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IDENTIFICATION AND ASSESSMENT OF WORK-RELATED NERVOUS SYSTEM LESIONS

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Abstract. Short historical data on occupational neurotoxicology, as well as on the pathogenic mechanisms of the nervous system impairments due to occupational factors are described. The main difficulties in the assessment of peripheral and central nervous system lesions are stressed.

Key words:
Neurotoxicology, Industrial neurology, Occupational neurotoxicants

INTRODUCTION

A comprehensive presentation of any subject should include its historical aspects. With regard to the work-related nervous system lesions this may not be possible, as neurological symptomatology constitutes an essential part of occupational pathology. Hence the earliest descriptions of diseases induced by occupational exposure may be regarded as a valid source of information about the nervous system impairments.

Long before hematological impairment due to lead exposure had been known, a detailed description of neurological symptoms was given by Nikander, an ancient Greek physician (4000 years ago).

In the European literature first reports on morbid symptoms which, according to contemporary knowledge, may be regarded as lead intoxication had appeared about 300 years before lead was considered a toxic agent. The described symptoms included severe encephalopathy with optic nerve atrophy, as well as pareses, symptoms rarely noticed nowadays in cases of saturnism.

The end of the 19th century witnessed the separation of neurology from internal medicine. Since then it has become an independent medical science. This fact marked the beginning of interest in potential neurological effects of occupational hazards. This was finally followed by the development of occupational medicine, as well as by the establishment of research centers dealing exclusively with this issue. The appointment of the Research Group on Industrial Neurology within the World Federation on Neurology as a result of growing interest in neurological aspect of occupational diseases proved to be one of the successive steps. The Group was established on the initiative of Eliska Klimkova-Deutschova from Prague, who held the position of its president for many years [1]. In Poland, the idea was promoted at the beginning of the 1960s, by Władysław Chłopicki, the then head of the Neurological Clinic of the Silesian Medical Academy [2].

The first handbook of industrial neurology in Europe, entitled ”Casna diagnoza u prumyslove neurologii”* was published in Prague, Czechoslovakia in 1965. In Poland, the most important textbook on ”Occupational Diseases of the Nervous System” was written by A. Prusiński in 1971.

* Early Diagnosis in Industrial Neurology.

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Numerous occupational factors may exert an adverse effect on the nervous system. The most prevalent are physical and chemical agents. While considering occupational hazards one should emphasize, that in the 21st century the environmental contamination may supersede the occupational one. Nowadays lead contamination is one hundred times higher than it was in the primitive man era. The adverse effect of drug addiction and abuse, as well as the high incidence of traumas, resulting from traffic accidents should also be taken into consideration. In view of the above, the evaluation of the nervous system lesions could be difficult or even impossible using an individual approach. The problem becomes even more complex and demanding when either multiple chemical agents or combined exposure to both chemical and physical hazards are involved [3,4].

The determination of etiology of the nervous system lesions is further hindered by the fact that the response of neuronal structures to any noxious agents is a non-specific one [3]. The nervous system impairments may be of functional or organic nature. With regard to the organic disorders, they may be manifested by peripheral neuron lesions (mono- or poly-neuropathies) and related to either of the central structures (CNS) or both the central and peripheral neurons [5,6].

The CNS changes may be manifested by the following syndromes: pyramidal (saturnism, solvent syndrom), extrapyramidal (manganese poisoning), cerebellar (metal mercury intoxication) and mixed lesions (carbon disulfide poisoning). Psychoses occur mainly in acute and sub-acute poisonings.

The so-called functional changes defined as neurotic, pseudoneurotic, or psychasthenic syndromes pose serious problems to occupational medicine. The high incidence of such disorders in the general population may be related to the conditions arising from modern civilization accompanied by all its side- effects.

The number of neurotoxic substances is growing every year, as the syntheses of new compounds continue. Practically, every new substance should be suspected of neurotoxic effect. It seems that both the clinicians and toxicologists must constantly be on the alert. It is often the physician, not the toxicologist who discovers the toxic effect of a given compound. Such was the case of n-hexane. It was used in shoe-making factories. This compound was not considered to be toxic until 1965 when a series of severe polyneuropathies was reported among Japanese workers producing sandals. At first, the symptoms were thoughts to be of viral etiology, but soon appeared that similar cases were reported in other shoe factories not only in Japan, but also in other countries. Since that time, MAC value for n-hexane has been established [7,8].

This short history of n-hexane polyneuropathy gives rise to the question on whether one could not predict toxic effect of a chemical agent with special regard to its neurotoxicity.

One of the contemporary toxicologists maintains that toxicology is an exciting intellectual rivalry and requires not only the perfection in developing particular elements, but also the capability of using them to build conceptual structures.

However, despite of continuous progress of research, the possibility of determining accurately the nervous system lesions is limited by scarce information on selective sensitivity of different cell types. This would be less complicated if a direct relationship between the concentration of a given agent in the workplace and the dose absorbed and the biological response would have exist.

Toxicity however, depends on numerous factors, including absorption, distribution in body organs, metabolic transformation and excretion. As to the nervous system, another factor is very important, namely the blood-brain barrier. Its permeability to some toxins has not as yet been sufficiently elucidated [9]. This also applies to individual predispositions that may be determined genetically. Different reactions to toxic stimuli because of sex differences are also taken into account. Lead is one of heavy metals that should be mentioned here. For example, a slower conduction velocity of cubical and fibular nerves in women than in men has been reported, although PbB in women reached half of the levels found in men [10].

As to neurotoxic area, the simple dose-response relationship cannot be expected since it is mostly dependent on the pathogenic mechanism. The toxic agents may:

- produce disturbances in oxidative processes and co-enzyme inhibition – the dose-depending response (e.g. lead);
- evoke allergic or immunological effects (calomel-Guillain-Barré syndrome type, vinyl chloride- scleroderma-like changes);
- produce primary and secondary impairments leading to vascular disturbances (eg. CS_2).

Neurotoxicity can be already manifested at a cellular level. Normal intracellular metabolism is the sum of all enzymatic reactions accompanying energetic exchange between the cell and its surroundings. High molecular compounds (enzymes, nucleid, acids) play an essential role in the adaptation processes that probably help to maintain human existence despite the deterioration of environmental conditions.

The detection of cellular disturbances, resulting from chronic exposure to neurotoxins (metals, ketons, aliphatic and aromatic hydrocarbons) is fairly easy in experiments on monocellular organisms. Neuron, a nervous cell with neuroaxons, is a dynamic structure. There occur perikaryotic processes of protein synthesis and protein transfer in ortho- and retrograde direction. This provides a proper impulse to the conduction, reception and maintenance of morphological structure [4].

The disturbances within the CNS structures at a cellular level may lead to subjective changes in emotional and cognitive spheres up to organic lesions, which can be detected by psychological tests. The behavioral toxicology seems to be a sensitive method for monitoring early neurotoxicity [11–14].

Another problem the psychologists deal with is the applicability of testing for neurotoxicity assessment, as well as the value of such a methodology. The electrophysiological methods were brought into practice for evaluating the state of neurons in the central and peripheral nervous systems. These methods are applied not only in the clinical diagnostics but also in the detection of early sub-clinical changes in the nervous system.

The neurophysiological methods used in the detection of early neurological impairments include mainly: electroencephalography (EEG), electroneuromyography (ENMG) and multimodal evoked potentials [15–17].

While considering the EEG findings in workers exposed to noxious agents, one should be aware that slight abnormalities or borderline recordings may occur in 10–20% of the general population. Isolated EEG abnormality cannot be decisive for diagnosis of a work-related disease. Higher frequency of abnormal EEG in the examined group as compared to the controls indicates the necessity to undertake relevant preventive measures. The EEG should be obligatory in the pre-employment examination for workers exposed to agents affecting the nervous system (mercury, solvents, electromagnetic fields). The most important information may be obtained during long-term EEG monitoring. In such a case even slight abnormalities should be regarded as early sub-clinical changes in the central nervous system.

The state of peripheral neurons can be determined on the basis of neurological examinations, both clinical and electrophysiological. The former allow to detect only advanced lesions, whereas the latter, also display sub-clinical symptoms. Electroneuromyography is useful for early detection of biological response to noxious agents, determination and verification of hygiene standards, evaluation of pathomechanism of adverse effects due to exposure to some noxious agents, as well as for application in experimental and epidemiological studies. The ENMG examination is undoubtedly very helpful in the neurological practice. The problem arises with proper interpretation, especially in the case of slight conduction velocity slowing down in an exposed person. There are many non-occupational agents, which may influence the neuronal transmission. It is generally presumed that slower conduction within one of the nerves can be found in 10–15% of the general population. Moreover, there also are some genetic predispositions. In hereditary neuropathies, single nerve conduction velocity may reach even 50% of the normal value without clinical symptoms of neuropathy.

Nevertheless, ENMG is very useful for monitoring workers occupationally exposed to noxious agents. A higher percentage of abnormal values in the exposed group than in controls may be regarded as an ”indicator” of occupa-

tional risk or may even imply the necessity to verify hygiene standards [15,18,19].

Electrophysiologic neuropathies due to occupational factors do not differ from neuropathies of other etiology, which pose a serious diagnostic problem.

Work-related chronic neuropathies are induced by chemical agents and physical factors. The epidemiology of particular occupational neuropathies cannot be precisely defined due to the fact that non-occupational factors, synergistic or masking effects in combined exposure and individual susceptibility very often overlap one another. In the majority of occupational neuropathies it is not possible to determine the dose-response relationship. However in organic lead exposure, the correlation between blood lead concentration and nerve conduction velocity, particularly of sensory fibers, has been determined.

At present, lead-induced neuropathies are only of subclinical type. As a rule, the locomotor function is not impaired. An opinion is widely shared that inorganic mercury does not produce lesions of peripheral nerves. Experience of other authors shows that neuropathies with slight conduction velocity slow down radial, median and cubical motor fibers [20,21].

Such chemicals as organic solvents from the group of aliphatic and aromatic hydrocarbons, as well as alcohols and ketones exhibit high affinity to peripheral neurons [19]. Severe polyneural impairments with motor lesions are caused by n-hexane. Triorthocresylphosphate usually induces intense neuropathies with paresis. In chronic CS_2 intoxication neuropathies are also of sub-clinical type. Severe cases of neuropathies with locomotor impairments recorded in the first half of the 20th century are no longer observed [15,18].

The application of multimodal evoked potentials can also be very useful in the assessment of adverse effects of occupational factors [22]. The method of evoked potentials, somatosensory, visual and auditory, provides the possibility to define the anatomical site of the sensory pathway impairment from the receptor to the cortical centre. Due to its high sensitivity, electrophysiological technique is a valuable tool in estimating neuronal transmission velocity. The method of multimodal evoked potentials has been successfully applied in evaluating subclinical disorders of sensory pathways, it may also be essential in detecting adverse effects of occupational factors, especially of toxic agents. According to many authors, this method facilitates the determination of a direct relationship between very low blood lead concentration (PbB 6–52 µg/dl) and abnormal values of somatosensory evoked potentials.

Abnormal values of visual evoked potentials and brainstem evoked potentials were reported in persons exposed to metallic mercury vapors [17].

It is important to stress that the nervous system response to various noxious agents is non-specific. This fact does not facilitate the diagnosis of occupational disease. The disorders due to occupational agents may take a form of chronic neuropathies, encephalopathies or encephalopolyneuropathies, while psychoses are very rarely observed. Moreover, no neurological syndromes may be regarded as specific for adverse affect of any noxious agent. Only a detailed analysis of sufficient amount of clinical signs, laboratory and electrophysiological findings may allow to relate a particular clinical picture to etiology of a respective case.

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