Review

Scand J Work Environ Health 1975;1(1):1-14

doi:10.5271/sjweh.2865

Applications of neurophysiological methods in occupational medicine. A review.

by Seppäläinen AM

The following articles refer to this text: 2015;41(5):421-507; 2016;42(3):177-255

Key terms: neurophysiological method; occupational medicine; review

This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/790562

Scand. j. work environ. & health 1 (1975) 1—14

Applications of neurophysiological methods in occupational medicine
A review

by ANNA MARIA SEPPÄLÄINEN, M.D.[1]

SEPPÄLÄINEN, A. M. Applications of neurophysiological methods in occupational medicine: A review. *Scand. j. work. environ. & health.* 1 (1975) 1—14.

Key words: occupational diseases, neurophysiological methods, electroneuromyography, electroencephalography, toxic neuropathy, toxic encephalopathy.

Involvement of the nervous system can be observed even in modern industrial plants, and, for example, in Finland occupational diseases with symptoms in the nervous system form the third largest group of occupational diseases. (They follow occupational skin diseases and hearing loss caused by noise.) Nervous system symptoms are at times vague, and it may be hard to find specific signs in purely clinical examinations. Early neurological symptoms have not been adequately taken into account in setting threshold limit values (TLVs).

The classical symptom of lead poisoning, paresis of the radial nerve leading to drop-hand, practically belongs to history in modern industrialized countries. Similarily, grave neurological symptoms of carbon disulfide poisoning are not met any more. But some workers still complain of numbness and pain in their limbs, headache, and dizziness. These early nervous symptoms can be studied with careful neurological examination, but various neurophysiological methods should also be added in order to gain sensitivity and objective proof of lesions at an early stage.

[1] Institute of Occupational Health, Helsinki, Finland.

Reprint requests to: Dr. Anna Maria Seppäläinen, Institute of Occupational Health, Haartmaninkatu 1, 00290 Helsinki 29, Finland.

Neurophysiological methods reveal certain types of lesions within the nervous system. Electroencephalography shows involvement of the central nervous system, especially dysfunction of the more superficial structures of the brain, and electroneuromyography differentiates lesions at different levels of the peripheral nervous system and muscles. The myoneural junction can be studied with repetitive stimulation of the peripheral nerves.

NEUROPHYSIOLOGICAL METHODS

Electroencephalography

Electroencephalography (EEG) is the recording of the electrical activity of the brain. This low-voltage activity is amplified with a specific apparatus (fig. 1) and is registered on paper. The EEG apparatus has at least 8 channels, but 16 channels are also widely used. According to the international 10—20 system 19 electrodes are placed on anatomically-fixed regions of the scalp, and one electrode is attached to each ear lobe. Resistance is lowered by rubbing the skin with alcohol and using an electrode paste under the electrodes, which are glued on or kept in place with a rubber net. Varying electrode combinations, i.e., montages, are then recorded during the next 30 minutes, which gives an ample possibility

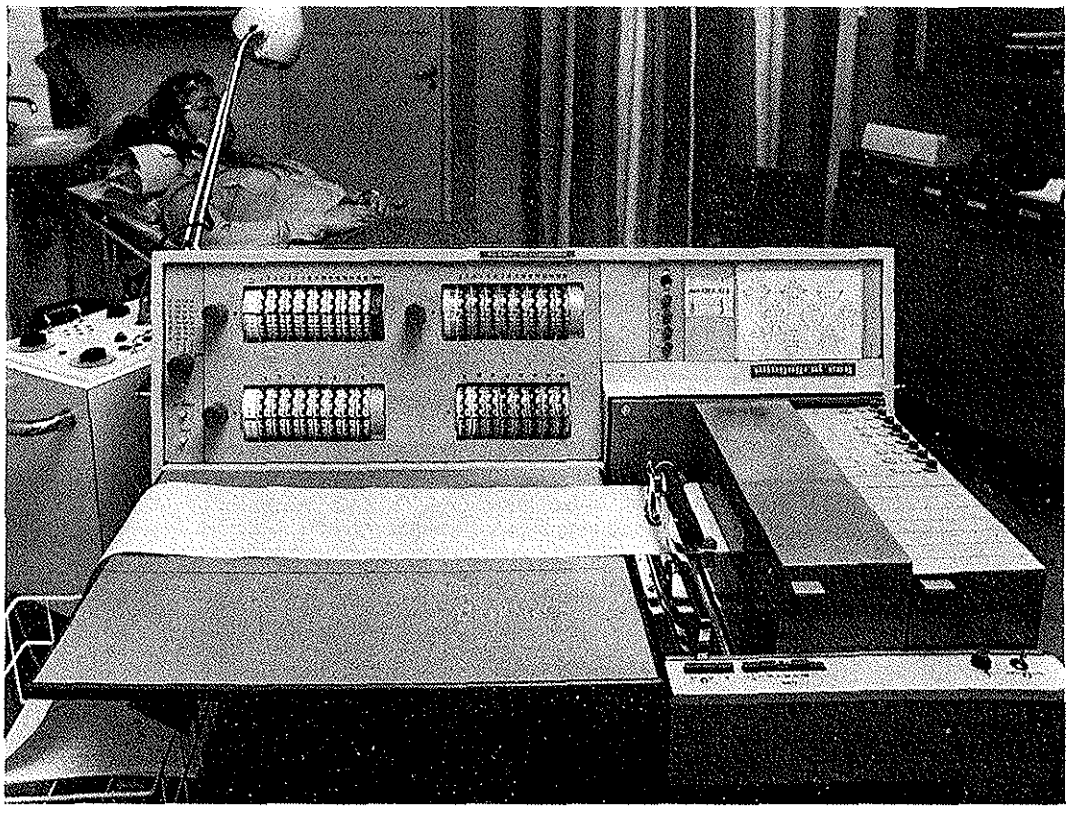

Fig. 1. An electroencephalograph.

for examining different areas of the brain since several regions are always studied at the same time. Activation methods include photic stimulation, trains of short pulses of intensive light with certain frequencies; hyperventilation for 3 minutes; and sleep, either natural or induced with the help of sedatives, e.g., chloral hydrate.

Specifically trained technicians register the electroencephalograms (EEGs) under the supervision of a physician, i.e., neurophysiologist. The neurophysiologist then interprets the EEGs according to well-documented principles (23, 33).

Different types of EEG abnormalities can be indentified. The most usual ones are slow wave abnormalities of varying degrees. They can be focal, i.e., localized in a certain area only, or diffuse or generalized. Slow wave abnormalities are connected to dysfunctions of nerve cells and brain structures or to anatomic lesions. They reveal encephalopathy of different origins — toxic, traumatic, metabolic, circulatory — or structural alterations like malformations or tumors or other expansive lesions. Increased intracranial pressure can also be revealed by slow waves.

Other EEG abnormalities include paroxysmal abnormalities, namely, sharp waves, spikes, and spike and wave discharges. Also these can be focal or generalized. Paroxysmal abnormalities are often seen in subjects with epileptic convulsions, but they can be found in the presence of other types of brain irritation too. For instance they are common in children with mental retardation or cerebral palsy, even without convulsions.

A good waking record is needed to gain general information on encephalopathy, but the amount of information can be increased by using different activation methods. Hyperventilation can activate slow wave abnormalities and is thus useful. In certain toxic encephalopathies it is important to look for possible irritative lesions; then photic stimulation and sleep are good auxiliary activation methods. Photic stimulation and hyperventilation should

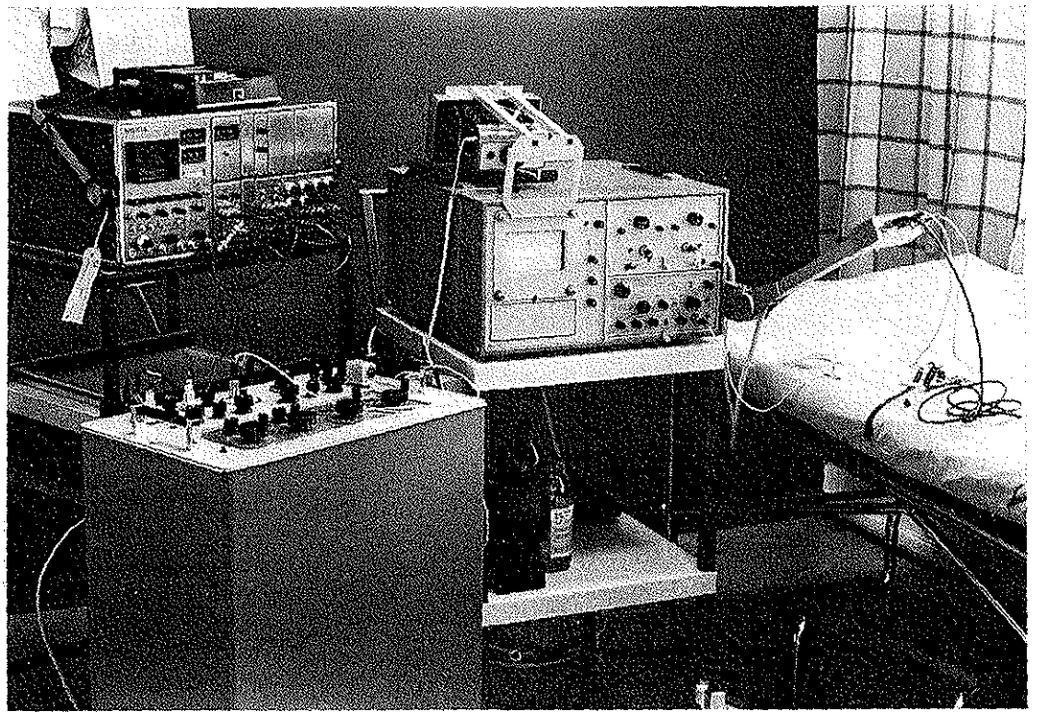

Fig. 2. Electroneuromyographic equipment: an electromyograph with a polaroid camera on the right, an electrical stimulator in the left foreground, and a small analog-digital computer in the left background.

both be included in every EEG examination because of differential diagnostic purposes. Natural sleep during a part of the recording can also be encouraged, but for ambulant patients sleep induced by drugs can be limited to the diagnostic problems of epilepsy.

An EEG mainly reflects the state of the brain at present. Therefore actively progressive diseases give severe EEG abnormalities, while slowly changing states like nonprogressive cerebral atrophy may leave the EEG intact. Deep lesions may well escape unnoticed because the activity diminishes in the distance between them and the scalp.

An EEG examination is indicated in suspected cases of occupational diseases which involve symptoms of the central nervous system, such as headache, poor memory, dizziness, and loss of muscular strength or tactile sense of a cerebral type, for example, hemisyndromes. It is of course also applicable in the differential diagnosis of neurological diseases like epilepsy, brain tumors, and brain injuries and can at times give prognostic hints.

Electroneuromyography

Electroneuromyography (ENMG) includes both electromyography (EMG) and the measurement of nerve conduction velocities. Diagnostic EMG is performed with concentric or bipolar needle electrodes inserted in appropriate muscles. The electrical activity of the muscles at rest and during a voluntary contraction is amplified with an electromyograph (fig. 2). The EMG activity is usually observed on the screen of an oscilloscope, and at the same time it can be heard through loud speakers. The human ear is good at separating the different sound frequencies in the spectrum of the EMG. EMG activity can also be photographed either on moving paper or with a polaroid camera. For later analysis it can also be recorded by tape recorders with a very large frequency spectrum. The evaluation of EMG activity

requires much training and experience and can be performed only by specialized physicians, i.e., neurophysiologists (28).

The electromyograph is also used to measure nerve conduction velocities. It is then combined with an electrical stimulator (fig. 2), which triggers the electromyograph at the time of the stimulus. Maximal motor conduction velocities (MCV) of the peripheral nerves are fairly easy to measure (64). The nerve is stimulated with a skin electrode at two separate spots along the course of the nerve, and the motor response is picked up with skin electrodes and amplified with the electromyograph. The latencies from the stimulus to the response are measured, and the MCV is calculated by dividing the distance between the stimulation points by the difference of the latencies.

Different nerves conduct the impulses at different speeds. The MCVs of the arm nerves range from 50 to 65 m/sec, and those of the leg nerves from 40 to 55 m/sec. The MCV of the deep peroneal nerve is usually higher than that of the posterior tibial nerve.

The age of the subject and the temperature of the nerve affect the MCV. Most MCVs slow down by about 1 m/sec for every 10 years of age between 20 and 60 years. The lower the temperature of the nerve, the slower the nerve conduction velocity. The skin temperature at the stimulation point is easily measured, and to ensure reliable results it should be above 30°C — usually it is between 31.5 and 33.5°C.

Series of normal values of MCVs, taking age into account, have been published (64), but each laboratory should have its own. In research projects control series matched by age are of utmost importance. If there is a question of disease or health, the controls should also be neurologically and medically healthy persons. If hazards of a certain occupational exposure are studied epidemiologically, the control subjects should probably not be prescreened neurologically, however.

More sensitivity can be added to nerve conduction studies by measuring the amplitude ratios of responses elicited by stimulation at different portions of the nerve, as well as by comparing the duration of the evoked muscle action potentials. Slower motor fibers can be studied separately by using paired stimuli based on the antidromic blocking technique (27, 56).

Sensory conduction velocities (SCV) can be measured orthodromically or antidromically with skin or needle electrodes. One practical method involves stimulating the finger nerve with skin electrodes and picking up the tiny nerve potential with skin electrodes on two separate spots along the course of the nerve. A series of amplified nerve potentials is then averaged in an analog-digital computer (fig. 2), after which latencies are measured and SCVs calculated.

Patients with myasthenia or myasthenic states exhibit abnormal fatigability because of disturbances in the myoneural junction. This abnormality can be shown electrophysiologically by observing the change, usually decline, in the amplitude of muscle action potentials elicited by repetitive stimulations of a motor nerve.

Muscle diseases appear in EMG as a decrease in the amplitude and duration of the motor unit potentials. Neurogenic diseases of the lower motor neuron type increase the duration and at times the amplitude of motor unit potentials and induce spontaneous activity in EMG in the form of fibrillations, fasciculations, or positive monophasic potentials. The number of recruitable motor units diminishes in neurogenic diseases, and thus during a maximal voluntary contraction only single motor units or a mixed pattern is achieved, instead of the normal interference pattern. If the neurogenic disease involves peripheral nerves, nerve conduction velocities are slowed. Conduction velocity of the slower motor fibers decreases earlier than the MCV. The neuropathy may be mainly sensory, however. Then only SCVs exhibit slowing. Thus with the help of ENMG it is possible to differentiate the levels and sites of peripheral neurogenic and myogenic diseases.

ENMG is indicated for patients with symptoms of disturbances in the peripheral nervous system, namely, flaccid paresis, muscular atrophy, muscular weakness, paresthesia and pain in the limbs, certain types of sensory loss, and abnormal fatigability. Even in cases with mild, mainly

sensory, symptoms abnormalities can be revealed by ENMG.

A specific etiological diagnosis based on neurophysiological studies alone is impossible in individual cases of suspected occupational disease. Usually sensitive methods give a greater number of false positive results than methods with low sensitivity. However, when exposure to a toxic agent can be documented and other evident causes for nervous system lesions can be excluded, positive neurophysiological findings give reasonable support for the diagnosis of occupational disease in the clinical work-up of patients with mild or nonspecific symptoms. The specific distribution of the lesions can also indicate the role of a certain exposure.

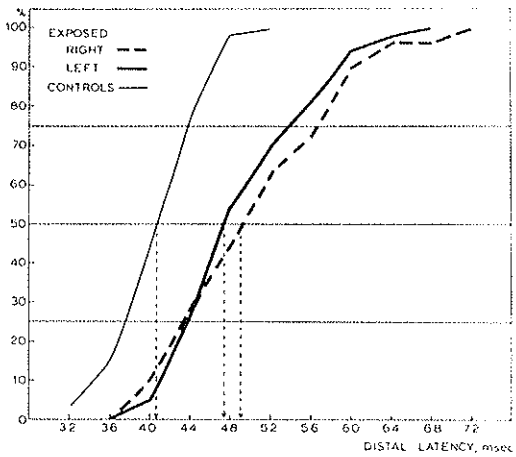

Fig. 3. Cumulative percentage distributions of the distal latency of the median nerve of vibration exposed forest workers and controls ($p < 0.001$, Kolmogorov-Smirnov test). [Reprinted from SEPPÄLÄINEN, A. M. *Work-environ.-health* 9 (1972) 106—111]

OCCUPATIONAL SOURCES OF NEUROLOGICAL SYMPTOMS

Certain physical and chemical agents causing occupational diseases with neurological symptoms are discussed in this section with special reference to neurophysiological findings.

Vibration

Physical factors may induce neurological symptoms. For instance vibrating tools cause the vibration syndrome, which consists of arteriolopathy and neuropathy. Workers complain of cold and white fingers and of numbness and pain in the extremities exposed to local vibration. Wallerian degeneration has been shown in the peripheral nerves of animals exposed to vibration (3).

Several studies have appeared on the decreased vibration sensitivity of workers using vibrating tools (48). However, Lidström (39) did not find permanent changes in the threshold of vibration sensitivity of 30 workers occupationally exposed to vibrating tools. The temporary threshold shift (TTS) to vibration sensation immediately after vibration exposure was, however, significantly greater among the lumberjacks than among the controls in Lidström's series (39).

ENMG examinations have revealed signs of neuropathy, i.e., damage in the peripheral nerves of workers who use vibrating tools. Damage of both the sensory and motor fibers has been reported for rock drillers and users of other pneumatic tools (15, 41), as well as for lumberjacks (53). The vibration frequency of the power saw has proved to be especially dangerous to the peripheral nervous system (31). One field study revealed frequent abnormalities in the conduction velocity of the slower motor fibers (CVSF) of the ulnar nerve and also in the distal motor fibers of the median nerve (fig. 3) among lumberjacks (54). Also Lukáš and Kužel (41) observed elongation of the distal latency of the median nerve in users of vibrating tools. They interpreted this observation as a sign of the carpal tunnel syndrome. I myself have found the combination of lesion in the distal portion of the median nerve and partial damage in the ulnar nerve to be quite common in the clinical vibration syndrome. Similarily, slowing in the distal portion of the sensory fibers of the arm nerves has been shown (36).

Other physical factors

It is possible that extensive exposure to noise causes changes in the brain and affects the EEG. Sudden alarming noise has been reported to induce specific EEG changes, the period of which corresponded well with the time during which the

subject was unable to take immediate, adequate steps to avoid an accident (52). Accidents have been reported to occur under such circumstances. Knowledge of EEG changes induced by long-term exposure to intensive noise are lacking, however. An Italian group has briefly reported that subjects with a mean exposure of 12 years to noise showed desynchronized, labile EEG traces (4).

Another physical factor which has been blamed for causing adverse effects in the nervous system is microwave radiation. Some studies describe electroencephalographic changes, namely, decreases in the alpha wave index and increases in the theta and delta wave percentages, as cited by Silverman (63). Well-controlled electrophysiological studies of persistent lesions in the nervous system after microwave exposure are, however, lacking.

Insecticides

Chlorinated hydrocarbon insecticides are basically neurotoxins. Hoogendam et al. (25) studied the EEG of 122 workers occupationally exposed to chlorinated hydrocarbon insecticides and found an increase in abnormal EEGs (20.5 % against 9 % among controls). Bilateral spike and wave discharges were noted in all cases that resulted in epileptiform convulsions. The EEGs returned to normal within 2 to 6 months after the termination of exposure. Later the same research group published a 9-year follow-up of the workers in an insecticide plant (26). During this period 17 workers, 5 % of the total labor force, suffered from epileptic convulsions. Most of them had typical EEG abnormalities when recordings were taken within 2 weeks of the convulsions. All the most recent cases of convulsions occurred in connection with unusually high exposure. As a consequence the authors submit the workers to EEG studies twice yearly. A similar prevalence (22 %) of abnormal EEGs among workers with exposure to chlorinated hydrocarbons has been found in Israel (43).

Organophosphorus pesticides at the exposure levels most common today do not induce measurable decreases in the blood cholinesterase activity, and it is impossible to measure their actual concentration in the blood or tissues. However, it has been shown electromyographically (14, 32) that organophosphorus pesticides cause a functional abnormality in the neuromuscular junction similar to that noted in the overtreatment of myasthenic patients. Namely, after daily pesticide exposure part of the workers exposed in a formulation plant and in agriculture exhibited a reduction in the amplitude of the first evoked muscle action potential of a short train of stimuli applied after a short voluntary muscle contraction. This phenomenon has been considered mild in degree and only suggestive of a necessity to improve workers' protection.

Only a few reports have listed persistent peripheral neuropathy or psychological defects of central nervous system function in connection with long-term occupational exposure to organophosphorus insecticides (45). The neurophysiological studies of workers in pesticide exposure mainly deal with acute effects, and therefore studies on long-term low-level exposure are lacking. As an international workshop (16) concluded, more studies and new methodology are needed. Also Kimura (34) has stressed the need of more sensitive electrodiagnostic methods for detecting subclinical effects.

Carbon monoxide

Acute carbon monoxide (CO) poisonig may lead to comas of various depths depending on the length and intensity of exposure to CO. During a CO-induced coma and shortly after it EEG abnormalities are common (20). They usually consist of slow waves prominently on the frontal areas. Revol et al. (49) described specific triphasic wave forms in some cases of comatose CO poisoning. The wave form looked similar to that noted in hepatic comas, sometimes called »pseudoparoxysmal spike and wave» or slow spike and wave. The authors thought that it was based on metabolic disturbances and considered it distinguishable from paroxysmal epileptiform discharges. Actually one EEG recording published by Geier et al. (20) had similar features. Epileptic convulsions do not belong to the picture

of acute CO poisoning, and EEG abnormalities disappear with time after an acute episode.

The existence of true chronic CO poisoning is a matter of dispute. Chronic symptoms probably originate from repeated attacks of acute CO poisoning, which might occur in certain work places, e.g., in foundries or garages. Neurophysiological studies on patients from such places are scarce. One report claimed that a policeman exposed to CO in heavy traffic began to suffer from seizures of the psychomotor type and also showed focal spike discharges in his EEG and that these abnormalities were due to chronic CO poisoning (21). Both the man and his EEG became symptomless when CO exposure ceased. In short-time exposure experiments with human volunteers changes in the visual evoked response appeared at a carboxyhemoglobin level greater than 20 % while carboxyhemoglobin levels approaching 33 % did not alter gross spontaneus EEG activity (30).

Acrylamide

When acrylamide was introduced, several workers in the first plant using it developed numbness of the fingers and weakness and unsteadiness of the legs. Because of these symptoms Fullerton and Barnes (19) conducted electrophysiological and histological studies on rats given repeated doses of acrylamide. Concomitantly with the appearance of major clinical symptoms the motor conduction velocity of the sciatic nerve was significantly slowed. A similar slowing of nerve conduction velocity, as well as a decreased excitability and decreased amplitude of the evoked muscle potentials, has been shown in rats and monkeys (38) and in the baboon (29).

Fullerton (18) described electrophysiological findings in human acrylamide poisoning. A slowing of maximal motor conduction velocity was rare, but dispersion of the muscle action potential to nerve stimulation was more striking. She especially noted a disproportionate slowing of conduction in the distal parts of the slower motor fibers. Japanese authors found electrophysiological abnormalities in the sensory conduction of workers handling acrylamide, mainly in the distal portions of the nerve, while disturbances in the motor nerves were slight and rare (69). They also observed a decrease in the amplitude of the muscle potential after stimulation of the motor nerve. Slight EMG abnormalities of a neurogenic type were reported for 7 of the 15 cases studied. Furthermore, slight EEG abnormalities occurred in three workers with complaints of dizziness and ataxic gait.

Lead

Improvements in occupational hygiene have abolished the occurrence of lead palsy in modern industry, but several studies have shown that subclinical lead neuropathy still exists. A reduction in the MCV of the ulnar nerve has been observed in some patients with lead poisoning, but without clinical neurological symptoms (62).

Since it has been shown in animal experiments (17, 51) that segmental demyelination can be found in some nerve fibers only, more refined techniques than measuring the MCV are needed in occupational medicine. More sensitivity was gained by Catton et al. (8), who showed a diminished ratio of the muscle action potential amplitudes following stimulation of the lateral popliteal nerve at the knee and at the ankle. This diminished ratio represented temporal dispersion in the muscle action potential and thus a slowing in some fibers of the nerve in question. The same phenomenon, slowing in a part of the nerve fibers, namely, in the slower fibers (CVSF) of the ulnar nerve has been demonstrated (fig. 4) in patients with lead poisoning at the Institute of Occupational Health in Helsinki as well (56). We also found some slowing in the MCVs of the arm nerves when a group of patients with lead poisoning was compared to a control group. A more distinct abnormality was found in the motor distal latency of the median nerve of patients with lead poisoning. A discriminant function analysis proved that the CVSF of the ulnar nerve and the motor distal latency of the median nerve formed the best combination for separating the cases of lead poisoning from the controls.

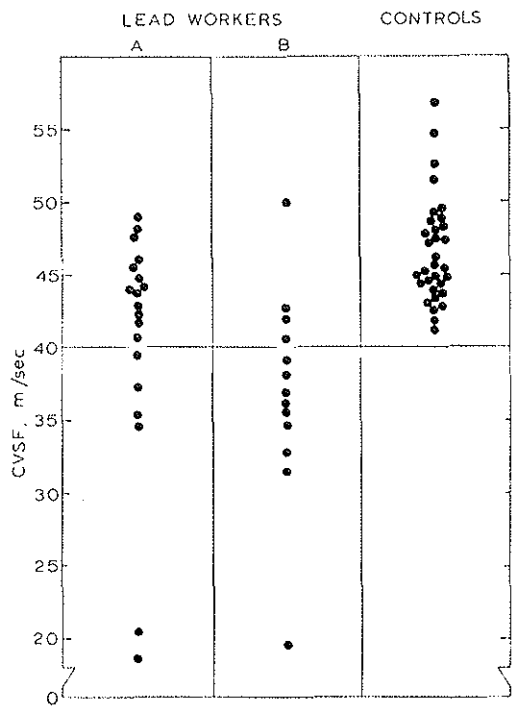

Fig. 4. CVSF of the right ulnar nerve of lead workers A, lead workers B, and normal controls. Lead workers A = first episode of excessive absorption or poisoning; lead workers B = subjects with one or more previous episodes of lead poisoning. [Reprinted from SEPPÄLÄINEN, A. M. and HERNBERG, S. *Br. j. ind. med.* 29 (1972) 443—449]

Recently, our team discovered partial damage of the ulnar nerve in lead workers whose blood lead levels had never exceeded 70 μg/100 ml during their entire period of exposure (mean exposure time : 4.6 years), ascertained by regular monitoring (59). Thus even blood lead levels previously regarded as safe do not necessarily protect the nervous system from slight damage.

Vasilescu (72) stressed the specific affection of lead to the radial nerve, but his study included subjects who had ingested illicitly distilled alcohol contaminated from leaded pipes. Thus the neurotoxic effect of other impurities in the alcohol, and of the alcohol itself, cannot be separated from the effects of lead.

In childhood lead poisoning encephalopathic signs of ataxia, hyperirritability, and lethargy, as well as seizures, are common. Psychological changes and the impairment of fine motor function as well as hyperactivity have been found in young children with slightly elevated blood lead levels (40—60 μg/100 ml) (2, 13, 47).

Dullness, irritability, headache, tremor, loss of memory, etc., have been described as symptoms of adult lead encephalopathy. Even recently lead encephalopathy was reported among heavy drinkers who used lead-contaminated whiskey and in cases of inhaled lead fumes (1, 74). However, EEG studies have not as yet gained interest among investigators of occupational lead poisoning.

Mercury

In the Minamata disease severe neurological symptoms and signs were common (12). However, in the Iraqi methylmercury catastrophe electrophysiological tests 7 to 8 months after the cessation of methylmercury intake did not reveal abnormalities in patients with mercury concentrations of 800 ng/ml or more in their blood (5). The only positive finding was myastheniform failure in the myoneural junction in 2 of the 14 patients studied. The connection of this finding to methylmercury intake requires further study.

Preliminary results from our laboratory show a frequent occurrence of a prolonged latency of muscle action potential after the stimulation of the facial nerve in fishermen with elevated blood mercury levels.

Neuropathological studies of rats by Cavanagh and Chen (9) have shown distinct differences in the pattern of neurotoxic degeneration caused by methylmercury as compared to other neurotoxic agents. The degenerative lesions after methylmercury intake were almost entirely confined to the primary sensory neurons of the dorsal root and trigeminal ganglia and to the granular cells of the cerebellar cortex. Even at an early stage the whole fiber was simultaneously undergoing fragmentation. The motor fibers seemed to be preserved intact. If the lesion caused by methylmercury is located almost exclusively in the sensory fibers in humans too, the lack of distinct findings in ENMG studies so far would be explained.

Only occasional reports of EEG studies in cases of metallic mercury exposure have been published. Some authors claim a

high prevalence of abnormal EEGs in chronic poisoning with metallic mercury or with signs of increased mercury absorption (37). A series of nine workers with metallic mercury vapor intoxication was reported in Florida (73). Their initial signs and symptoms were tremor, rigidity, irritability, memory disturbances, and, rarely, sensory loss. Five of the patients showed diffuse slowing in their EEGs. Slightly slower nerve conduction velocities on a group basis was noted in the distal portion of the median nerve both in motor and sensory fibers as well as in the MCV of the tibial nerve. Mild neurogenic changes were noted in motor unit potentials in the EMG of all the patients, and for five of them the change was statistically significant when compared to the controls.

A power spectra analysis of the surface EMG of workers with inorganic mercury exposure revealed an increased band width (10). A retest after 4 to 6 months in a greatly reduced exposure shifted the EMG band width towards a more normal value.

Carbon disulfide

Several studies have shown a slowing of the maximal motor conduction velocities of the peripheral nerves in subjects with carbon disulfide (CS_2) poisoning (40, 42, 61, 71). EMG investigations have revealed neurogenic abnormalities which have partly been interpreted as signs of damage at the spinal cord level, especially in cases with normal nerve conduction velocities (61). Some disturbance also appeared in the myoneural junction (61), as judged from the fact that abnormal fatigability was demonstrated for several patients with manifest poisoning with the tetanic stimulation test. The nerves of the legs are more often involved in CS_2 neuropathy, as has been shown by Vasilescu (71).

Similar findings of neurotoxicity were found when workers with long-term CS_2 exposure were compared to paper mill workers (60). Both groups were strictly comparable with regard to age, type of work, social background, and other relevant factors. The CS_2 exposed workers, most of whom were actively working and displayed minor complaints only, had significantly slower MCVs in the leg

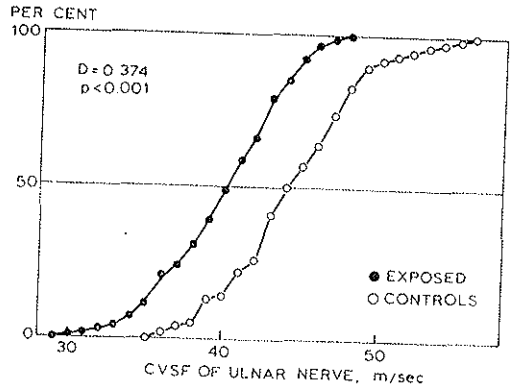

Fig. 5. Cumulative percentage distributions of the conduction velocity of slower motor fibers (CVSF) of the ulnar nerve of the CS_2 exposed and unexposed groups. [Reprinted from SEPPÄLÄINEN, A. M. and TOLONEN, M. *Work-environ.-health* 11 (1974) 145—153]

nerves as well as statistically significant slowing of the CVSF of both the ulnar (fig. 5) and the deep peroneal nerves. Prolongation of the motor distal latency of the median and the ulnar nerves among the CS_2 exposed workers proved that the distal portions of the nerves in the upper limbs were affected as well.

EEGs have been used to detect encephalopathy among workers exposed to CS_2. Stýblová and Holanová (67) found a high percentage of abnormal EEGs, namely, 37 % of 187 workers exposed to CS_2. The prevalence of abnormal EEGs was higher among workers suffering from a temporary or permanent disability as compared to workers who did not require a transfer from exposed work. A Finnish study also showed that 39 % of 54 workers with long-term CS_2 exposure had abnormal EEGs, while in the control group of 50 paper mill workers only 6 abnormal EEGs were found (60). The EEG is thus a suitable tool for demonstrating the toxic encephalopathy caused by CS_2.

Hydrocarbon solvents

Hine and Zuidema (24) tested the toxicological properties of several hydrocarbon solvents in rats and rabbits with oral administration, vapor inhalation, percutaneous administration, aspiration, and skin and eye irritation tests. Acute intoxication

was usually characterized by a depression of central nervous activity followed by incoordination and varying degrees of coma. Convulsions were occasionally seen. Electrophysiological tests were not applied in this study.

Clinical symptoms in long-term exposure to organic solvents are often attributable to central nervous involvement. However, EEG studies of workers with solvent exposure are few. Chalupa et al. (11) published a small series of acute poisonings from CO and industrial solvents; only ten subjects had been exposed to solvents, six of them to trichloroethylene. EEG abnormalities were frequent among the subjects, especially among those with solvent exposure. On the other hand, Mitchell and Parsons-Smith (44) stated that the EEG is usually unaffected. The EEG of a Japanese with a transverse lesion of the spinal cord after accidental exposure to trichloroethylene was reported to be normal also (50).

Benzene compounds induced EEG abnormalities in 40 out of 100 women employed at gluing plastic elements (65). Methylene chloride exposure also caused frequent EEG abnormalities among shoeworkers (22). Preliminary reports from our laboratory (55, 57) have shown a high prevalence of EEG abnormalities among workers with occupational exposure to solvents or with chronic solvent poisoning. Among the 240 subjects studied, EEG abnormalities were more frequent among those with high exposure levels. Affections in the peripheral nervous system were not as common as central nervous involvement, but also polyneuropathic signs in electroneurography increased in number as exposure became higher.

Short-term exposure to 500 to 1,000 ppm of methylene chloride induced changes in the visual evoked response from two of three volunteers (66), the findings were interpreted as signs of central nervous system depression.

Trichloroethylene or some of its breakdown products have caused cranial polyneuropathy, most marked in the fifth cranial nerve, in workers in industry (7, 44, 70). Similar case reports have appeared earlier in connection with general anesthesia of trichloroethylene and soda lime in a closed circuit as cited by Buxton and Hayward (7). These findings indicate that electromyography of facial muscles should be employed in the study of the neurotoxic effects of trichloroethylene.

Japanese authors have shown that n-hexane, especially as a component of glue, causes polyneuropathy. At lower exposure levels (up to 900 ppm) the polyneuropathy is predominantly sensory. With increasing concentrations the motor nerves are also involved and, especially among sniffers, motor polyneuropathy with muscular atrophy is severe. The sensory disturbances were few if any in the four cases reported in the Japanese literature (68). Some Italian bootmakers, working at home or in small factories, also showed motor polyneuropathy and abnormal EMG and MCV findings (6).

The voluntary, repeated inhalation of commercial lacquer thinner caused severe peripheral neuropathy in seven young male sniffers (46). Three of them were completely paralyzed, including bulbar involvement. Nerve conduction velocities were greatly decreased. The authors thought that methyl-amyl-ketone was the component of the thinner responsible for the severe symptoms.

The most severe polyneuropathic symptoms connected with hydrocarbon solvents seem to be caused by high concentrations either in accidental exposure or during sniffing.

Styrene is used in the manufacture of fiber glass products. It belongs to the organic solvent group and also produces neurotoxic symptoms. EEG abnormalities and an increased tendency to sleep have been noted in styrene exposure in Czechoslovakia (35). At the Institute of Occupational Health in Helsinki we have also demonstrated EEG abnormalities, the prevalence of which increased with increasing mandelic acid concentrations in the urine of the workers (58). Peripheral nervous lesions could not be connected to styrene exposure in our study, however.

CONCLUSIONS

The most common lesion of the peripheral nervous system caused by an occupational agent is polyneuropathy. In many instances

the neuropathy is more striking in the distal portions of the nerves, as in the case of lead-, acrylamide-, CS_2- and vibration-induced neuropathy. Only alkyl mercury neuropathy distinctly involves the whole length of the sensory axon at an early stage. In most cases neuropathy at current exposure levels is mild or subclinical; this is displayed well by the fact that more sensitive and more refined techniques are being developed in order to detect the effects of neurotoxic substances.

Myopathy caused by industrial poisonings has not been reported, but disturbances of myoneural juction are found in insecticide exposure and in CS_2 poisoning.

Encephalopathy is no doubt a potential danger, especially in exposure to various solvents — CS_2, styrene or other hydrocarbons — and perhaps in chronic CO exposure. A combination of EEG abnormalities and signs of peripheral neuropathy is suggestive of effects of a neurotoxic substance.

EEG abnormalities with clinical significance are found not only after workdays but also during periods without exposure to toxic chemicals. Within a period of a few months without exposure, EEG abnormalities tend to disappear in most cases, if the toxic effect has not been long-acting and if encephalopathy has not been severe. Normal EEGs in connection with symptoms of the psycho-organic syndrome or dysfunction of the autonomous nervous system are found in a fair number of people, especially when encephalopathy is slowly progressive and mainly involves the deep brain structures. Thus a normal EEG does not rule out toxic encephalopathy.

Neurophysiological methods in occupational medicine are useful in the following aspects:

1) In the study of neurotoxicity of known or new chemicals or the neurological involvement caused by physical factors. Strictly controlled epidemiologic studies of humans or well-planned animal experiments are the most informative. However, the knowledge derived from animal experiments cannot be directly applied to man, since certain species-specific variations in effects are common.

2) In the setting of safety norms. Nervous involvement must always be considered unacceptable, and, when such signs are present, exposure levels should be lowered.

3) In the early diagnosis in cases of suspected occupational diseases. Furthermore, neurophysiological examination may aid in deciding whether or not the patient qualifies for workmen's compensation.

4) In making the decision whether or not a worker may remain exposed. It is important to lower the exposure level, or to stop harmful exposure periodically or totally, early enough to prevent permanent lesions. At an early stage neurotoxic effects are often reversible.

5) In detecting especially vulnerable workers. Persons with nervous system diseases should be excluded from work with exposure to neurotoxic chemicals.

REFERENCES

1. ABED, D., BOLLINELLI, R., BROUSSY, G., CARLES, P. and SORBARA, R. Encéphalopathie saturnine mortelle. A propos d'une observation anatomo-clinique. *Arch. mal. prof.* 34 (1973) 599—608.
2. ALBERT, R. E., SHORE, R. E., SAYERS, A. J., STREHLOW, C., KNEIP, T. J., PASTERNACK, B. S., FRIEDHOFF, A. J., COVAN, F. and CIMINO, J. A. Follow-up of children overexposed to lead. *Environ. health perspect.* 7 (1974) 33—39.
3. ANDREEVA-GALANINA, E. T., and KARPOVA, N. I. On degeneration and regeneration of peripheral nerves under the effect of experimental vibration. *Gig. tr. prof. Zabol.* 13 (1969): 2, 4—7.
4. ANGELERI, F., FALEG, G., GRANATI, A. and LENZI, R. Aspects expérimentaux des effets du bruit sur le système nerveux central. *Acta otorhinolaryngol. belg.* 25 (1971) 221—232.
5. BAKIR, F., DAMLUJI, S. F., AMIN-ZAKI, L., MURTADHA, M., KHALIDI, A., AL-RAWI, N.Y., TIKRILI, S., DHAHIR, H. I., CLARKSON, T. W., SMITH, J. C. and DOHERTY, R. A. Methylmercury poisoning in Iraq. *Science* 181 (1973) 230—241.
6. BATTISTINI, N., LENZI, G. L., ZANETTE, E., FIESCHI, C., BATTISTA, F., FRANZINELLI, A. and SARTORELLI, E. Some observations on polyneuropathies due to organic glues. *Abstracts: 2nd industrial and environmental neurology congress,* Prague-Czechoslovakia 1974, p. 6.
7. BUXTON, P. H. and HAYWARD, M. Polyneuritis cranialis associated with industrial trichloroethylene poisoning. *J. neurol. neurosurg. psychiatry* 30 (1967) 511—518.
8. CATTON, M. J., HARRISON, M. J. G.,

FULLERTON, P. M., and KAZANTZIS, G. Subclinical neuropathy in lead workers. *Br. med. j.* 2 (1970) 80—82.
9. CAVANAGH, J. B. and CHEN, F. C. K. The effects of methyl-mercury-dicyandiamide on the peripheral nerves and spinal cord of rats. *Acta neuropathol.* (Berl.) 19 (1971) 208—215.
10. CHAFFIN, D. B. and MILLER, J. M. Behavioral and neurological evaluation of workers exposed to inorganic mercury. In: C. XINTARAS, B. L. JOHNSON and I. DE GROOT (eds.), *Behavioral toxicology.* U. S. Department of Health, Education and Welfare, Washington, D. C. 1974, pp. 214—239.
11. CHALUPA, B., SYNKOVÁ, J. and SEVČIK, M. The assessment of electroencephalographic changes and memory disturbances in acute intoxications with industrial poisons. *Br. j. ind. med.* 17 (1960) 238—241.
12. DALES, L. G. The neurotoxicity of alkyl mercury compounds. *Am. j. med.* 53 (1972) 219—232.
13. DAVID, O., CLARK, J. and VOELLER, K. Lead and hyperactivity. *Lancet* II (1972) 900—903.
14. DRENTH, H. J., ENSBERG, I. F. G., ROBERTS, D. V. and WILSON, A. Neuromuscular function in agricultural workers using pesticides. *Arch. environ. health* 25 (1972) 395—398.
15. DYLEWSKA, D. The study of conduction in the motor and sensory nerves of upper limbs in vibration disease [In Polish]. *Neurol. neurochir. pol.* 4 (1970) 28—31.
16. Epidemiological toxicology of pesticide exposure: Report of an international workshop. *Arch. environ. health* 25 (1972) 399—405.
17. FULLERTON, P. M. Chronic peripheral neuropathy produced by lead poisoning in guinea-pigs. *J. neuropathol. exp. neurol.* 25 (1966) 214—236.
18. FULLERTON, P. M. Electrophysiological and histological observations on peripheral nerves in acrylamide poisoning in man. *J. neurol. neurosurg. psychiatry* 32 (1969) 186—192.
19. FULLERTON, P. M. and BARNES, J. M. Peripheral neuropathy in rats produced by acrylamide. *Br. j. ind. med.* 23 (1966) 210—221.
20. GEIER, S., TUTIN, M., PASQUIER, P., NAJMAN, A., FOURNIER, A. and BOUR, H. Les aspects électro-encéphalographiques au cours des intoxications oxycarbonées aigues et ses sequelles. *Anesth. analg.* (Paris) 23 (1966) 241—251.
21. GILBERT, G. J. and GLASER, G. H. Neurologic manifestations of chronic carbon monoxide poisoning. *N. engl. j. med.* 261 (1959) 1217—1220.
22. HANKE, C., RUPPE, K. and OTTO, J. Untersuchungen zur toxischen Wirkung von Dichlormethan bei Fussbodenlegern. *Z. gesamte Hyg.* 20 (1974) 81—84.
23. HILL, D. and PARR, G. *Electroencephalography.* MacDonald, London 1963.
24. HINE, C. H. and ZUIDEMA, H. H. The toxicological properties of hydrocarbon solvents. *Ind. med. surg.* 39 (1970) 215—220.
25. HOOGENDAM, I., VERSTEEG, J. P. J. and DE VLIEGER, M. Electroencephalograms in insecticide toxicity. *Arch. environ. health* 4 (1962) 86—94.
26. HOOGENDAM, I., VERSTEEG, J. P. J. and DE VLIEGER, M. Nine years' toxicity control in insecticide plants. *Arch. environ. health* 10 (1965) 441—448.
27. HOPF, H. C. Untersuchungen über die Unterschiede in der Leitgeschwindigkeit motorischer Nervenfasern beim Menschen. *Dtsch. Z. Nervenkeilkd.* 183 (1962) 579—588.
28. HOPF, H. C. and STRUPPLER, A. (eds.). *Elektromyographie.* Georg Thieme Verlag, Stuttgart 1974. 229 p.
29. HOPKINS, A. P. and GILLIATT, R. W. Motor and sensory conduction velocity in the baboon: Normal values and changes during acrylamide neuropathy. *J. neurol. neurosurg. psychiatry* 34 (1971) 415—426.
30. HOSKO, M. J. The effect of carbon monoxide exposure on the visual evoked response in man: And the spontaneous electroencephalogram. *Arch. environ. health* 21 (1970) 174—180.
31. HYVÄRINEN, J., PYYKKÖ, I. and SUNDBERG, S. Vibration frequencies and amplitudes in the aetiology of traumatic vasospastic disease. *Lancet* I (1973) 791—794.
32. JAGER, K. W., ROBERTS, D. V. and WILSON, A. Neuromuscular function in pesticide workers. *Br. j. ind. med.* 27 (1970) 273—278.
33. KILOH, L. G. and OSSELTON, J. W. *Clinical electroencephalography.* Butterworths, London 1966. 147 p.
34. KIMURA, J. Electrodiagnostic study of pesticide toxicity. In: C. XINTARAS, B. L. JOHNSON and I. DE GROOT (eds.), *Behavioral toxicology.* U. S. Department of Health, Education and Welfare, Washington, D. C. 1974, pp. 174—181.
35. KLIMKOVÁ-DEUTSCHOVÁ, E., JANDOVÁ, D. SALCMANOVÁ, Z., SCHWARTZOVÁ, K. and TITMAN, O. Recent data concerning the neurological picture of occupational styrene exposure. *Cesk. neurol.* 36 (1973) 20—25.
36. KUŽEL, V., LUKÁŠ, E. and NEDVIDKOVÁ, H. Vergleichung der Befunde auf dem peripheren Nervensystem der oberen Gliedmassen bei Personen mit professioneller und nichtprofessioneller Vasoneurose. *Abstracts: 2nd industrial and environmental neurology congress,* Prague-Czechoslovakia 1974, p. 60.
37. LANGAUER-LEWOWICKA, H. and GRUDZINSKA, B. Clinical and electroencephalographic correlations in chronic poisoning with metallic mercury. *Med. pr.* 24 (1973) 337—342.
38. LESWING, R. J. and RIBELIN, W. E. Physiologic and pathologic changes in

acrylamide neuropathy. *Arch. environ. health* 18 (1969) 22—29.
39. LIDSTRÖM, I.-M. Lokala vibrationers inverkan på övre extremiteterna *Arbete och hälsa* (1974) 8, 128 pp.
40. LUKÁŠ, E. Leitgeschwindigkeit peripherer Nerven bei Schwefelkohlenstoff ausgesetzten Personen. *Int. j. clin. pharmacol. ther. & toxicol.* 2 (1969) 354—358.
41. LUKÁŠ, E. and KUŽEL, V. Klinische und elektromyographische Diagnostik der Schädigung des peripheren Nervensystems durch lokale Vibration. *Int. Arch. Arbeitsmed.* 28 (1971) 239—249.
42. MANU, P., LILIS, R., LANCRANJAN, I., IONESCU, S. and VASILESCU, I. The value of electromyographic changes in the early diagnosis of carbon disulphide peripheral neuropathy. *Med. lav.* 61 (1970) 102—108.
43. MAYERSDORF, A. and ISRAELI, R. Toxic effects of chlorinated hydrocarbon insecticides on the human electroencephalogram. *Arch. environ. health* 28 (1974) 159—163.
44. MITCHELL, A. B. S. and PARSONS-SMITH, B. G. Trichlorethylene neuropathy. *Br. med. j.* 1 (1969) 422—423.
45. NAMBA, T., NOLTE, C. T., JACKREL, J. and GROB, D. Poisoning due to organophosphate insecticides. *Am. j. med.* 50 (1971) 475—492.
46. PROCKOP, L., ALT, M. and TISON, J. Peripheral neuropathy secondary to lacquer thinner inhalation. *Abstracts: 2nd industrial and environmental neurology congress.* Prague-Czechoslovakia 1974, p. 80.
47. PUESCHEL, S. M. Neurological and psychomotor functions in children with increased lead burden. *Environ. health perspect.* 7 (1974) 13—16.
48. RADZUYKEVICH, T. M. and MIKULINSKY, A. M. Sensitivity to vibration in workers exposed to the effect of vibration of dissimilar spectral composition and practically healthy subjects of different age. *Gig. tr. prof. zabol.* 16 (1972) 16—20.
49. REVOL, M., MONIER, P., COURJON, J., FOURNET, A. and GERIN, P. L'E.E.G. dans l'intoxication oxycarbonée aigue. *Anesth. analg.* (Paris) 23 (1966) 235—239.
50. SAGAWA, K., NISHITANI, H., KAWAI, H., KUGE, Y. and IKEDA, M. Transverse lesion of the spinal cord after accidental exposure to trichloroethylene. *Int. Arch. Arbeitsmed.* 31 (1973) 257—264.
51. SCHLAEPFER, W. W. Experimental lead neuropathy: A disease of the supporting cells in the peripheral nervous system. *J. neuropathol. exp. neurol.* 28 (1969) 401—418.
52. SEM-JACOBSEN, C. W. Sudden, alarming noise: Effect on brain functions and EEG changes. *Acta otorhinolaryngol. belg.* 25 (1971) 218—220.
53. SEPPÄLÄINEN, A. M. Nerve conduction in the vibration syndrome. *Work-environ. -health* 7 (1970) 82—84.
54. SEPPÄLÄINEN, A. M. Peripheral neuropathy in forest workers: A field study. *Work-environ.-health* 9 (1972) 106—111.
55. SEPPÄLÄINEN, A. M. Neurotoxic effects of industrial solvents. *Electroencephalogr. clin. neurophysiol.* 34 (1973) 702—703.
56. SEPPÄLÄINEN, A. M. and HERNBERG, S. Sensitive technique for detecting subclinical lead neuropathy. *Br. j. ind. med.* 29 (1972) 443—449.
57. SEPPÄLÄINEN, A. M., HINTZE, G. and LINDSTRÖM, K. Sensitive methods for evaluation of subclinical effects of solvents. Paper presented at the international conference of occupational health, Slanchev Bryag, Bulgaria 1971.
58. SEPPÄLÄINEN, A. M. and HÄRKÖNEN, H. Neurotoxicity of styrene in humans. *Abstracts: 2nd industrial and environmental neurology congress,* Prague-Czechoslovakia 1974. p. 88.
59. SEPPÄLÄINEN, A. M., TOLA, S., HERNBERG, S. and KOCK, B. Subclinical neuropathy at «safe» levels of lead exposure. *Arch. environ. health* 1975, in press.
60. SEPPÄLÄINEN, A. M. and TOLONEN, M. Neurotoxicity of long-term exposure to carbon disulfide in the viscose rayon industry: A neurophysiological study. *Work-environ.-health* 11 (1974) 145—153.
61. SEPPÄLÄINEN, A. M., TOLONEN, M., KARLI, P., HÄNNINEN, H. and HERNBERG, S. Neurophysiological findings in chronic carbon disulfide poisoning: A descriptive study. *Work-environ.-health* 9 (1972) 71—75.
62. SESSA, T., FERRARI, E. and COLUCCI D'AMATO C. Velocita'di conduzione nervosa nei saturnini. *Folia med.* 48 (1965) 658—668.
63. SILVERMAN, C. Nervous and behavioral effects of microwave radiation in humans. *Am. j. epidemiol.* 97 (1973) 219—224.
64. SMORTO, M. P. and BASMAJIAN, J. V. *Clinical electroneurography.* Williams & Wilkins, Baltimore, Md. 1972. 234 p.
65. SOBCZYK, W., SIEDLECKA, B., GAJEWSKA, Z. et al. EEG recordings in workers exposed to benzene compounds. *Med. pr.* 24 (1973) 273—283.
66. STEWART, R. D., FISHER, T. N., HOSKO, M. J., PETERSON, J. E., BARETTA, E. D. and DODD, H. C. Experimental human exposure to methylene chloride. *Arch. environ. health* 25 (1972) 342—348.
67. STÝBLOVÁ, V. and HOLANOVÁ, V. The electroencephalogram of workers exposed to carbon disulfide. *Prac. lék.* 25 (1973) 90—96.
68. SUZUKI, T., SHIMBO, S., NISHITANI, H., OGA, T., IMAMURA, T. and IKEDA, M. Muscular atrophy due to glue sniffing. *Int. Arch. Arbeitsmed.* 33 (1974) 115—123.
69. TAKAHASHI, M., OHARA, T. and HASHIMOTO, K. Electrophysiological study of nerve injuries in workers handling acrylamide. *Int. Arch. Arbeitsmed.* 28 (1971) 1—11.
70. TOMASINI, M. and SARTORELLI, E. In-

tossicazione cronica da inalazione di trielina commerciale con compromissione dell VIII paio di nervi cranici. *Med. lav.* 62 (1971) 277—280.
71. VASILESCU, C. Motor nerve conduction velocity and electromyogram in carbon disulphide poisoning. *Rev. roum. neurol.* 9 (1972) 63—71.
72. VASILESCU, C. Motor nerve conduction velocity and electromyogram in chronic lead poisoning. *Rev. roum. neurol.* 10 (1973) 221—226.
73. VROOM, F. Q. and GREER, M. Mercury vapour intoxication. *Brain* 95 (1972) 305—318.
74. WHITFIELD, C. L., CH'IEN, L. T. and WHITEHEAD, J. D. Lead encephalopathy in adults. *Am. j. med.* 52 (1972) 289—298.

Received for publication: 1975-01-02