response; MDL ↑ after 6 months (4 h/day); AMP ↓ after 8 months; histology: 200 hours of vibration → slight disruption of myelin sheath and detachment of sheath from the axon, slight changes in the node of Ranvier; 500 hours of vibration → myelin sheaths disrupted along SLIs, detached clearly from axolemma and protruded into the axons, vacuoles accumulated in Ranvier nodal gap; 800 hours of vibration → part of myelin sheaths disrupted, part of axons destroyed	MCV ↓, reflecting disruption of myelin sheaths the first change, MDL ↑ a later finding, AMP ↓, reflecting degeneration of the axon seen only at the end of the experiment
Strömberg et al (38)	10 male patients exposed to vibration undergoing wrist denervation, 12 male cadaver referents of similar age	Exposure to vibration (median length 25.5 years) from various tools	Histological findings in dorsal interosseus nerve biopsies 5 cm proximal to the wrist	Light microscopy showed changes in 9 patients (slight in 2 and moderately severe in 7); endoneurial fibrosis of varying degree present in all 9, lipid deposition and loss of myelin and a reduced number of myelin sheaths in 6; similar changes found in one control patient whose history revealed Raynaud's symptoms	The results of having neural effects of vibration above the level of carpal tunnel suggest that vibration may induce effects on nerves in the carpal tunnel

kPa) compression for 4 hours resulted in slight changes in nerve function, mild symptoms, and an altered vibratory perception (28).

Experimentally induced vibration causes epineurial edema as the first change within days (34). According to Lundborg, this first change is similar for mechanical, ischemic, and chemical trauma, and endoneurial edema is a later finding. Early-stage ultrastructural changes consist of deranged axoplasmic structure or accumulation of smooth axoplasmic reticulum that have been reversible in animal models after a short duration of vibration exposure. These ultrastructural changes were first seen in unmyelinated fibers. Since sympathetic activity is mediated by thin unmyelinated fibers, disturbed sympathetic function may result in disturbance in the regulation of microvascular flow. Later changes associated with vibration exposure are disruption of the myelin sheath simultaneously with decreased motor conduction velocity and several changes at the nodes of Ranvier reflected as prolonged motor distal latency (37). Axonal degeneration has been seen after several months of exposure in animal studies (35, 37).

In humans, a 32-minute period of hand-arm vibration leads to a temporary threshold shift of the vibration perception threshold in fingers concurrently with paresthesia and numbness (39). Ultrastructural changes similar to those seen in animals have been seen in the nerves of the fingers of subjects with long-term vibration exposure (40), but also more proximally in the upper extremity in the dorsal interosseus nerve in the distal forearm (38). The latter finding suggests that changes could be induced also in the median nerve in the carpal tunnel.

The tonic vibration reflex is a gradually increasing involuntary contraction that results in either slow joint movement or increases in active tension. When it is superimposed on a voluntary contraction, as in holding a tool, increased forceful exertion results (41, 42).

In principal, CTS in association with the use of vibrating hand-held tools could be a result of effects of vibration on the median nerve at the carpal tunnel, and effects of sustained forceful gripping of the tool with the hand. The tonic vibration reflex and tactile disturbances as a possible effect of vibration tend to increase the force of gripping the tool.

Contact stresses have been poorly quantified in experimental studies. In the study of Ochoa et al (23), in which nerve compression was induced by a pneumatic cuff, the displacement of the nodes of Ranvier was the most severe under the edges of the cuff. Also in the study of Rydevik & Lundborg (24), in which local compression was induced by a compression chamber, intraneural edema appeared earlier and was later more severe beneath the edges of the chamber. The authors suggested that the maximization of injury beneath the edges of the cuff is probably a result of special physical forces acting on the nerve and resulting in intraneural shear stresses. The role of contact stresses in the etiology of nerve injury in compression neuropathies has been stressed by other authors also (29, 43). Besides mediating destruction of Schwann cells and decreased axonal transport, contact stresses may also mediate localized ischemic changes.

From their results of median nerve excursion and strain during active finger flexion in different postures of the wrist, Bay et al (22) emphasized the potential role of stretch of the median nerve as a pathomechanical cofactor in CTS. The nerve can be stretched as a result of elongation of the nerve bed in wrist extension or as a result of interaction with adjacent structures by means of frictional forces or fascial or fascicular tethering.

Risk factors for carpal tunnel syndrome

The studies on physical load factors with respect to CTS have been grouped into those on posture, force, repetition, external pressure, and vibration. This distinction presents problems in the analysis of many epidemiologic studies because they have often addressed combinations of these factors. The distinction is, in our opinion, however, appropriate to be able to reveal maximal information as the basis for prevention.

Under each physical load factor, we start our review with selected epidemiologic studies, with an emphasis on the results concerning exposure-response relationships between the physical load factor and CTS. In some of the experimental studies the changes in CTP have been measured in healthy volunteers under different loading situations. Some psychophysical studies are briefly reviewed in order to see whether the critical levels of exposure correspond to those from other types of studies. The few experimental studies on CTP changes under different loading situations using CTS patient populations have been included to understand any special characteristics in response to loading in association with the disease. Finally, some cadaver studies are reviewed to learn about the responses of CTP to loading and to study the dynamics of the structures in the carpal tunnel.

Posture

Epidemiologic studies. The review published by the National Institute for Occupational Safety and Health (NIOSH) (10) on epidemiologic evidence of the work-relatedness of physical load factors and carpal tunnel syndrome concluded that there was insufficient evidence for "nonneutral postures" to be an independent risk factor for CTS. In combination with other factors of physical load a causal relationship was established.

The duration of nonneutral wrist postures has shown an exposure-response relationship with CTS in 2

population studies. DeKrom et al (44) performed a case-referent study with the case definition based on clinical and electrodiagnostic assessment and exposure assessment based on subjective assessment. The odds of being a case increased significantly with increasing exposure (hours per week) to wrist extension or wrist flexion, but not to pinching or typing. In another case-referent study, by Nordstrom et al (45), case definition was based on the results of a clinical examination, and exposure was assessed by a telephone interview. The authors found a significant quadratic dose-response relationship for hours per day of bending or twisting hands or wrists. The questions on the duration of the nonneutral postures were not validated in either of the studies, and it is therefore not known how well the reported durations of postures correspond to the actual durations.

In a retrospective study among slaughterhouse and chemical workers, slaughterhouse workers, especially deboners, showed a clearly higher risk of electrodiagnostically confirmed CTS than the chemical workers (46). The work analysis of the deboners showed 4.8—6.3 nonneutral postures of the dominant hand per minute, and they spent 18—28% of the time with the dominant hand in a nonneutral posture while deboning. Unfortunately, the corresponding physical load factors were not assessed for the referents.

In a small case-referent study by Armstrong & Chaffin (47), the cases (18 sewing-machine operators) with a history of clinically defined CTS were compared with nonsymptomatic referents with the same occupation. Cinematographic assessments of posture and electromyographic (EMG) estimations of forearm flexor force showed that the cases tended to use pinch grip and exerted more force in the pinch grip than the referents did. They also tended to use nonneutral wrist postures more often and exerted more force in these postures than the referents did.

In a magnetic resonance imaging and electrophysiological study of the carpal tunnel region in 24 female floor cleaners compared with 19 female office worker referents, Pierre-Jerome et al (48) reported similar carpal tunnel volumes between the 2 groups but a slightly more intense signal of the median nerve (P=0.05), longer mean motor latencies (P=0.03), and lower sensory amplitudes (P=0.01) in the cleaners than in the referents. While the authors noted no significant correlation between the magnetic resonance and electrophysiological parameters and no significant effects of age, height or years of work, they interpreted their findings as suggesting repetitive flexion-extension in mopping leading to higher intermittent CTP values and concomitant nerve damage. The authors reported no level, frequency, or duration of repetitive flexion-extension. The lack of effect of years as a cleaner may have been due to the misclassification of exposure duration, frequency, or intensity.

Studies on healthy subjects. Some researchers investigated different postural loads on CTP (table 2) (49—58). Ham et al (49) used magnetic resonance imaging to assess changes in the carpal tunnel due to the action of the flexor tendons in 12 healthy volunteers. Going from full finger extension to finger flexion, the lumbrical muscles moved into the carpal tunnel, expanding the tunnel to different degrees (range 21—30 mm^2). The tunnel expanded more the closer the lumbricals came from distal to proximal to the hamate, when compared with full extension. Flattening of the median nerve and fat compression was observed in all 12 subjects when the lumbricals were present in the carpal tunnel.

Werner et al (50) found that wrist extension and flexion resulted in the greatest increase in CTP, followed by forearm pronation and supination. Radial and ulnar deviation and hand posture had smaller effects. The comparison of multiple linear regression models showed that the subject-to-subject variability made the largest contribution to the variance.

Rempel et al (51, 52) conducted some carefully executed in vivo laboratory studies looking at the effect of different postures, sometimes in combination with loads and frequencies, on CTP. The underlying assumption of these studies was that a persistent elevation in CTP

Table 2. Experimental studies on posture. (MRI = magnetic resonance imaging, CTS = canal tunnel syndrome, CTP = carpal tunnel pressure, ANOVA = analysis of variance, MCP = metacarpophalangeal, EDS = electrodiagnostic studies, → = leading to, 1 mm Hg ≈ 0.133 kPa)

Study	Species or subjects	Exposures	Measures of effect	Results	Comments
Studies on healthy subjects					
Ham et al (49)	12 healthy humans	Full finger flexion to extension	MRI to assess change in tunnel size	Range from 21—30 mm^2 depending on how close the lumbricals came from distal to proximal to the hamate. Nerve flattening when lumbricals in the tunnel	Relationship of size and volume to CTS is unclear. Finger flexion may increase pressure due to presence of lumbricals in the tunnel

(continued)

Table 2. Continued.

Study	Species or subjects	Exposures	Measures of effect	Results	Comments
Werner et al (50)	7 healthy humans	Flexion/extension, ulnar/radial deviation, supination/pronation, fist, pinch, extended fingers	CTP	Greatest increase in CTP with wrist extension or flexion, followed by pronation or supination	Large variation between subjects
Rempel et al (51)	17 healthy humans	Forearm position combined with MCP flexion	CTP	Full MCP flexion + full supination → 55 mm Hg; all ranges of MCP flexion combined with 45 degrees pronation had lowest CTP; nonadditive interactions between forearm posture and MCP flexion	Suggest 45 degrees of MCP flexion and pronation should be considered in tool design
Keir et al (52)	14 healthy humans	Wrist flexion/extension and MCP joint angle; ulnar/radial deviation	CTP, repeated measures ANOVA	Significant interaction between flexion/extension and MCP angle. Wrist extension (40 degrees)+finger extension (MCP=0) had greatest effect	Flexor belly activity in the tunnel may contribute to higher pressures, entering at about 30 degrees of extension
Clinical studies					
Gelberman et al (53)	15 CTS patients, 12 referents, mean age 56	Wrist flexion	CTP	Patient CTPs averaged 32 mm Hg (SD 3.8, range 2—50) with neutral wrist. Maximum wrist flexion → 94 mm Hg in patients and extension → 110 mm Hg. Immediately postoperatively mean CTP 5 mm Hg and 2 months postoperatively 3.5 mm Hg (7 patients). Referents (2.5 mm Hg in neutral) → 31mm Hg in flexion, 30 mm Hg in extension	
Werner et al (54)	CTS patients undergoing release	Finger flexion, wrist extension/flexion	CTP	CTP values higher with straight fingers than with flexed fingers with wrist flexion; wrist extension → higher CTP but finger extension did not significantly increase CTP; provoked isometric and isotonic contractions significantly increased CTP; more abnormal EDS → more elevated CTP	No comparison group
Okutsu et al (55)	46 CTS patients pre/post endoscopic surgery, 16 referents	Maximum passive flexion/extension, active grip	CTP	Preoperative nonresting or nonneutral postures in patients → 5 times greater CTPs than neutral resting postures, passive extension was the highest; postrelease dramatic reductions in all CTPs but passive flexion CTP greater than extension and both greater than 10 times the resting CTP. Postsurgical CTPs less than referents' for all positions	
Szabo & Chidgey (56)	22 CTS patients (5 advanced CTS), 6 referents	Maximum passive flexion/extension, repetitive passive flexion/extension 30 times per minute for 1 minute	CTP	CTP values in neutral or flexion did not differ between patients and referents but were higher in extension. Mild or moderate CTS patients differed significantly from referents in all postures but there was no difference between severe cases and referents	9 patients had other associated conditions; CTP level does not appear to be an indicator of increasing severity of CTS
Cadaver studies					
Cobb et al (57)	Series of cadaver studies with 5 cadavers	Lumbricals intact and then excised; 1kg loads on flexor tendons, with different degrees of finger flexion	CTP	Pressures increased progressively from finger extension to flexion (cumulative increase of 62mm Hg); removal of lumbricals → CTP no longer significantly different based on finger flexion angle; fist had greater CTP than other postures	Authors speculate that manual workers have lumbrical hypertrophy which increases CTP (report no studies demonstrating hypertrophy in manual workers)
Kang et al (58)	6 fresh frozen cadavers	Wrist flexion	Tendon excursion	Tendon excursion, load, efficiency before and after cutting ligament → in wrist flexion smallest mean cross-sectional area of carpal tunnel because of volar shift of tendons and pressure on ligament. When ligament was cut → increased space but more bowstringing of tendons, less frictional forces. In flexion → weakening of finger flexion, increased tendon excursion. Demonstrated transverse carpal ligament is a true A0 pulley	Supports work of Armstrong & Chaffin that increased pressure on median nerve is function of tendons wrapped around carpal bones in extension or of transverse carpal ligament in flexion

causes or aggravates CTS. The highest pressures were observed at full metacarpophalangeal (MCP) flexion with full supination of the forearm (55 mm Hg, 7.3 kPa), although with no MCP flexion, the mean pressure was 54 mm Hg (7.2 kPa). The lowest pressures were achieved at all MCP angles with 45 degrees of pronation. There were significant nonadditive interactions between MCP and forearm position with CTP. The authors speculated that the increased pressure had something to do with the orientation of the tendons as they pass through a tunnel that alters volume or that the shape of the space changes. The role of the lumbricals with MCP flexion is consistent with the findings of Ham et al (49), but it does not explain the increase seen with extension. The authors suggested that the lowest pressures achieved at 45 degrees of pronation and 45 degrees of MCP flexion should be considered in job and tool design.

Keir et al (52) found wrist angle, MCP angle, and the interaction between these 2 to be significant predictors of CTP. Finger extension (MCP joint angle of 0 degrees) induced greater pressures than MCP flexion for wrist extension and up to 10 degrees of wrist flexion. The highest pressures were with 40 degrees of wrist extension and 0 degrees of MCP flexion. The authors suggested that flexor belly movement into the tunnel may account for the results. They tested the possibility of this explanation using the lumbrical excursion data from Cobb et al (57) and the tendon excursion regression equations of Armstrong & Chaffin (16). The extrinsic flexor belly can enter the carpal tunnel at about 30 degrees of extension, acting opposite of the lumbricals. A recent cadaver study investigated the relationships of the flexor digitorum profundus and flexor digitorum superficialis muscles with the proximal limit of the carpal tunnel. The results showed that 46% of the women and 8% of the men had the muscle bellies in the tunnel (59).

Clinical studies. Gelberman et al (53) reported the CTP values of 15 CTS patients to average 32 mm Hg (4.3 kPa), with those of 12 referents averaging 2.5 mm Hg (0.3 kPa). The average CTP values of the patients in maximum flexion and extension were 3-fold those of the referents. Immediately and 2 months postoperatively the values of the patients in the neutral posture were close to those of the referents.

Werner et al (54) studied CTS patients undergoing surgical release. For these patients, the CTP values were higher with straight fingers than with flexed fingers with wrist flexion. Overall the wrist extension CTP values were higher than with flexion, but straight fingers did not appear to increase the pressure substantially when compared with flexed fingers. There were dramatic increases in pressure over resting pressures when the nerve stimulator provoked isometric contractions and isotonic contractions. Pressure increased as the muscle contraction became stronger. Furthermore, these investigators demonstrated, at least for the CTS patients, that the more abnormal the electrophysiological tests, the higher the CTP values.

Okutsu et al (55) studied the CTP values of 46 CTS patients before and after endoscopic surgery and compared them with the pressures of 16 referents. The cases were diagnosed according to clinical signs and distal sensory latencies of more than 3.5 milliseconds or motor latencies of more than 4.5 milliseconds. Preoperative nonresting or nonneutral postures of the CTS patients resulted in significantly greater CTP values than neutral resting posture (approximately 5 times greater), with passive extension having the highest CTP. After the surgical procedure, there were dramatic reductions in all the CTP values. However, passive flexion had a slightly higher CTP than extension, and both were more than 10 times the resting neutral posture pressure of 6.2 (SD 5.5) mm Hg [0.8 (SD 0.7) kPa]. The postsurgical CTP values were lower than the reference group pressures for all positions.

Szabo & Chidgey (56) measured the CTP with a slit catheter preoperatively in 22 patients with clinically and electrodiagnostically confirmed CTS and also in 6 referents. Nine of the patients had other medical conditions associated with CTS. Five patients had advanced CTS and 17 an early or intermediate stage of CTS. Pressures were measured at rest in neutral and in maximum passive flexion and extension. The wrist was then repetitively passively flexed and extended to maximum position at a rate of 30 full cycles per minute for 1 minute. The CTP of the entire group of patients did not differ from that of the referents in the neutral posture or in flexion, whereas in extension the pressure was higher in the patients than in the referents. When the 17 patients with early or intermediate CTS were compared with the referents, there was a difference for all 3 postures at rest. Immediately postexercise, and also 10 minutes after the exercise, the pressures in the early and intermediate CTS patients were higher than those of the referents, and also higher than the pressures of the same group of patients at rest. The pressures of the patients with advanced CTS and the referents immediately after and 10 minutes after the exercise did not differ from their values at rest.

The pressure elevations at rest and during flexion and extension agreed with the results of other studies on patient populations (53—55). The more interesting result with regard to the understanding of the development of CTS was the sustained elevation of CTP after the relatively short flexion-extension exercise of 1 minute. The authors speculated that this latter result suggests that the dynamics of the carpal tunnel are similar to those in a closed compartment.

Cadaver studies. Cobb et al (57) conducted cadaver studies to assess the impact of the lumbrical muscles on CTP

while the fingers are flexed 100% (a tight fist), 75% (fingertips to thumb web space), 50% (distal fingertips even with distal palm), and full extension. To ensure that the flexor tendons remained taut (simulating active flexion) during the experiment, 1-kg weights were applied. The hook of the hamate was used as the reference point for the distal end of the transverse carpal ligament. After measuring pressures with the lumbricals intact, they were excised and the flexion-extension pressures were measured again. In all the specimens, the pressures increased progressively from extension to 100% flexion with the lumbricals in place. The cumulative mean increase was 62 mm Hg (8.3 kPa). When the lumbricals were removed, the CTP was no longer significantly different for the different finger positions. Pressures recorded with 100% fist position were significantly greater than for other positions (probably due to the small sample size, 5 cadavers). The possible role of manual work in causing lumbrical hypertrophy and thereby increasing CTP was suggested by the authors and has been proposed also by other researchers (60).

Kang et al (58) used 6 fresh-frozen cadaver hands to investigate the effect of wrist position, transverse carpal ligament, and palmar fascia on the biomechanics of finger flexion. These researchers demonstrated the importance of the transverse carpal ligament as a true A0 pulley by comparing tendon excursion, load, and efficiency before and after the ligament was cut. Wrist flexion resulted in the smallest mean cross-sectional area of the carpal tunnel because of the volar shift of the tendons and their pressure on the ligament. While cutting the ligament increased the space, there was more bowstringing of the tendons and decreased work requirements (due to less frictional forces). In flexion, there was a weakening of finger flexion and increased tendon excursion not seen in either neutral or extended wrist postures. This study supports the work of Armstrong & Chaffin (16), who described the increase in pressure on the median nerve as a function of the tendons wrapped around the carpal bones in extension or transverse carpal ligament in flexion.

Summary of studies on posture. Forearm pronation-supination, wrist deviation, and MCP and finger flexion all affect CTP. Forearm pronation-supination angle and MCP angle and wrist flexion-extension angle and MCP angle have significant interactions. Interactions between other combinations of joint postures are likely but have not been adequately addressed.

The CTP appears to be lowest at 45 degrees of pronation and 45 degrees of MCP joint flexion. Upon MCP flexion the CTP increases as a result of lumbrical muscle excursion into the carpal tunnel. Both wrist flexion and extension increase the CTP. The pressure in wrist extension is higher with the fingers in extension than in flexion, the highest pressures being obtained for 40 degrees of wrist extension with straight fingers. The excursion of the extrinsic finger flexor muscle belly into the carpal tunnel is a possible factor contributing to the pressure increase in wrist and finger extension. In extreme wrist flexion the carpal tunnel area is reduced and the median nerve is compressed against the transverse carpal ligament. Clinical studies among patients show high CTP values during wrist flexion and extension. The study of Szabo & Chidgey (56) suggested a sustained pressure increase after repeated wrist flexion and extension among patients with early or intermediate CTS, the mechanism of which is not easy to explain.

According to experimental studies, forearm, wrist and finger postures are a powerful predictor of CTP and contact stress. If it is assumed that an elevated CTP and high contact stresses are an important pathomechanical step in the development of CTS, postural factors should be considered important risk factors.

The results of experimental studies on wrist postures support the results from epidemiologic studies. Some epidemiologic studies suggest that the duration of wrist flexion and extension may have importance with regard to the development of the disease. The lack of validation of the used questions and likely overestimates of exposure duration in these epidemiologic studies hinder the use of these data as reference values for being confident about safe levels of exposure.

Pinch grip has been discussed in association with force.

Force

Epidemiologic studies. The NIOSH review (10) concluded that there is evidence of a positive association between forceful work and CTS, and strong evidence of a positive association between exposure to a combination of risk factors (eg, force and repetition, force and posture) and CTS.

Silverstein et al (61) studied 652 industrial workers and classified their jobs into the following 4 categories of repetition and force: low-force + low-repetition (group 1), high-force + low-repetition (group 2), low-force + high-repetition (group 3), and high-force + high-repetition (group 4). The classification was based on a walk-through survey, and force was validated against EMG estimations of forearm flexor force requirements. A mean adjusted force exceeding 6 kg was considered high force. The diagnosis of CTS was based on a physical examination. The prevalences of CTS were 0.6%, 1.0%, 2.1%, and 5.6% in groups 1 to 4, respectively. The odds ratio for group 2 versus group 1 was 1.8 and nonsignificant, and the odds ratio for group 4 versus group 1 was 15.5 [95% confidence interval (95% CI) 1.7—142]. In a separate logistic model the odds ratio for force was 2.9 and nonsignificant.

Chiang et al (62) studied 207 fish-processing workers using a classification similar to that of jobs by Silverstein et al (61), except that groups 2 and 3 were combined as a high-force or high-repetition group. Using less strict criteria based on a physical examination than was the case with Silverstein et al, they found the prevalences of CTS to be 8.2%, 15.3%, and 28.6% in the 3 groups. In a separate model the odds ratio for force was 1.8 (95% CI 1.1—2.9).

Stetson et al (63) performed nerve conduction studies among 240 industrial workers (78% men) in the automotive industry, 103 with pain, numbness, or tingling in the hand or volar wrist ("symptomatic hand population") and 137 asymptomatic workers. The referents were 105 subjects (59% men) employed in administrative and professional positions. The jobs of the industrial population were evaluated by observation and interview with the use of a checklist. The risk factors in the checklist consisted of repetitiveness (work cycle <30 seconds or >½ cycle spent repeating same exertions), force [carry an object weighing >10 pounds (>4.5 kg), hold an object weighing >6 pounds (>2.7 kg) per hand], mechanical stress, and posture (pinch grip, wrist flexion, extension, or ulnar deviation). The median sensory amplitudes were statistically significantly smaller, and the motor and sensory distal latencies longer, in the industrial asymptomatic hand than in the reference population. Within the industrial population, the median sensory amplitudes were statistically significantly lower and the latencies longer for those exposed to high grip forces [both carry >10 pounds (>4.5 kg) and grip >6 pounds (>2.7 kg)] when compared with those without such exposure. Within the industrial population, the median sensory distal latencies were longer in the symptomatic hand group than among the asymptomatic workers. The longer sensory latencies are indicative of segmental demyelination, axonal stenosis, or conduction block of large diameter axons and smaller amplitudes of axonal degeneration, conduction block, or multifocal demyelination. The careful design of the study and the consideration of the most potential confounding factors suggest that the differences in nerve conduction measures are likely to reflect effects of physical loads. Yet, without a follow-up showing to what extent asymptomatic subjects with abnormal nerve conduction studies develop symptoms or a clinical stage of CTS, the significance of these findings remains partially unexplained. In another study, abnormal median sensory nerve conduction velocity in asymptomatic workers did not predict hand or finger complaints (64).

Studies on healthy subjects. Rempel et al (65) determined the relationship between fingertip loading and CTP among 15 healthy volunteers (8 women, 7 men, age 23—50 years, medical and electrodiagnostic examination normal). The subjects pressed a load cell (pinch meter) with the tip of the index finger at 0, 6, 9, and 12 N force for 2 seconds. The task was performed with the wrist in the neutral posture, 10 and 20 degrees of ulnar deviation, 10 degrees of radial deviation, and 15, 30 and 45 degrees of both flexion and extension. All the tasks were performed with the forearm in full pronation. The CTP values were measured with a saline-filled, blunt-tipped, multiperforated catheter connected to a pressure transducer.

The results showed that the CTP values increased with all the loads, and the increase was independent of the angle of the wrist. In the neutral posture, the relationship between CTP and fingertip load loosely fit the form of a second order polynomial. With the forces and postures of this study, finger force had greater effect than wrist angle on CTP.

As a possible mechanism behind the increase in CTP, the authors mentioned the migration of flexor tendons toward the transverse carpal ligament, which creates pressure gradients within the tunnel. The authors concluded that it is unlikely that relatively short periods with comparable loads have any adverse health effects but that, if such loads are sustained, an ischemic process may be initiated that triggers symptoms in patients with CTS, or initiates events leading to CTS.

Keir et al (66) studied CTP among 20 healthy subjects during pressing and pinching with the index finger with 0, 5, 10, and 15 N force with the forearm in 45-degree pronated posture. For both pressing and pinching, the CTP values increased almost linearly with increasing force, the pressures for pinching being almost 2-fold in comparison with those for pressing. It should be noted that upon pinching, a force of 5 N was sufficient to cause a CTP of 30 mm Hg (4.0 kPa), whereas the same level upon pressing required a force of 15 N.

The authors suggested that the linear relationship between force exertion and CTP is probably due to the posture of the forearm (45-degree pronation, posture with the lowest pressure in the carpal tunnel), in comparison with their earlier study (65), in which the forearm was in full pronation and the relationship between force and CTP was close to a second-order polynomial. The increase in CTP upon pinching is likely to be due to the exertion of the thumb (flexor pollicis longus and opponens pollicis) to counteract the pinching force of the index finger. The results have implications for task and tool design, where the force upon pinching should be minimized and attention should be paid to frequent pauses in work activities requiring pinching.

Cadaver studies. Smith et al (67) studied 8 cadaver forearm specimens. The median nerve was removed and replaced with compliant, water-filled cylindrical balloon transducers (long 4.5 cm and short 1.5 cm, diameter 3 mm). The short balloon was placed separately into the proximal and distal tunnel and under the distal

antebrachial fascia. Nylon cords were attached to the tendons of the flexor digitorum profundus and superficialis, flexor carpi radialis, and flexor pollicis longus. Static forces of 5 and 10 pounds (2.3 and 4.5 kg) were applied along the lines of the muscle force actions (measured with spring scales).

The results showed that the 10 pound (4.5 kg) load always created a higher pressure than the 5 pound (2.3 kg) load, pressures were greater with the wrist in flexion than in a neutral position or in extension, and the pressure increased with increasing flexion angle. Moreover, pressures caused by loading of the digitorum profundus tendons of digits 2 and 3 were greater than for any other tendons (the loading effects of flexor digitorum superficialis being minor). The effects of simultaneous loading of digits 2 and 3 were no different from those of the loading of digits 2, 3, and 4. Passive wrist flexion and extension caused significant effects only at the extremes of the range of motion. During loading of the tendons of the flexor digitorum profundus of digits 2 and 3, the pressure changes were much higher in the proximal and distal carpal tunnel than under the antebrachial fascia, whereas during passive wrist flexion and extension the pressure changes were the most pronounced under the antebrachial fascia. This latter finding is explained by the median nerve being compressed by the distal radius and folded antebrachial fascia in flexion and between the lunate and taut antebrachial fascia in extension.

Keir et al (43) used a pressure catheter to measure hydrostatic pressures in the carpal tunnel and a 45-mm rubber bulb, containing a 30-mm long measuring portion replacing the median nerve, to measure contact stresses to the median nerve during different loading situations in varying degrees of flexion-extension and radial-ulnar deviation of the wrist in 8 cadaver hands. The muscles that were loaded separately by 9.8 N were the palmaris longus, second and third superficial, and deep finger flexors and the flexor pollicis longus. The pressures were also measured in a no-load situation. The forearm was in supination, and the fingers were placed around a 30-mm cylinder in order to obtain a 2-finger pinch posture.

In flexion-extension, the pressures obtained via both the catheter and the bulb showed a U-shape curve for all the loading conditions, with the highest values in extension and the lowest in neutral or slight flexion. In radioulnar deviation, the angle of the wrist had no effect on pressures measured with the catheter, whereas the recordings with the bulb showed a U-shape for all loading conditions. In flexion-extension recorded via the catheter, the effects of loading from greatest to lowest were the loading of the palmaris longus, the finger flexors, flexor pollicis longus, and no loading, except for the most extreme flexion (45 degrees), for which the pressure was highest for finger flexor loading. With the bulb, the pressure responses due to the loading of the finger flexors were higher than those for the palmaris longus. A similar order of pressure response was obtained with the catheter for loading the muscles in various angles of radioulnar deviation as in flexion-extension. With the bulb, very high pressures were obtained when the finger flexors were loaded in ulnar deviation beyond 20 degrees.

The authors noted that the divergence in the pressure measurements obtained with the catheter and the bulb suggests that they measured different phenomena, the catheter measuring hydrostatic pressure and the bulb measuring a combination of hydrostatic pressure and contact force. The high catheter recordings obtained by loading the palmaris longus, especially in extension, is a new finding. The authors explained this finding by the insertion of the palmaris longus into the palmar aponeurosis, the distal portion of the flexor retinaculum. In extension, the pull of the palmaris longus may flatten the retinaculum and thereby decrease the carpal tunnel volume. The high pressure values obtained by the bulb suggest direct mechanical effects on the median nerve when the flexor tendons are loaded with the wrist in flexion. High bulb values were also obtained for the flexor tendons and the flexor pollicis longus tendon in ulnar deviation. The authors explained this phenomenon by the tendons "trapping" the bulb as they would the median nerve. This result suggests that forceful grip in ulnar deviation would provide high compression to the median nerve.

Summary of studies on force. Epidemiologic studies suggest that high force requirements of the hand are an independent risk factor of CTS, but they do not provide any dose-response relationships. In the study by Silverstein at al (61), force was a weaker risk factor than repetition, but in the study of Chiang et al (62) force was a stronger risk factor than repetition. Force and repetition increased the risk of CTS in a multiplicative way in the Silverstein et al study. In the case-referent study by Armstrong & Chaffin (47), the cases with CTS exerted more force in pinch grip and in nonneutral wrist postures than the referents.

Experimental studies suggest that CTP is very sensitive to loading of the long flexors of the 2nd and 3rd digit and also the long flexor of the thumb. With the forearm in 45-degree pronation, increasing loading results in an almost linear increase in CTP in both pressing and pinching types of tasks. The same level of force in the pinch grip causes CTP values to double those in the power grip.

The study of Keir et al (43), measuring the CTP both with a catheter and a bulb as a replacement of the median nerve, clearly demonstrated that, depending on the wrist posture and the loaded fingers, the response may be detected more clearly either with the catheter, measuring true hydrostatic pressure, or with the bulb, measuring the combination of hydrostatic pressure and contact stress. In the same way, the effects of forceful

exertions may be mediated via 2 pathways, through raised hydrostatic pressure and through increased contact stresses on and deformation of the nerve. Loading the finger flexor tendons with the wrist in ≥45-degree flexion and ≥30-degree ulnar deviation is likely to induce the highest contact stress to the median nerve.

Repetition

Epidemiologic studies. The NIOSH review (10) concluded that there is evidence of a positive association between highly repetitive work alone and CTS and strong evidence of a positive association between exposure to a combination of risk factors (eg, force and repetition) and CTS.

In the aforementioned study of Silverstein et al (61), the odds ratio for group 3 versus group 1 (low force + high repetition versus low force + low repetition) was 2.7 and nonsignificant, and the odds ratio for group 4 versus group 1 (high force + high repetition versus low force + low repetition) was 15.5 (95% CI 1.7—142). In a separate logistic model the odds ratio for repetition was 5.5 ($P<0.05$).

In the study of Chiang et al (62), the odds ratio for repetition was 1.1 and nonsignificant. There was no statistically significant interaction between repetition and force.

Latko et al (68) performed a cross-sectional study to look at the associations between various levels of repetition and the prevalence of CTS. A preliminary job selection or classification was performed to obtain jobs encompassing 3 levels of repetition (low, medium, and high). Three companies with a total of 352 workers with a minimum of 6 months seniority in their job participated in the study. The workers represented a total of 39 jobs. Repetition, force, and posture were estimated with an observation method for 1 representative worker per job. The rating of repetition was performed with a 0—10 scale, based on the amount of recovery time within the cycle and speed of hand movement. CTS was defined by (i) a hand diagram score, (ii) median mononeuropathy (a difference in peak latency of at least 0.5 milliseconds between ipsilateral ulnar and median nerves), and (iii) a combination of 1 and 2. The prevalence of CTS according to the hand diagram score was 6.8%, 14.5%, and 17.4% in the low, medium, and high repetition categories, respectively, the overall differences and linear trend being statistically significant. The prevalence of median mononeuropathy was not associated with the level of repetition. The prevalences of CTS based on both the hand diagram score and the median mononeuropathy were 2.7%, 4.9%, and 7.9%, showing a borderline significant linear trend ($P=0.06$). Hand repetition and wrist ratio (ratio of wrist depth to width >0.73 versus ≤0.73) were statistically significant predictors in the final logistic models for both hand diagram and hand diagram + median mononeuropathy, the odds ratios being 1.16 (95% CI 1.00—1.34) and 1.22 (95% CI 0.98—1.53) per unit of repetition, respectively.

Barnhart et al (69) studied the prevalence of CTS among 173 ski manufacturing workers in repetitive and nonrepetitive jobs. Using either positive Tinel's sign or Phalen's test and electrodiagnostic evidence as the criterion for CTS, the prevalence of CTS was 15.4% for repetitive jobs and 3.1% for nonrepetitive jobs (OR 3.95, 95% CI 1.0—15.8).

Wieslander et al (70) performed a case-referent study with 34 men operated on for CTS as cases. For each case, 2 gender- and age-matched referents undergoing surgery for other reasons and 2 population referents were chosen. Altogether 143 referents were included in the analysis. There was a dose-response relationship between years at work involving repetitive movements of the wrists, the odds ratio being significant for more than 20 years versus less than 1 year of such exposure.

In a cross-sectional study of 93 symptomatic and 91 asymptomatic active workers with median mononeuropathy (≥0.5 ms difference between the median and ulnar evoked peak sensory latency, 25% of the entire study population), Werner et al (71) found significant postural differences between the 2 groups in univariate analyses, including finger and wrist nonneutral postures. Other statistically significant differences between the 2 groups were gender, triceps skinfold thickness, history of diabetes, job insecurity, average hand force, and repetition level. In the multivariate logistic regression analysis, only repetition level and gender remained as significant factors.

Studies on healthy subjects. Experimental studies on nonsymptomatic subjects, investigating the effects of various degrees of repetitive movements or tasks on, for example, CTP, are almost nonexistent. Rempel et al (72) studied CTP values among 19 healthy subjects during a repetitive task of loading and unloading 1 pound (0.45 kg) cans from a box at a rate of 20 cans per minute for a period of 5 minutes. The task was performed with and without a flexible wrist splint. Without the splint, CTP rose from a median base-line level of 8 (SD 6) mm Hg to 18 (SD 13) mm Hg [1.1 (SD 0.8) to 2.4 (SD 1.7) kPa] during activity, with considerable variation in pressure during the activity. Preactivity levels were reached within 14 (SD 15) seconds after the exercise. The splint had minimal effects on these values. The authors postulated that the pressure levels observed during repetitive activity, although low, may be enough to reduce blood flow in the epineurial venules.

Several psychophysical studies have looked at tradeoffs between wrist posture, grip type, resistance load, and frequency and duration with respect to maximum accept-

able levels as perceived by participants. The relationship between these maximum acceptable limits and CTP changes was not reported per se. In the absence of connecting data, an assumption would have to be made that the same mechanisms that increase pressure also increase perceptions of discomfort or affect function.

Snook et al (73) studied maximum acceptable torque, which was the number of Newton-meters of resistance with repetitive wrist flexion or extension at 2—20 motions per minute with a pinch or power grip. The tasks were performed over 8-hour shifts twice a week for 20 days by 15 women in the first experiment and by 14 different women working 5 days a week for 23 days in the second experiment. The second experiment used only flexion or extension 15 times a minute in a power grip. The maximum acceptable torque decreased with duration and frequency. The maximum acceptable torque was higher for flexion than for extension. Although the symptoms increased with the frequency of motions and with the duration of exposure over the day, so did the tactile sensitivity. The symptoms also increased more with extension than with flexion. Symptoms of soreness and stiffness gradually decreased from day 5 to day 23 for the 2nd experiment and therefore suggested that the initial symptoms were due to unaccustomed work. Symptoms of numbness were greater among the 5-days-per-week group than among the 2-days-per-week group, and they were primarily concentrated on the palmar side of the fingers and thumb. There were no significant differences with respect to grip type. The maximum acceptable torque of the persons who worked 5 days a week was 36% lower than that of the persons who only worked 2 days a week. The independent variables for this group were number of repetitions in flexion with a power grip. The 36% reduction was then applied to all the other variables measured in the first experiment to derive a table of acceptable limits. The authors used these data to derive maximum acceptable forces for women on the basis of repetition rate, grip type, and wrist posture. Although most studies indicate a greater decrease in force capacity with wrist flexion than extension, the opposite was true in this study. The authors speculated that the design of the flexion task was such that it took advantage of gravity, whereas the extension task did not. The maximal acceptable force tables therefore apply only to work situations that are similar to those of this study (ie, the direction of the flexion force is in line with the direction of gravity).

It is unclear whether these studies contribute anything to the understanding of the pathomechanisms of CTS. Perhaps the finger or thumb numbness reported by some participants is not a part of the training effect but rather the effect of repeated CTP elevations due to the lumbricals in the carpal tunnel during forceful grips, as well as to the tendons and transverse carpal ligament compressing the nerve during extension and flexion. There may be some increase in swelling due to the repetitive forceful unaccustomed work. Perhaps this reaction causes subjects to self-regulate to lower acceptable force levels by the end of the day and with increasing repetition.

There have been a series of studies by Fernandez et al using psychophysical methods to assess maximal acceptable levels for various combinations of wrist postures, grips, frequencies, durations, and loads (74—76). Data were also collected on muscle fatigue and function using surface EMG, grip dynamometers, perceived exertion, and some more-global measures, such as heart rate and blood pressure. These experiments usually had 12—15 healthy men or women performing the tasks for relatively short durations [compared with the studies of Snook et al (73)]. Maximum acceptable frequencies (MAF) were significantly lower for increasing wrist flexion during a drilling task simulating work at a nearby factory when using a pistol-shaped 1.3-kg drill during 10 different 25-minute simulation sessions. There was no significant independent effect of ulnar deviation or, when combined with flexion, on MAF, EMG, blood pressure, grip strength, or perceived exertion. Flexion had a significant effect on MAF, grip strength, flexor EMG, wrist, forearm and shoulder ratings of perceived exertion. When static exertions of 3 minutes replaced repetitive exertions, evidence of muscle fatigue was the greatest in the flexor EMG during wrist flexion. Similarly, the researchers found that the MAF values were significantly reduced as lateral pinching force, wrist flexion, and task duration increased (75).

Of interest for this review is the fact that the lateral pinch position with wrist flexion probably pushes the lumbricals into the carpal tunnel and increases pressure, and the flexion adds to compression of the nerve by wrapping it around the transverse carpal ligament. It would be interesting to know if flexor EMG findings can be a surrogate measure for CTP values in the workplace. The strength of these studies is that the variables of frequency, force, and posture domains resemble those observed in many manufacturing facilities. If the relationship to CTP values can be determined, they may provide some guidance for job design based on short-term intermediate measures. The drilling simulation was comparable with a job in which an elevated prevalence of CTS and other hand or wrist disorders had been reported. It is not known whether these short-term acceptable levels would be protective enough in the long term.

Clinical studies. In the aforementioned study of Szabo & Chidgey (56), a 1-minute flexion-extension exercise with the rate of 30 cycles per minute was enough to increase CTP values among the cases with early and intermediate CTS above those of the healthy referents and maintain such a difference to 10 minutes postexercise. This is the

only identified clinical study experimentally investigating the effects of repetition among patients.

Summary of studies on repetition. An association between CTS and repetitive tasks has been fairly consistently reported in epidemiologic studies. The diagnosis of CTS was confirmed by electrodiagnosis in several studies. One study reports a dose-response relationship between the prevalence of CTS and the level of repetition (68). There is some evidence that the risk of CTS increases with increasing duration of exposure to repetitive wrist movements at work (70). In the study of Silverstein et al (61), repetition was a stronger risk factor than force, and repetition and force together increased the risk of CTS multiplicatively.

One study on rabbits indicated that uninterrupted flexion-extension movements around the radiocarpal joint at a rate of 80 cycles per minute for 10 hours produce swelling of the structures within the carpal tunnel and decrease the median nerve conduction velocity over a period of days (33) (table 1). The repetition rate of 80 cycles per minute corresponded well to a moderate pace of light manual work, but the lack of rest pauses and the long duration of the activity spell were clearly more extreme than in most actual work situations. The same study showed that, although the water content of carpal tunnel tissues increased both with intact and cut tranverse carpal ligament, an intact transverse carpal ligament was needed for the development of functional disturbance of the median nerve. Although CTP values were not measured in this study, one can speculate that with a cut ligament, CTP does not increase enough to induce disturbance in nerve function.

A human study on patients reported sustained elevated CTP values after flexion-extension exercise with a rate of 30 cycles per minute for 1 minute (56). Overall, only few experimental studies exist investigating the effects of various degrees of repetitive movements or tasks on, for example, CTP or median nerve conduction velocity.

The psychophysical studies indicate that maximum acceptable levels of hand or wrist activity decrease with increasing force, postural extremes, and frequency. Most of these studies have been short-term and have looked at performance or acceptability. The relationship between these indices and CTP or CTS is currently unknown. The relationship between psychophysical indices and CTP values should be relatively straightforward to study. The relationship to CTS could only be studied prospectively.

External pressure

Information regarding external pressure in relation to CTS or CTP is available only from clinical case series and cadaver studies. Clinical case series suggest that symptoms of CTS can be produced as a result of prolonged direct pressure on the palm by tools such as chisels, screw drivers, and handles of some other tools (77). No epidemiologic studies have been reported addressing specifically the role of external pressure in CTS.

Cadaver studies. Cobb et al (78) investigated the effects of externally applied force on CTP in 5 cadavers at 16 locations in the wrist and palm. A 1-kg force was applied by means of a force dial to the palm in a palmar-to-dorsal direction (the authors gave no proper unit for force, or the cross-sectional area or the diameter of the tip of the device by which force was applied). The application of force to the distal parts of the palm resulted in pressures ranging from 3 to 9 mm Hg (0.4—1.2 kPa). Higher pressures were obtained for the hypothenar area, and applying pressure just distal to the hook of the hamate resulted in an average pressure of 37 mm Hg (4.9 kPa). Applying pressure in the thenar region resulted in an even higher CTP, the medial aspect of the base of the thenar eminence yielding a total mean pressure of 75 mm Hg (10.0 kPa). Applying pressure over the flexor retinaculum at the midline of the palm resulted in the highest pressures, the peak pressure (136 mm Hg, 18.1 kPa) being obtained upon pressure at the level of the hook of the hamate.

As possible mechanisms the authors considered attachment of the thenar and hypothenar muscles to the flexor retinaculum, distribution of pressure through compartmental anatomy, including the flexor tendon sheaths, and a simple effect of soft-tissue compression, the last alternative gaining support from the concentric distribution of pressures around the catheter tip.

Cobb et al (79) studied the role of lumbrical muscles and tool size in CTP with upper-extremity specimens from 5 cadavers. The flexor profundus and superficialis tendons of the 2nd to the 5th digits were loaded each with a 1-kg weight. The CTP values were measured first with a full fist. Then a 1-inch (2.54 cm) diameter cylindrical tube was placed in the fist and the CTP was measured. The measurement was repeated with the fingers kept in the same posture after the tube was removed. Similar measurements were then made with and without a 2-inch (5 cm) tube. The whole procedure was repeated with the lumbricals removed. The effects of the lumbrical muscles, presence of tubing, and tube size on the change in CTP were assessed by a 3-way repeated-measures analysis of variance.

The highest CTP values were obtained in the 1st experimental situation with full fist. The greatest decrease in CTP was seen when the lumbricals were removed and the tubes were removed. With intact lumbricals, the CTP values decreased when the fingers moved from fully flexed to more extended positions. After the removal of the lumbricals no such change was seen in the CTP. With intact lumbricals, the removal of the 2-inch (5 cm) tube resulted in a slightly higher decrease in CTP than did the

removal of a 1-inch (2.54 cm) tube. The authors concluded that lumbrical muscle incursion and pressure on the palm cause significant increases in CTP. Moreover, the amount of increase in CTP from the use of a tool depends on the distribution of forces on the palm, which are affected by the size and shape of the tool.

Summary of studies on external pressure. On the basis of available information, it can be concluded that the application of external forces at or around the carpal tunnel area results in considerably high CTP values even at relatively low force levels. In work situations, tool size and shape are crucial factors in determining the CTP. The additive effects of successive elevations of CTP as a result of tool use in a work environment are not known. Clinical case series suggest that CTS may result from the use of certain tools, but no data exist to suggest any length or time pattern of tool use with the potential of causing disease.

Vibration

Epidemiologic studies. The NIOSH review (10) concluded that there is evidence of a positive association between work involving hand or wrist vibration and CTS.

The associations between CTS and the use of hand-held power tools have been investigated in 2 population studies. In the National Health Interview Survey, the odds ratios of self-reported and medically-called CTS (diagnosis of CTS made by a medical person) were 1.7 (95% CI 1.3—2.2) and 1.9 (95% CI 1.2—2.8), respectively, for work with hand-held or hand-operated vibrating tools or machinery (80). In the population-based case-referent study of Nordstrom et al (45), the association between CTS and mean hours per day using power tools or machinery showed borderline significance in a bivariate analysis, but not in the final multivariate model.

In a carefully conducted study, Nilsson et al (81) investigated the effects of vibration exposure from hand-held tools on median nerve function. Sixty platers, 58 assemblers, and 61 office workers were included. Vibration exposure was estimated from measurements of the tools and the duration of tool use. The duration of repetitive and forceful gripping was estimated from observations of a group of platers and assemblers. Sensory and motor nerve conduction velocity, distal latency time, and amplitude of the median nerve were measured. The case definition of abnormal nerve conduction was based on the 95% confidence interval of the mean of the office workers not exposed to vibration. In a logistic regression model of prolonged distal latency time over the carpal tunnel segment both on the right and left side, duration of vibration exposure was a significant predictor when included together with age and consumption of nicotine, and it remained significant after the inclusion of assembling and plating work. Moreover, sensory conduction velocity over the wrist was slower among the platers than among the office workers on the left side. In general sensory conduction velocity was slower on the right than on the left side, but the rate ratios were higher for the left side than for the right. The authors explained this finding as a result of more physical load in general on the right side. Therefore the relative effect of some specific exposure may be greater for the nondominant hand, due to a lower total work load. The effects of vibration and other physical loads could not, however, be separated in the study. The vibration exposure from plating was considered moderately high and low from assembling.

In the Silverstein et al (61) study, the use of vibrating tools was viewed from videotapes of at least 3 workers performing the job. The crude odds ratio of CTS for vibration was 5.3 ($P<0.1$). Jobs with vibration exposure were, however, all highly repetitive and mostly high-force jobs. The crude odds ratio for high force + high repetition jobs with vibration compared with high force + high repetition jobs without vibration was 1.9 and non-significant. This result suggests confounding between high force + high repetition and vibration.

In the case-referent study of Wieslander et al (70), there was a dose-response relationship between surgically treated CTS and number of years using hand-held vibrating tools, the odds ratio for 1—20 years and >20 years versus <1 year being 4.3 (95% CI 1.4—12.9) and 16.0 (95% CI 2.8—90.2), respectively.

Bovenzi & Zadini (82) clinically examined 65 forestry workers using chain saws and 31 maintenance workers. The acceleration of vibration was measured for 3 chain saws of the 2 different types that were used. From measurements and workhours, daily vibration exposure was characterized in terms of 4-hour energy-equivalent frequency-weighted acceleration for each worker. Checklists were used to characterize other physical load factors, such as postures, forces, and the repetitiveness of work movements. Maintenance workers were reported to have a higher proportion of work cycles shorter than 30 seconds (ie, their work was considered more repetitive), but the forestry workers were considered to have more physically demanding jobs overall. They also had a colder work environment. The work analysis concerning other physical load factors than vibration was not, however, described or reported in detail. The prevalence of CTS was 38% for the forestry workers and 3% for the maintenance workers (adjusted odds ratio for age and body mass index 21.3, $P<0.001$). The prevalence of CTS increased with increasing daily vibration exposure.

In another study, Bovenzi and his associates (83) studied 570 quarry drillers and stonecarvers exposed to vibration and 258 stone workers performing only manual activity. Exposure to vibration was assessed in terms of 8-hour energy-equivalent frequency-weighted

acceleration and as lifetime vibration dose based on tool use. The prevalence of CTS, based on physical examination, was 8.8% for workers using vibrating tools and 2.3% for reference workers (adjusted odds ratio 3.4). The prevalence of CTS increased with increasing lifetime vibration dose.

Koskimies et al (84) clinically and neurophysiologically investigated 125 male forest workers who had used chain saws for a minimum of 500 hours during 3 years. The diagnosis was based on nocturnal numbness in fingers, physical signs, and electrophysiological findings, although explicit diagnostic criteria were not defined. CTS was present in 25 men (20%), of which 12 (48%) had bilateral involvement.

Clinical studies. A clinical study analyzed a series of 100 male patients exposed to vibration from hand-held tools and referred to a hand surgery department for examinations because of neurosensory or vasospastic problems, pain, or muscle weakness (85). Isolated neurosensory symptoms were present in 48%, isolated vasospastic problems in 20%, and combined neurosensory and vasospastic problems in 32% of the patients. Neurosensory symptoms were more common than vasospastic symptoms, especially during the first 20 years of vibration exposure. Of 80 patients with neurosensory symptoms, 22 (28%) had CTS according to the physical examination. It was concluded that vibration-induced neurosensory symptoms are often not due to CTS.

Sakakibara et al (86) measured fractionated median sensory nerve conduction velocity for 56 patients treated in 3 hospitals for hand-arm vibration syndrome and 43 healthy referents selected from residents near the hospitals. The patients had used rock drills or chain saws for an average of 21 years. Sensory nerve conduction velocity was measured in the digital (3rd finger, the right hand for all but 4 cases with injuries), finger-to-palm, palm-to-wrist, and wrist-to-elbow segments. The nerve conduction velocity was slower in the cases than in the referents in the digital and wrist-to-palm areas, whereas there was no difference between the groups in the palm-to-finger and elbow-to-wrist velocities. A slowed sensory conduction velocity (below the 5th percentile of the referents) was found in 20 (36%) patients in the digital area, in 11 (20%) patients in the wrist-to-palm area, and in 7 (13%) in both areas. A slowed sensory conduction velocity in the digital area but not in the wrist-to-palm area was associated with the sensorineural stage for hand-arm vibration syndrome according to the Stockholm classification.

Summary of studies on vibration. Several cross-sectional studies have shown an association between CTS and the use of hand-held vibrating tools. Dose-response relationships have been obtained between CTS and daily vibration exposure (82), number of years using hand-held vibrating tools (70), and lifetime vibration dose (83). The results of Silverstein et al (61) suggest that exposure to vibration has additional effects beyond those of forcefulness and repetitiveness, but it has mostly been impossible to separate the effects of vibration from those of especially forceful gripping.

In none of the reviewed studies was CTS defined in the most recommendable way, according to symptoms and electrodiagnostic testing (4). As the sensorineural symptoms of the hand-arm vibration syndrome can mimic those of CTS, and the validity of the most commonly used Tinel's and Phalen's test are not very high, considerable misclassification of the used outcomes is possible. The study of Nilsson et al (81), using measurements of nerve conduction velocity, shows convincing evidence of nerve injury in the carpal tunnel level.

Clinical case series suggest that patients exposed to hand-arm vibration have symptoms and findings of CTS (85, 86). The case series of Sakakibara et al (86) with fractionated measurements of nerve conduction velocity on heavily exposed subjects showed slowing of nerve conduction at 2 sites, the digital and the carpal tunnel area, slowing at the digital area being more common. The nerve biopsies in the study of Strömberg et al (38) demonstrated nerve injury in the interosseus nerve even more proximally in the distal forearm. On the other hand, the electrodiagnostic findings in the study of Nilsson et al (81) among subjects with low-to-moderate exposures suggested that the carpal tunnel area is the predisposed site of nerve injury. Because the effects of gripping forces and other physical load factors are inseparable from those of vibration in the studies, one can only speculate whether, in heavy vibration, the fingers are predominantly affected and whether, in association with a lower exposure to vibration, the findings in the carpal tunnel area are primarily a result of other physical loads than vibration.

Concluding remarks

CTP values are higher for CTS patients than for referents. Experimental studies have shown that certain forearm, wrist, and finger postures, even moderate hand loads and external pressure on the palm, can increase the CTP at least temporarily to levels in which nerve viability may be threatened. Acute effects on the nerve are usually followed by rapid recovery. However, some experimental studies have shown that prolonged pressure in the carpal tunnel or very high pressure can result in prolonged or potentially irreversible effects on the nerve. What is not known is whether *intermittent* high pressures over extended periods of time (as in forceful repetitive work for

20—40 hours a week over weeks, months or years) are necessary and sufficient to cause CTS or whether some other mechanism besides high CTP is also required. Contact stresses on the median nerve have been inadequately quantified and their effects are not well known.

Forceful repetitive work, vibration, and extreme wrist postures have been associated with CTS in a number of epidemiologic studies. Individual factors, such as age, gender, and obesity, have also consistently been associated with CTS. It should be noted that women and men are segregated into different types of jobs, and the variable gender may include exposure factors that differ between the genders. In clinical case series, CTS seems to be associated with systemic diseases, but in working populations these diseases seem to play a minor role. A range of other individual risk factors is likely to exist. It has also been seen in experimental studies that a certain forearm, wrist, and finger posture combination can result in a wide range of CTP values. Moreover, people seem to differ in their tolerance to increased CTP values.

This review is consistent with the "cascade model" of upper-limb musculoskeletal disorders (87), in which an external load has an internal response that, in turn, leads to a series of responses. These cascading responses can be salubrious or detrimental, depending on the level, duration, and frequency of the load and on the individual's capacity to withstand the load. It is realistic to assume that the individual characteristics behind these differences in the responses to the physical load factors will never be fully understood. Another important factor is that of known individual risk factors; only few, such as obesity, trauma, and some rheumatic diseases, are, according to current knowledge, modifiable, whereas all physical workload factors are, in principle, modifiable and can be a target for preventive measures.

Well-designed epidemiologic studies with acceptable diagnostic criteria and valid exposure assessment are needed to obtain more knowledge of the role of physical load factors and, especially, of exposure-response relationships for a more effective prevention of CTS. When feasible, extending the duration of the protocols in experimental studies may bring useful information of more long-term effects of quantifiable exposures. Some avenues for future research include determining the correlation between various psychophysical indices and CTP values. Because it is unlikely that CTP values can be used epidemiologically, if there is high correlation with the psychophysical indices, these could be used as surrogate intermediate measures in future studies.

While more research is needed, there is sufficient information to suggest that reducing the duration, frequency, or intensity of exposure to forceful repetitive work, extreme wrist postures, and vibration is likely to result in a reduction of the incidence or severity of CTS in working populations.

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