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MULTI-LEVEL DAMAGE OF PERIPHERAL NERVOUS SYSTEM IN CLINICAL PRACTICE OF NAVAL AND MILITARY MEDICINE

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Damage to the peripheral nerves and spinal roots in natural anatomical tunnels is not only a common form of damage to the nervous system, but also an important medical and social problem; because tunnel neuropathy and degenerative-dystrophic diseases of the spine are the most common reasons for draft exemption, dismissing from the Armed Forces of the Russian Federation, seafarers, changes in the category of fitness for military service. According to various authors, a compression- ischemic neuropathy combined with signs of spinal cord disorders occurs in 30 - 70% of cases with tunnel syndromes. This is especially relevant for seafarers, because they are more likely to have musculo-skeletal/mobility disabilities, as long-term, monotonous load can lead to micro-traumatization and microbleeding, followed by scarring of muscles, tendons, ligaments, fascia and, as a consequence, the narrowing of natural anatomical tunnels. Relationship between the work at sea and the frequency of injuries of spinal cord and shoulder girdle with the rotational cuff syndrome and tunnel syndromes was revealed. In military personnel, this may occur during excessively long compression of the upper arms when shooting, training, working in low temperatures and vibration.
Key words: marine medicine, tunnel syndrome, radiculopathy, polyneuropathy, double crash syndrome, multifocal neuropathy, myelopathy.

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Damage to the peripheral nerves and spinal roots in natural anatomical tunnels is not only a common form of damage to the nervous system, but also an important medical and social problem. Degenerative-dystrophic diseases of the spine and musculoskeletal system are one of the most common reasons for the release of citizens from the draft call, the dismissal of military personnel from the Armed Forces of the Russian Federation, seafarers, changes in the category of fitness for military service.

According to various sources, this circumstance is due to the fact that lesions of peripheral nerves and plexuses in everyday clinical practice take up to 60% of all diseases of the nervous system. According to the research, tunnel neuropathy and radiculopathy are the most common forms of damage to the nerve trunks, but their etiology is established only in 75% of cases and then only in specialized hospitals [1, pp. 31–36]. There are zones of increased vulnerability of the peripheral nerves and spinal roots - anatomically narrow channels (tunnels) formed by bones, muscles, fascia and ligaments in the human body. Compression in these zones can lead to mechanical deformation and prolonged ischemia of the nerve fibers, which ultimately contributes to the formation of foci of local demyelination with the formation of impulse transmission blocks. According to the literature, tunnel syndromes lead to temporary, and in some cases, permanent disability of citizens, including military personnel and seafarers [2, pp. 37–38]; moreover, today they are also one of the urgent problems of modern traumatology, accounting for 3–10% of all complications of injuries of the musculoskeletal system [3, pp. 557-562]. According to some authors, the majority of patients (up to 80%) with lesions of the peripheral nervous system (PNS) are young people of working age [4, pp.31-41].

According to published research results, tunnel neuropathies and radiculopathies occur not only as a result of injuries, but are a polyetiological pathology that includes a large number of somatic diseases, such as endocrine disorders (diabetes, hypothyroidism), diffuse connective tissue diseases (primarily nodular polyarteritis, systemic scleroderma and systemic lupus erythematosus), rheumatoid arthritis, deforming osteoarthritis, gout. According to most authors, somatic pathology induces an increase in osmotic intra-neural pressure, especially in case of diabetes (due to the accumulation of sorbitol), with the gradual development of nerve edema and tendons, which causes a volume discrepancy between the inner space of the

tunnel and its contents, followed by compression, development of hypoxia and nerve ischemia. This mechanism explains the frequent cases of tunnel neuropathy and radiculopathy in diabetes.

According to foreign literature data, patients with chronic renal failure 3–5 years after the start of program hemodialysis may develop amyloid disease. Attention is drawn to the fact that amyloid infiltration of the synovial membrane within the tunnel channels is a factor contributing to nerve compression [5, pp. 1090-1094]. Local factors leading to compression of nerves or spinal roots, including spondyloarthrosis, changes in the ligament and fascial apparatus, and muscles are also noted.

The acquired pathology of the musculoskeletal system is particularly relevant in the formation of various lesions of the PNS in seafarers. According to research hold by L. Kaerlev and colleagues, the most common diseases among seafarers are the lesions of the musculoskeletal system, various injuries and poisonings. The relationship between the work at sea and the frequency of injuries of spinal cord and shoulder girdle with the syndrome of rotational cuff and tunnel neuropathies is also noted [6, p.8]. Attention is drawn to the fact that a long, monotonous load when being on duty contributes to microtraumatization and microbleeding with subsequent scarring of muscles, tendons, ligaments, fascia and, consequently, the narrowing of natural anatomical tunnels.

It is known that the risk of damage to the PNS, including that among military personnel, is relatively increasing during an excessively long compression of the upper parts of the arms during firing, training, working in the conditions of vibration and low temperatures. So, hypothermia leads to spasm of arterioles and stasis of perineurium capillaries, which leads to disorder of endothelium permeability [7, pp. 522]. It was repeatedly emphasized that the service in the fleet is connected with an additional psychological burden that is a cause of frequent alcoholization among personnel [8, pp. 26-29]. Thus, alcohol abuse can lead to an increase in the sensitivity of nerve fibers to the negative effects of occupational factors, which increase the risk of neuropathy, radiculopathy, polyneuropathy and their severity [9, pp. 26–31].

According to numerous scientific publications, alcoholic polyneuropathy is formed by the direct toxic effect of ethanol and its metabolites (acetaldehyde) on peripheral nerves. Lack of intake of thiamine, including that associated with an unbalanced diet, also plays a significant role. At present, the question of the rational nutrition of the personnel of ships and submarines on long voyages has not been fully solved. As studies have shown [2, pp. 27–38; 10, pp. 776–783], a decrease in the resistance of PNS to various negative influences of the environment and professional activity can develop with a deficiency of B vitamins. The military personnel, whose work is associated with numerous adverse factors (transportation of weights, performing uniform movements, forced posture, fluctuations in ambient temperature), suffer from early development of degenerative-dystrophic changes of the spine. The senior officers often do staff work that is connected with a sedentary lifestyle accompanied with high psycho-emotional stress. The interrelation of insufficient physical activity with the development of neurological complications of degenerative-dystrophic diseases of the spine was noted [10, pp. 776-783]. It is known that the prolonged exposure of various kinds of physical factors to seafarer is an integral part of a sailoring [12, pp. 12-26; 13, pp. 534-545]. For example, regular local influence of vibration can play a huge role in the formation of tunnel syndromes and sensory polyneuropathy [1, pp. 31–36; 14, pp. 131–139; 15, pp. 31–34]. According to experimental data, the vibration causes an increased excitability of the receptors and leads to a disturbance of the regulatory effects of the central nervous system on the vascular tone and, as a result, to nerve dystrophic changes [14, pp. 131–139] (Table).

Table

Some unfavorable factors of military service, which may contribute to peripheral nervous system damage

Unfavorable factors of military service	Some aspects of the pathogenesis of a disease	Preventive measures
Natural: — cold; — change of atmosphere pressure; — change of temperature; — high humidity	Hypothermia leads to spasm of arterioles and stasis of perineurium capillaries, which leads to a violation of their permeability	Proper uniform for military personnel, elimination of their long-term outdoor

Technical: — vibration; —microwave electromagnetic interference (SHF EMI) — ionizing radiation; — heavy metals, organic substances	Vibration causes an increased excitability of the receptors, that interrupts the regulatory effects of the central nervous system on vascular tone and, as a result, trophic nerves.	Eliminate the long-term effects of these factors, comply with the regimes of work and rest of military personnel
Social: — chronic stress; — mental strain; — closed collective	Disorders of the mediator and immune processes, changes in tissue metabolism, energy expenditure and energy production occur under stress (extreme conditions)	Working with a psychologist, control of commanders over personnel
Nutrition: — deficiency of B vitamins	B vitamins are coenzymes involved in various biochemical processes. B vitamins improve the energy of the nerve cell, play an important role in the biosynthesis of many neurotransmitters	Proper menu including vitamin B complex for fleet personnel
Physical: — long-time work at ECM (operators); — hypodynamia; — traumatism	Specific position of the body or limbs, monotonous repetitive actions can contribute to the infringement, microtraumatization and swelling of the nerve tables in narrow anatomical canals.	Performing morning physical exercises, leading an active lifestyle, alternating work and rest time

The hypothesis of a multilevel PNS lesion first described in 1973 by A. R. Upton and A. J. McComas, arose in the twentieth century. It was developed after a comprehensive clinical and electrophysiological examination of 115 patients with tunnel syndromes. Electrophysiological, clinical and anamnestic data confirming the presence of cervical radiculopathy were obtained in 81 patients. It is the essence of the hypothesis that individual axons, restrained in one area, become especially susceptible to damage elsewhere [16, pp. 359]. From the point of view of neurophysiology, A. R. Upton and A. J. McComas substantiated their hypothesis by impaired axoplasmic current, which predisposes to the occurrence of tunnel neuropathies and is designated in the literature as “double crush syndrome” [4, pp. 31–41; 16, pp. 359; 7, p. 522; 18; pp. 1171-1175]. In this regard, the compression of nerve fibers at the level of the spinal roots causes their partial degeneration of neurofilaments that provide axonal substances transport. In this situation, there is no degeneration of the distal part of the axon, however, additional compression can cause a dysfunction of the saved neurofilaments and lead to violations of the trophic supply of the nerve [18, pp. 1171–1175]. Clinical studies have confirmed this hypothesis [19, pp. 1256-1259]. According to various authors, a combination of compression neuropathies with signs of damage to the roots of the spinal nerves is found in 30–70% of cases of tunnel syndromes [20, p. 367; 21, p. 376]. Literary data indicate that the compression of nerve fibers can be not only double, but also triple, and even more. And therefore, some authors have proposed the term “multiple axoplasmic compression” - MAS syndrome [4, pp. 31–41].

In 1987, K. Nemoto et al. conducted an experiment on dogs using electrophysiological and histological methods. The study has shown that a nerve compressed in the proximal part becomes especially susceptible to additional compression in the distal region. In other words, a proximal nerve compression can reduce its ability to withstand further compression in a more distal part. Moreover, it has been found that two low intensity compressions along the nerve is worse than more intense compression, but at the same level [7, p. 522].

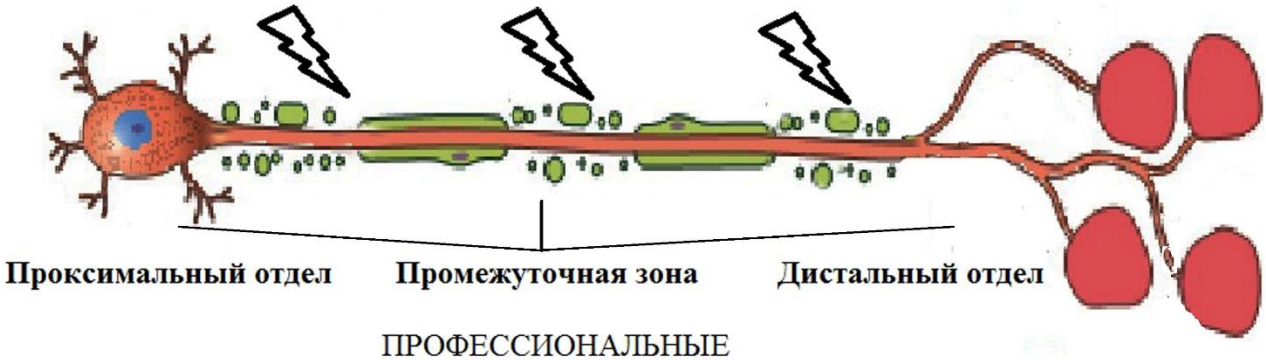
The article “Frequency and severity of carpal tunnel syndrome according to level of cervical radiculopathy: Double compression syndrome?” (2006) describes the results of a retrospective study of 277 patients with cervical radiculopathy C6, C7, C8, among whom 39 had carpal syndrome. A correlation between carpal tunnel syndrome and radiculopathy level was revealed: the degree of decrease in sensory responses was more pronounced with C6, C7 radiculopathy, and motor disturbances were more significant with C8 radiculopathy. Analysis of the electrophysiological results in carpal syndrome did not reveal a significant correlation between sensory impairments and C6, C7 radiculopathy, and no relationship was observed

between motor indices in C8 radiculopathy. The analysis performed did not confirm the hypothesis of the double compression syndrome (DCS) [19, pp. 1256-1259].

D. W. Flatt developed the primary theory of double compression of the median nerve at the wrist and in the neck area. He applied the theory to explain the damage to other nerves, for example, the infrapatellar saphenous nerve [22, pp. 395–397]. R. E. Carroll et al. described the combination of the upper thoracic aperture and carpal tunnel syndrome in one patient [23, pp. 149-153]. Nevertheless, at the moment the discussions revolve around the problem of multilevel nerve damage, as well as around the underlying mechanisms of syndrome development. Given that the rationale for the DCS hypothesis was formulated many years ago and has not been updated and revised since, despite modern advances in neurophysiology, it is necessary to clarify the concepts of the mechanisms underlying multilevel compression hypothesis [3, pp. 557-562]. The traditional definition of DCS is narrow, it is necessary to take into account that somatic pathology (for example, diabetes mellitus), medicinal and toxic neuropathies contribute to nerve damage.

In 2011, the large-scale “Delphic study” with the participation of 50 experts from various countries was completed. Of these, 59% agreed that the presence of the initial “defect” of the nervous system determines the suspectibility to the secondary disorder of the nervous system in the same segment; 12% refrained from withdrawal and 29% did not agree [3, pp. 557-562]. According to the research results, the main mechanisms promoting the development of multilevel neuropathy were formulated: axonal transport disorder, changes in the regulation of ion channels above and below the compression area, immune inflammation in the posterior roots, spinal ganglia, central sensitization [3, pp. 557-562].

In 2016, B. H. Cohen et al. of the medical school of Brown University (USA) published an article in which they proposed to replace the term DCS with multifocal neuropathy. According to the authors, the term multifocal neuropathy is more appropriate and includes a multiple etiology of damages to peripheral nerves [18, pp. 1171-1175] considering that the majority of the patients, especially in old age, have a confluence of factors (the interaction between mechanical, systemic, pharmacological, and environmental factors), leading to a complex nerve damage (Figure).



	ПРОФЕССИОНАЛЬНЫЕ ФАКТОРЫ РИСКА: Природные (холод, перепады давления, температуры и т.п.); Технические (вибрация, СВЧ-излучение и т.п.); Физические(гиподинамия, длительная работа за ЭВМ); Социально-бытовые (стресс, психическое перенапряжение). СИСТЕМНЫЕ ФАКТОРЫ: Диабет; Гипотиреоз; Наследственные невропатии; Недостаточность витаминов В; Хронический алкоголизм; Заболевания соединительной ткани и т.п.	
Шейная радикулопатия Поясничная радикулопатия Плечевая плексопатия Синдром грудной аппертуры Травма		Дистальные компрессионно-ишемические невропатии Травма

Figure. Confluence of factors that result in complex nerve damage

Проксимальный отдел	Proximal segment
Промежуточная зона	Middle segment
Дистальный отдел	Distal segment
ПРОФЕССИОНАЛЬНЫЕ ФАКТОРЫ РИСКА:	Occupational health risks
Природные (холод, перепады давления, температуры и т.п.)	Natural (cold, changes of atmosphere pressure, temperature, etc.)
Технические (вибрация, СВЧ-излучение и т.п.)	Technical (vibration, EMI interference, etc.)
Физические (гиподинамия, длительная работа за ЭВМ)	Physical (hypodynamia, long-time work at ECM)
Социально-бытовые (стресс, психическое перенапряжение)	Social (stress, mental strain)
СИСТЕМНЫЕ ФАКТОРЫ:	Systemic factors:
Диабет	Diabetes
Гипотериоз	Hypothyroidism
Наследственные невропатии	Hereditary neuropathies
Недостаточность витаминов В	Deficiency of B vitamins
Хронический алкоголизм	Chronic alcoholism
Заболевания соединительной ткани и т.п.	Connective tissue diseases, etc.
Шейная радикулопатия	Cervical radiculopathy
Поясничная радикулопатия	Lumbar radiculopathy
Плечевая плексопатия	Brachial plexopathy
Синдром грудной аппертуры	Thoracic outlet syndrome
Травма	Trauma
Дистальные компрессионо-ишемические невропатии	Ischemia-induced distal compression neuropathies

Nash H. Naam of the Southern Illinois Hand Surgery Center Effingam (USA) agreed that “multifocal neuropathy” is an appropriate term for the multiple etiology of nerve damage, but noted that it is used by clinicians to describe an autoimmune disease, multifocal motor neuropathy [24, p. 1176].

The relationship of carpal syndrome and cervical radiculopathy is the most widely studied. However, in 1998, G. Morgan et al. examined about 12,000 patients using clinical and neurophysiological criteria and did not find a relationship between cervical radiculopathy and tunnel syndromes; the frequency of concomitant carpal and cubital syndromes with cervical radiculopathy was less than 1%. The obtained data are in sharp contrast to the initial findings [18, pp. 26–29; 25, p. 2].

Proponents of this theory recommend a careful approach to the diagnosis of diseases of PNS, especially in middle-aged and elderly people. However, it should be noted that many practitioners are not sufficiently familiar with this hypothesis; therefore, combined lesions of the PNS as a multilevel compression of peripheral nerves present diagnostic difficulties. In particular, cervical radiculopathies can both aggravate the clinical picture of tunnel neuropathies, as well as mask the main pathological process, imitating the symptoms of peripheral tunnel neuropathies, leading to incorrect diagnostic and therapeutic measures.

Electrophysiological methods are traditionally considered the “gold standard” for detecting disorders of the conductive nerve function. The study of the functional state of the motor and sensory nerves is carried out by the method of stimulation ENMG, which allows to investigate the M-response, S-response, F-wave. M-response is the total electrical potential of a muscle in response to a single electrical stimulation of a motor or mixed nerve. S-response allows to evaluate the conductivity of the sensory nerve fibers, involves the analysis of the sensory spread of nerve excitation and the amplitude of the action potential of the nerve. The F-wave is the response of a muscle to an impulse sent by a motor neuron as a result of its excitation by an anti-dromic wave, which occurs when the distal indirect stimulation of a nerve is caused by a supramaximal current. Analyzing the parameters of the time delay (latency) and the propagation speed of the F-wave, it can be inferred the conductivity by the most proximal segments, as well as the excitability of motoneurons and their functional state [26, p. 151].

Electrophysiological diagnosis of vertebral radiculopathies includes F-wave studies, radicular delay analysis, needle EMG. However, at present, the diagnosis of radiculopathy is clinical and does not require the mandatory performing of ENMG, and electrophysiological methods are used only in the differential diagnosis of complex clinical cases. The following parameters are estimated in the study of F-waves: minimum latency, chronodispersion, tacheodispersion, coefficient of dispersion, minimum speed, blocks of F-waves. The study of radicular delay is based on the analysis of the minimum latency of the F-wave and registration of the induced motor response during segmental magnetic stimulation [28, pp. 25–31]. A sensitive method in the diagnosis of lesions of the spinal roots is needle electromyography, its sensitivity according to some data is up to 70%.

To determine the treatment management, a doctor often had to detect the exact location and degree of injury of the peripheral nerve, as well as evaluate possible damage to the muscles, vessels, tendons. ENMG does not allow to assess the state of the tissues surrounding the nerve and detect the location of the injury. Ultrasonography (USG) of peripheral nerves is a relatively "new" method of research and is quite reliable, and is also a valuable addition to the clinical analysis of the neurological status and electrophysiological data. During ultrasonography of peripheral nerves, the detection of a significant increase in the longitudinal-cross-section (PPS) of the peripheral nerves, more often proximal to the level of compression with a decrease in its echogenicity during longitudinal scanning is an important result. A disorder of internal differentiation of the nerve into fascicular groups, swelling of the surrounding soft tissues and hypervascularization occur at the site of compression. In addition, ultrasonography helps to detect injuries of the brachial plexus trunks, tumors and nerve injuries [15, pp. 31–34]. According to different authors, the sensitivity of ultrasonography of PNS ranges from 55 to 95%, and a comparative analysis of the results of scientific work shows that ultrasound examination of nerves is as sensitive method for diagnosing disorders as ENMG [27, pp. 207–234].

Magnetic resonance imaging (MRI) forms the “gold standard” in diagnosis the degenerative-dystrophic changes in the spine that cause the damage of the PNS. Unlike X-ray examination methods, MRI offers the best evaluation of soft tissue structures: it gives the clear picture of the pathological changes in the intervertebral discs, allows to define the degree of compression of the dural sac and roots. An important advantage of MRI is the ability to assess the compression of the spinal cord with the development of myeloischemia, as well as the presence of edema of the nervous tissue. Due to the high resolution, the possibility of a multiplane MRI study accurately determines the localization of peripheral nerve damage: in the T2-VI mode, the damaged nerve, due to edema, has a hyperintense signal, but during the regenerative process, the hyperintensity gradually decreases and approaches the baseline values, corresponding to the degree of nerve regeneration [29, pp. 157-165].

In everyday clinical practice, affected military personnel and seafarers often have signs of peripheral nerve damage, both at the distal level in the area of natural anatomically narrow canals with the development of tunnel syndromes, and at the proximal level with the involvement of spinal roots. Often, in both young and old people, on the background of pronounced degenerative-dystrophic changes in the spine, the effects of compression of the roots with compression of the spinal cord by various structures (myeloradiculopathy) occur [30, pp. 13-17; 31, pp. 359; 32, pp. 538–546]. At the same time, changes of the MR signal in the compression zone of the spinal cord do not always correspond to focal neurological symptoms and severity of myelopathy [23, pp. 149-153].

The treatment of multilevel disorders can be both conservative and surgical. At the initial stages of the disease (recurrent paresthesias, lack of muscle atrophy), therapeutic exercises, removing provoking factors, wearing corsets, orthotics of joints for sleep and during physical work, taking B vitamins, as well as local administration of corticosteroids are considered effective as a conservative therapy. The peculiarity of conservative therapy is that the impact of therapeutic factors is throughout the peripheral nerve - from the parent motor neuron to the innervated tissues. When encountering with the ineffectiveness of the above measures for 3 months or when treating patients with severe forms of neuropathy (with contractures and muscle atrophy), surgical treatment methods become relevant. For example, surgical treatment of patients with cubital syndrome is aimed at the ulnar nerve decompression, which consists of neurolysis and / or transposition of the nerve into more favorable conditions. Surgical treatment of carpal tunnel syndrome involve the dissection of the transverse ligament of the wrist by an open or endoscopic method. According to the literature [33, pp. 30–34], most elderly patients show much longer sensory and motor impairments recovering after surgical treatment of tunnel neuropathies due to degenerative-dystrophic spinal disease with the development of cervical radiculopathy or myelopathy, that is, the multi-level damage of nervous system.

Thus, tunnel syndromes are the most common form of PNS damage. The service in the Armed Forces of the Russian Federation and in the fleet is closely related with additional psychological and physical loads that

increase the risk of compression-ischemic neuropathies and radiculopathy in servicemen and seafarers. Development of the tunnel syndromes is strongly dependent on the baseline state of the peripheral nerve throughout and the higher parts of the peripheral and central nervous systems. A multi-level damage to the peripheral nervous system may occur with “compromised axonal systems” in the proximal (double axoplasmic compression syndrome with radiculopathy) or distal (polyneuropathy) segment, against the background of axoplasmic current deficiency. Therefore, doctors may encounter problems of timely diagnosis in PNS damage in several segments of the nerve in patients, which can lead to high financial costs and dissatisfaction with the results obtained by stakeholders. In this regard, further development of the concept of multilevel damage of the peripheral nervous system and the development of a new terminology that could cover a wide range of damage factors is required in order to improve the quality of medical care for patients affected with this disease.

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