National Consensus on Diagnosis and Treatment of Pain of Neurological Origin

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By initiative of the Bulgarian Headache and Pain Association

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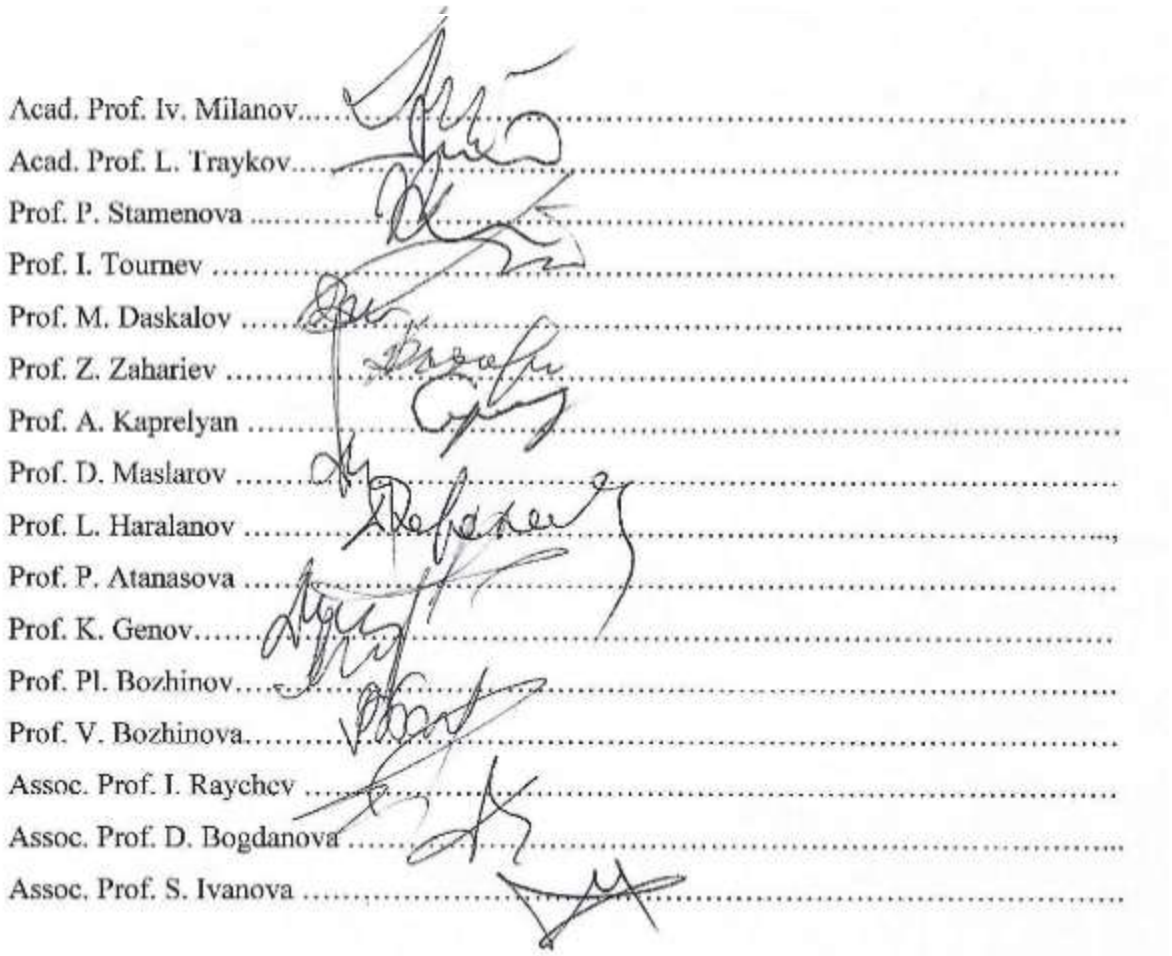
Today, November 10, 2018, we, the undersigned experts, have reached a consensus on the diagnosis and treatment of pain of neurological origin:



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Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.

Classification

By its duration pain is classified as acute and chronic. Acute pain is a symptom, chronic pain is a disease.

Acute pain is related to clearly identified tissue injury and lasts no more than 1 month from its onset. It is protective and gradually resolves as the injured tissues heal, when the environment surrounding the nociceptors is normalized and their hyperactivity resolved.

Chronic pain persists for more than 3 months. It is caused by tissue damage but continues even after the causative lesion heals. It is not due to activation of nociceptors and has no protective effect.

According to the underlying pathophysiological mechanisms pain is classified as nociceptive or neuropathic. The combination of both types (mixed) pain is common.

According to its anatomical location pain is classified as head, face and mouth pain; cervical pain; pain in shoulders and arms; thoracic; abdominal; lumbar pain; pain in lower limbs; pelvic; anal, perianal and genital pain.

Nociceptive pain

It is caused by injury to any organ or system other than the nervous system, and its diagnosis and treatment is associated with a number of medical specialties. It is subdivided into physiological nociceptive pain, caused by temporary dysfunction (cramps, colics), and pathological nociceptive pain, caused by tissue injury.

Neuropathic pain

It is pain caused by dysfunction, lesion or disease directly affecting the somatosensory nervous system.

The prevalence of neuropathic pain is between 3 and 8.2% of the adult population.

Etiologically it represents a heterogenic group of conditions that vary from neoplasms compressing peripheral nerves, traumas, damage to a peripheral nerve after surgery, inflammation, immunological, metabolic, intoxication, endocrine, degenerative and ischemic injuries of peripheral nerves to ischemic injuries of the brain and dysfunctions. Neuropathic pain varies according to the causative pathology and anatomic location of injury. Injury may be located anywhere in the nervous system – from the peripheral nerve to the brain. It is subdivided into peripheral and central neuropathic pain. It may be also subdivided into physiological, in case of neural structure

compression with transitory dysfunction or pathophysiological changes, and pathological, in case of destruction.

It may be spontaneous or stimulus-induced. Usually, the two types of pain are manifested simultaneously. Neuropathic pain is chronic or remittent and is rarely acute (in herpes zoster). It is characterized by different symptoms that are not necessarily present at the same time, and could manifest in different combinations.

Clinical signs are characterized by changes in intensity, quality, local and time characteristics of pain. It is located in anatomic regions of partial or complete sensory loss. Motor and autonomic disturbances are possible.

There are **two basic types of symptoms:** positive and negative. Negative symptoms are associated with deficit, and positive symptoms are related to abnormally increased activity of the sensory system. The burden of negative and positive symptoms is not the same and negative symptoms are frequently masked by positive symptoms. Positive symptoms depend on affected systems and include pain, paraesthesia, dysesthesia and hyperalgesia (somatosensory system), fasciculations and myokymia (motor system), hyperhidrosis, piloerection – "goose bumps" and vasoconstriction (autonomic system). Negative symptoms depend on affected systems and include hypoesthesia and analgesia (somatosensory system), paresis (motor system) and hypohidrosis (autonomic system).

Pain symptoms are subdivided, according to the causative factor, into spontaneous (positive) and induced (positive and negative).

Spontaneous (non stimulus-induced) symptoms are characterized by ***pain*** of different *duration*: continuous, intermittent or paroxysmal. Paroxysmal pain is typical for neuralgia, compression mononeuropathies, tabes dorsalis, neuropathy in Fabry's disease and phantom limb pain.

Causalgia is a burning pain in the region of one or more peripheral nerves.

Phantom limb pain is a combination of central and peripheral neuropathic pain. It is experienced in amputated limbs or in parts of the body that are under general anaesthesia due to lesion of peripheral nerves, plexuses, roots and the spinal cord.

Reflected pain and hyperalgesia are experienced in parts of the body that are different from those where the harmful stimulus occurs, and are stimulus-induced. The most typical is the reflected visceral pain.

Projected pain originates from a certain region and is experienced in another part of the body along the spinal roots or peripheral nerves.

Paraesthesias may be spontaneous and induced. They are abnormal unpainful sensations of numbness or 'stinging', which are not unpleasant for patients.

Dysesthesias are abnormal spontaneous or induced sensations such as painful numbness, which are unpleasant for the patient.

Symptoms induced by test stimuli are subdivided into positive (pain, hyperalgesia, allodynia and hyperpathia to mechanic, thermal or chemical stimuli) and negative (hypoalgesia). Allodynia and hyperalgesia are not associated with specific type of pain.

Hyperalgesia, according to the test stimulus, which is perceived as the most painful, is subdivided into mechanical, thermal, cold and chemical.

Hyperpathia is hypoalgesia with increased reaction to pain stimuli. It is characterized by elevated sensory threshold, delayed perception of stimulus and abnormal pain reaction, with summation to repeating stimuli (pain increase). Pain continues long after stimulus termination and is caused both by stimuli that usually cause pain and stimuli that do not evoke pain.

Allodynia is a sensation of pain elicited by a non-noxious stimulus (touch). Allodynia pain is diffuse, continues even after stimulus termination and depends on the emotional state. Depending on the stimulus applied, there is mechanical, thermal (cold and heat) and motor allodynia.

Spatial alterations (dyslocalization) are the common symptom of neuropathic pain. Stimulus application in one region causes pain in another region.

Diagnosis

Neuropathic pain, unlike nociceptive pain, is accompanied by other positive and negative neurological symptoms, therefore it is diagnosed and treated by neurologists. Diagnosis is based on a medical history, neurological examination, criteria for diagnosis and some laboratory methods.

Medical history is intended to describe the pain. It is necessary to clarify the mode of onset, its location, duration, severity, inducing and relieving factors. Patients with neuropathic pain use specific definitions to describe their pain. On that basis different *verbal pain scales* have been developed to differentiate the neuropathic from nociceptive pain. The most frequently used is the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS).

Neurological examination is intended to ascertain the presence of neurological lesion and its relation to patient‘s pain. Sensory disorders in the region of pain are examined. A detailed study of the temperature and pain sensations conducted through different systems is required. The examination assesses the velocity (conduction velocity) and accuracy of patients’ responses. It is necessary to ascertain the existence of positive and negative pain disorders and their location. During patient’s examination consideration should be given to trophic changes in the skin, autonomic, auxiliary neurological (motor, coordination, etc.) and internal organs symptoms.

Pain irradiation helps to determine the location of injury (root, plexus, neural, central), because every type of pain has a relatively stereotypic propagation.

Hyperalgesia may be examined by pinching the skin between the thumb and forefinger which causes an unpleasant feeling in the area of hyperalgesia.

Allodynia is examined by touching the skin with a cotton ball, which evokes pain.

Manual palpation may find muscle hypersensitivity that underlines various methods which determine the affected visceral organ.

Intravenous administration of lidocaine only relieves neuropathic but not nociceptive pain and can be used for its differentiation.

Diagnostic criteria with different levels of certainty are used: definite, probable and possible neuropathic pain.

Definite neuropathic pain is diagnosed upon fulfilling 4 criteria:

1. Pain in an anatomic region that is innervated by a peripheral nerve or root or corresponding to topographic representation in the central nervous system.

2. A history of disease or injury to the peripheral or central somatosensory nervous system associated with pain.

3. Definite neuroanatomical damage determined by the neurological examination.

4. Confirmation of the lesion or disease by at least one diagnostic test (neurophysiological, neuroimaging or neurosurgical methods).

Probable neuropathic pain is diagnosed in the presence of the first three criteria, and *possible* neuropathic pain – in the presence of the first two criteria. Possible neuropathic pain requires additional tests conducted to specify the diagnosis.

There are various **methods for quantification of pain.** These methods are subjective and are determined by patient's attention, fatigue and alertness. They examine the spontaneous pain and pain induced by various stimuli (mechanical, thermal, electric, chemical and ischemic). Every sensory modality may determine the pain threshold and pain tolerance.

Pressure algometry is used to quantify the local sensitivity in muscle trigger points by pressure algometer. The pressure threshold is measured – the minimum pain-inducing pressure. The pressure tolerance is determined as the maximum pressure which is tolerated by the patient and represents the sensitivity to pain stimuli.

There are various **scales to determine the intensity of pain:**

Visual Analogue Scale (0-10) is a 10-cm horizontal straight line with a mark only in the beginning and at the end of the scale. On the left-hand end of the scale is "no pain" and on the right-hand end is "unbearable pain". Patients mark their pain sensation and the investigator measures the distance from the beginning of the line in centimetres or millimetres. This way the pain is digitalized.

Numerical Rating Scale for Assessment of Pain Intensity uses numbers from 0 to 10 for patient-reported pain intensity. A rating of 0 to 4 corresponds to mild pain; 5 to 6, to moderate pain, and 7 to 10, to severe pain.

Verbal Rating Scale for Assessment of Pain Intensity is a list of words describing the incremental increase in pain intensity – from no pain to worst pain.

The *Wong-Baker Faces Pain Rating Scale* is used in children under 8 years who find it hard to use adjectives or numbers for self-assessment of pain. It uses a series of illustrated faces showing a very happy and smiling to stressed and crying state.

Multidimensional scales are harder to apply and interpret. They are used by psychologists in patients with chronic multifactorial pain that hardly respond to treatment. The *McGill Pain Questionnaire* is the most frequently used instrument. It allows the assessment of sensory, affective and evaluative components of pain. The patient must select descriptive terms from the suggested groups of words that are listed according to pain intensity. He/she also has to mark themselves, on a diagram of a human figure, the location of the source of pain. *Brief Pain Inventory* is a widely used instrument to assess the pain impact on patients' daily functions. *Multidimensional Pain Inventory* is a questionnaire that consists of 64 items, 3 sections and 12 subscales. The first 2 sections asses the pain impact on different aspects of patient's life and his/her perception of his/her family members' attitude to his/her condition. Section 3 makes assessements of how often the patient performs 18 daily activities. It is appropriate to evaluate the treatment outcome.

Neurophysiological methods are used to ascertain nervous system damage.

The *EMG study* only detects damage of thick myelinated fibres in peripheral nerves. Conventional methods cannot test fine Aδ and C fibres conducting autonomic impulses and nociceptive afferentation, neither can identify positive symptoms. Therefore, the test cannot confirm or rule out the peripheral nerve damage as the cause of neuropathic pain. Nevertheless, electromyography and electroneurography find application in diagnosing polyneuropathies, compression neuropathies, radiculopathies and other peripheral nerve damages that could be a source of pain. The test makes it possible to evaluate damage duration and prognosis by the clinical significance of changes detected on neuroimaging methods. It is absolutely indicated in identifying negative neurological symptoms. The electromyographic evaluation of muscle activity and of the F-wave allows for accurate detection of the root affected.

The *Sympathetic Skin Response* is used to examine the small non-myelinated sudomotor sympathetic fibres. The electric stimulation of a peripheral nerve is caused by adrenergic stimulus that leads to sweating and change in the skin electric potential. The sensitivity of the method to diagnose small fibre neuropathy is low.

Brain stem reflexes (blink reflex and masseter inhibitory reflex) are a method for assessment of trigeminal, brainstem functions and of craniofacial pain.

The blink reflex consists of R1 and R2 components that are evoked by mechanical or electric stimulation in the supraorbital region. The masseter inhibitory reflex consists of SP1 and SP2 components that are evoked by mechanical or electric stimulation of the maxillary or mandibular region. Such reflexes assess the function of thick myelinated trigeminal afferents, as well as the central trigeminal neural circuits in medulla oblongata, pons and mesencephalon.

Somatosensory Evoked Potentials (SEPs) are obtained when applying low-intensity electric stimuli that mainly activate thick, fast-conducting afferent fibres with a lower electrical stimulation threshold than the one for the small nociceptive afferent fibres. The increase in electrical stimulus intensity causes increase in pain severity, as nociceptive afferent fibres are also activated. Detection of "nociceptive" evoked potentials starts. Somatosensory evoked potentials N1-P2 (or N140-P250) reflect the cortical pain response.

Skin biopsy is used to diagnose painful neuropathies. Small pieces of skin (3 mm) are taken from different areas of the body to study the axons and nociceptive nerve endings in it. According to standard, puncture skin biopsy of the leg is performed at 10 cm above the external malleolus. Diagnosis is based on the decreased below 5% density of nerve endings. The quantitative study is carried out in the epidermis where axons are divided into individual enumerable intraepidermal nerve terminals.

N. suralis biopsy is widely used as the nerve is clearly sensory and its injury does not lead to muscle weakness. Light microscopy study of non-myelinated nociceptive axons is capable of diagnosing neuropathy.

Neuroimaging methods used to determine the cause of pain are radiography, myelography with non-ionic contrasts, computer tomography and magnetic resonance tomography. Neuroimaging methods are absolutely indicated in neurological deficit, weight loss, history of tumour disease, serious injury, motor neurological deficit, continuous administration of corticosteroids, clinical evidence of rheumatoid arthritis, ankylosing spondylitis and metabolic disorders.

Radiography is routinely used in patients with low back pain. The correlation between the radiographic findings and patient's symptoms is very poor. It visualizes spinal cord degeneration that reflects normal ageing but not the compression of roots.

Computer tomography (CT) is a method of choice in patients with neurological deficit. It is not possible to visualize well the outlines of the spinal cord without applying CT myelography.

Myelography is an invasive method, which should only be used in patients with neurological deficit. Water-soluble contrast agent is applied intrathecally by lumbar puncture. It decreases the

postmyelographic reactions and arachnoidites but nevertheless it poses a high risk. Another limitation of the method is the impossibility to visualize the accompanying pathology distally of the complete contrast block.

Magnetic resonance imaging (MRI) allows for imaging of changes that are not visible with CT scan. The high sensitivity of the method bears the risk of overdiagnosing due to imaging of early degenerative changes. The administration of contrast agent (gadolinium) increases the method sensitivity and is especially indicated for differentiation of tumours and postoperative complications of repeated disc prolapses.

Scintigraphy is a method of early diagnosis of mostly metastatic tumours, osteomyelitis and osteoporotic fractures.

Evaluation of the autonomic nervous system by means of dermographic methods and Head's procedure helps to detect hyperalgesia in the skin and subdermis.

With the *dermographic procedures,* 2 parallel vertical lines about 2 cm apart are made through a blunt dermatograph pencil. A constant pressure of 500 g is applied. It is possible to use the dorsum of the investigator's finger. Two red lines appear on the skin (vasodilation), which normally fade away gradually and simultaneously. An early interruption of these lines occurs in hyperalgesic areas, indicating a prevalence of the ischemic phase of dermographism.

For *Head's procedure,* concentric lines are scratched over the skin surface at constant pressure of 40 g and angle of inclination of the dermatograph's nib of 25^0. A painful reaction by the patient is indicative of reaching the border of the hyperalgesic area.

Laboratory methods for testing serum and urine are used to determine the injury's aetiology. If there is evidence for small fibre neuropathy, blood sugar must be tested, in case of suspicion of collagenosis – antinuclear antibodies, rheumatoid factor, cryoglobulin and ESR should be tested. Every specific study is determined by the presumptive diagnosis.

General Practitioner, if neuropathic pain is suspected, refers the patient to a neurologist.

Neurologist

1. Following a clinical examination, refines the indications for testing. In order to undergo myelography, the patient should be consulted by a neurosurgeon. The execution of neuroimaging studies must be made more precisely.

2. Diagnoses neuropathic pain with a degree of certainty determined by the criteria and according to the results of studies carried out.

Peripheral Neuropathic Pain

It may result from any type of damage or dysfunction of peripheral nerves, gangliopathy (sensory and autonomic ganglia injury) or radiculopathy (dorsal root injury). Typical precipitating factors are trauma, infection, inflammation, metabolic and vascular abnormalities, malnutrition, ischemia, neurotoxins (incl. chemotherapeutic agents), radiation, autoimmune diseases and inherited disorders. According to aetiology, the clinical presentation is different. Disease progression rate helps identify the aetiology. Typically, pain develops incrementally because it is caused by pathophysiological mechanisms that develop gradually in the peripheral and central nervous system. The onset is acute with sudden damage, inflammatory, autoimmune, toxic or vascular disorders. The onset is subacute in toxic, deficiencies and systemic diseases, and chronic, in inherited and metabolic disorders.

Craniofacial Pain

Pain in any area of the face and around the mouth is reported in 13% of population. It is subdivided into 4 large groups: caused by local diseases, by peripheral nerves and their central pathways, by extrafacial anatomical structures (ears, eyes, heart, cervical spinal cord) and chronic atypical pain.

Atypical Facial Pain (neuralgia, orofacial dysesthesia)

It is persisting facial pain, in which no organic lesions and neurological symptoms are identified.

The *prevalence* is about 0.7 per 100,000 population, more common in females in middle and old age.

Aetiology and pathogenesis of pain are not clear; it is supposed to be neuropathic resulting from subclinical small fibre neuropathy. The onset is frequently associated with trauma – dentistry, tooth extraction or sinus surgery.

The *clinical course* is associated with deep but not well located burning pain, in the region of the lower or upper jaw. Pain is unilateral but in 30% it could be bilateral. At the beginning, it is experienced in the fold between cheek and nose or the midface but, as disease progresses, it involves a larger area and goes beyond the cervical region. It does not irradiate along the peripheral nerves or roots and goes beyond the area innervated by the trigeminal nerve. The pain is burning, drawing, piercing, constricting or pulsating, fluctuating from moderate-to-severe intensity. It may be constant, daily or it may be missing during some months of the year. It may be accompanied by slight subjective sensory disorders in the same region, dysaesthesias, paresthesias and symptoms of sympathetic and vascular dysfunction, such as sensation of swelling and heat. Patients present with headache, low back pain, hyperirritable bladder, depression, psychological distress preceding the

onset of disease and other mental disorders.

Diagnosis is based on ruling out all other possible systemic, neurological and dental diseases and trigeminal nerve injury.

Burning Mouth Syndrome

Terms such as glossodynia, glossopyrosis, stomatodynia, stomatopyrosis, sore mouth and oral dysaesthesia are used.

The *prevalence* is about 3.7% of adult population. This condition affects women (5.5%) more than men (1.6%). With aging, the prevalence increases in both sexes and is as high as 12% in women for the 60-70-age group. The risk factors are unknown, except for the increased risk in menopausal women.

The syndrome's *aetiology and pathophysiology* are not known. Changes in the peripheral and central nervous system, with minor injuries of the central and peripheral part of the trigeminal system, which cause neuropathic pain are suspected.

Clinical course is with continuous bilateral burning, moderate to severe pain in the area of normal-looking oral mucosa, in lips, the front part of the tongue and of the hard palate or in several regions. No anatomical innervation of peripheral nerves is followed. It is intensified while talking, under stress and when feeling tired, and is ameliorated when the patient is distracted, working, eating and consuming cold food and drinks. The pain is the mildest upon awakening and progressively increases till evening. The symptoms gradually intensify to development of the full clinical picture. Dry mouth is an associated symptom (in 50%), although there is no decreased salivary secretion. 70% of patients report distortion of the sense of taste and persisting dysgeusia (bitter or metallic taste). Patients have chronic pain syndromes, depression, anxiety, somatization, personality disorders and sleep disorders.

The mouth examination may reveal hyperaemia, inflammation and ulcerations, which intensify the pain.

Diagnosis is made after ruling out systemic and local diseases of the oral mucosa, such as candidiasis, infections, allergic reactions, decreased salivary secretion and dental problems. Iron deficiency, vitamin B_{12} and folic acid, hormonal disorders (estrogenic deficiency), diabetes and Sjogren's syndrome must be ruled out. Diagnosing requires the use of local anaesthetics that suppress the glossodynia but not the pain radiating from other structures.

Pain from peripheral nerves and their central pathways

It is divided into two big groups: a group without impairment of the central nervous system (neuralgias) and a group with impairment of the central nervous system.

Neuralgias

They are classified as idiopathic (with unknown aetiology) and symptomatic – arising from another underlying disease. They run with neuropathic paroxysmal pain in the region innervated by the respective sensory nerves. Pain is short and resembles an electric impulse followed by refractory pain-free periods. The existence of trigger points of pain is typical. There is also persistent, milder burning pain.

Orofacial Neuralgias

Trigeminal Neuralgia

The *incidence* is 6 per 100,000, and the prevalence is 70 per 100,000 population. Women are affected 3 times more often than men and the incidence rate increases in both sexes with age (over 60 years).

The *aetiology* is associated with compression of trigeminal roots of an aberrant blood vessel, most often the posterior cerebellar artery. It is divided into idiopathic, atypical and symptomatic.

Clinically, the onset is in the fifth decade and the symptomatic form is manifested between 30 and 35 years. Attacks are represented by unilateral, severe, brief (electric-like) pain in the mandibular and/or maxillary and more rarely (18%) on the ophthalmic branch of the nerve. Attacks happen in periods followed by remission. They can be clustered one after another but an attack is followed by a refractory period of several minutes in most cases. 10% of patients experience bilateral pain but attacks are not experienced at the same time. It lasts for seconds to 1-2 minutes but it is at its peak right after onset and causes the patient to wink involuntarily, hence the name ‘tic douloureux’ (painful tic). They occur during the daytime, rarely at night, and are induced by touching specific trigger zones on the face, lips or gums. Eating, talking, smiling, grimacing, teeth brushing or even wind may trigger an attack.

The sensitivity at the exit areas of the affected nerve branches is increased on palpation. No sensory or motor disorders are detected, there could be slight trophic changes in the skin of the affected area.

Symptomatic neuralgia is observed in 2% of patients with trigeminal neuralgia. It is caused by structural lesion: pontocerebellar angle tumour (in 5% neurinoma of the auditory or trigeminal nerve, meningioma in the posterior cranial fossa), syringomyelia, multiple sclerosis (in 5% plaque located close to the root entry zone in the pons), aneurism of basilar artery or vascular anomaly. The clinical course is associated with constant, dull, more often bilateral pain and hypoesthesia in the trigeminal area. It may be accompanied by facial hemispasm (tic convulsif) and manifests impaired sensation in the zones innervated by the nerve or its roots.

Trigeminal neuropathy is due to a structural nerve lesion resulting from injury, inflammation, ischaemia or systemic disease. It is caused by more massive lesions in the distal part of the nerve following sport traumas, car accidents, tumors affecting the peripheral branches of ganglion Gasseri, surgeries and severe arterial compression by the ectatic basilar artery. It is most common after impairment of the dental branches of the trigeminal nerve due to tooth extraction (1-5%), injecting of local anaesthetic, neuroablations in the mouth cavity or treatment of dental tubules.

The *clinical manifestation* is associated with chronic burning pain, which increases episodically and becomes acute. Trigger zones are not so well pronounced. There could be sensory disturbances, paraesthesia, dysaesthesia, mechanic allodynia and weakness of m.m. masseter and pterygoideus.

Glossopharyngeal Neuralgia

The *incidence* is 0.8 per 100,000 population.

The *idiopathic form* is due to vascular compression of the vertebral artery or a. cerebellaris posterior inferior in the root entry zone of IX and X cranial nerve.

The *symptomatic form* (in 25%) is associated with peritonsillar abscess, carotid aneurysm, carcinoma or epithelioma in the oropharyngeal area, pontocerebellar angle tumor, infections, trauma, multiple sclerosis, Eagle's syndrome.

Glossopharyngeal neuropathy is continuous pain due to surgical interventions.

The *clinical picture* appears similar to that of trigeminal neuralgia. The onset of the disease may be in childhood to old age, mostly middle age. It presents with short-lasting, paroxysmal, unilateral, intensive and piercing pain in the zone of IX and X cranial nerve. It spreads to the throat (fossa tonsillaris), ear (auricular branch of n. vagus), tongue base and mandibular angle or is primarily located there. This condition is induced by swallowing, talking, chewing, coughing, yawning, food with certain tastes and touch on the neck or the external auditory meatus. Paroxysms last for seconds to minutes with constant dull pain between them, persisting for minutes or hours. Attacks happen every day in a period of weeks or months followed by a longer period of remission. The number of attacks reaches 12 or even more daily, including at night while sleeping. It can be accompanied by bradycardia, tachycardia, hypotension or syncope due to triggering of cardioinhibitory reflexes of pain afferentation (from IX cranial nerve to tractus solitarii and the dorsal motor nucleus of X cranial nerve). It may be accompanied by cough and hoarse voice. No sensory or motor disorders are detected.

Occipital Neuralgia

Occipital neuralgia is very common. The existence of idiopathic and symptomatic form and its relationship with cervicogenic headache remains unclear.

The *pathogenesis* is associated with damage of the occipital nerve upon its passing through m. semispinalis capitis due to chronic spasm of the muscle in myofascial syndromes. The involvement of roots is caused by hereditary anomalies and degenerative changes in the spinal cord, tumours, ankylosing spondylitis, rheumatoid arthritis, osteomyelitis, hernia of the cervical disc and trauma (whiplash injury in car accident).

The *clinical* onset is between the third and fifth decade of life. It is associated with deep paroxysmal burning pain in the region of the major (C_2) or minor occipital nerve (C_3) – suboccipital, occipital and posterior parietal areas. It increases in the afternoon and may spread to the ipsilateral side of the forehead and temple. Palpation detects paraesthesias and increased sensitivity in the occipital area on palpation.

Postherpetic Neuralgia

Between 20 and 35% of patients with herpes zoster infection develop postherpetic neuralgia. The risk factors are old age, female gender, prodromal and severe pain with marked rash in the acute phase, ophthalmic nerve injury, diabetes mellitus, immunocompromised patients and psychological factors. 50% of patients aged over 60 have neuralgia, with a tendency to spontaneous remission, as contrasted with neuralgia in younger patients. In younger people, postherpetic neuralgia continues for 2-3 weeks after the skin lesions heal, and in adults it lasts for more than 2 months but hyperesthesia may persist for a longer period.

This neuralgia is caused by persisting sensitisation of nociceptors after the infection is resolved and by changed central mechanisms of pain control.

This disorder affects *clinically* the cranial (herpes zoster auricularis and ophthalmicus) and spinal nerves and plexuses. There are two main types of pain: constant, superficial and burning accompanied by hyperpathia and dysaesthesia, and second, paroxysmal, stronger piercing or lightning pain in the affected dermatome. Pain occurs spontaneously or as a result of skin contact with clothes, physical activity, changes in temperature and stress. Some areas in the dermatome trigger the pain on touch and relieve it on compression. Hypo- or anaesthesia, allodynia, hyperalgesia, itching, dysaesthesia or hyperesthesia to touch are identified in the affected dermatome. Pain intensity varies and is only mitigated at night but then hyperpathia intensifies and disturbs patient’s sleep.

Diagnostic Methods in Craniofacial Pain

1. Medical history of the pain character and **clinical** examination (particularly of facial

sensation) are essential for diagnosis.

2. Neurophysiological methods (EMG study of the brainstem reflexes and SEP) are applied to reveal injuries to the trigeminal nerve and brain stem nuclei. The presence of injuries supposes symptomatic neuralgia and requires the use of neuroimaging methods to identify the cause.

3. Neuroimaging methods (radiography, CT, MRI scans) are used to rule out sinus conditions, nasopharyngeal and pulmonary carcinoma, pontocerebellar angle tumour, multiple sclerosis. Detection of changes in the spinal cord with neuroimaging methods do not confirm the diagnosis because they are a common finding.

4. Consultation by a dentist to rule out dental pathology.

5. Consultation by an ophthalmologist to rule out glaucoma and refractive disorders.

Differential Diagnosis in Craniofacial Pain

Primary differentiation is made between symptomatic neuralgia and neuropathy, pain of sinus conditions, jaws, teeth, eyes, ears, nose and neck. Secondly, cluster headache (Sluder) in the lower face, neck-tongue syndrome, Hunt's neuralgia (of n. intermedius), idiopathic otalgia, with pain in or around the ear, cluster-tic syndrome, SUNCT, Tolosa-Hunt syndrome, cervicogenic, tension headache and some forms of migraine or similar must be differentiated.

Cluster-tic syndrome occurs in episodic and chronic form and combines three types of pain. The first type resembles trigeminal neuralgia – severe, paroxysmal and short-lasting. The second type resembles cluster headache and is accompanied by autonomic symptoms (lacrimation and rhinorrhoea). The third type is a combination of the first two types and is evoked by trigger points or neck movements.

Costen's syndrome is a form of craniofacial pain that should be differentiated from trigeminal neuralgia.

Tolosa-Hunt syndrome manifests as unilateral, constant, severe and acute pain behind the eye followed by ophthalmoplegia and diplopia a few days later. It is caused by granulomatous lesions, tumours or arteritis in the orbital region and involvement of III, IV, V (ophthalmic branch) and VI cranial nerve. The response to corticosteroid treatment is a diagnostic test.

Raeder's paratrigeminal neuralgia is a result of trauma, tumours in the middle cranial fossa, syphilis, sinuites, aneurisms, carotid artery dissection, granulomatous processes and injuries to the parasellar area or sinus cavernosus. It is characterized by unilateral, constant, severe and acute, deep and pulsating or burning, frontotemporal pain in the trigeminal nerve region – around the eye, forehead and cheek, which cannot be induced. It can wake the patient from sleep. It is accompanied by hypoesthesia and dysaesthesia, ptosis and myosis (incomplete Horner's syndrome). There is a migrainous variant with episodic pain lasting for hours or days and a symptomatic variant

that manifests with more constant pain.

Reflex sympathetic dystrophy of the face occurs after dental surgery or penetrating facial injury. It is characterized by acute, burning pain and hyperpathia, without sudomotor, vasomotor and trophic skin changes.

Central neuropathic pain in damage of the central nervous system may cause a syndrome that is indistinguishable from trigeminal neuralgia.

Neck-tongue syndrome runs with acute occipital pain and numbness of the ipsilateral half of the tongue, on sharp turning of the neck. It is due to extension of the C_2 nerve root, which contains proprioceptive fibres from the tongue.

General practitioner must refer the patient for consultation by a neurologist so that to timely differentiate symptomatic neuralgias.

Neurologist performs the necessary tests and determines the diagnosis.

Back Pain

It is not a specific disease but rather a symptom of a number of underlying diseases, the exact aetiology of which in many cases remains unknown. Back pain can occur in any region of the spine (cervical, thoracic or lumbosacral) but is most often localised in the low back.

The prevalence of low back pain reaches up to 80% of population and the incidence is 5% per year. Neck pain occurs more rarely. The prevalence increases from the age of 30 years on, and peaks around the age of 55-64.

Aetiology and pathogenesis. The pain syndrome may be due to disorders of bone structures, apophyseal joints, ligaments, muscles or intervertebral discs, subsequently affecting the spinal cord and peripheral nerves. The pain is not associated with neurological injury in 85% of patients. Neoplasm is found in 1% of patients, a compression fracture is found in 4%, and disc protrusion is found in 8%. The causes of pain in the absence of root compression are nerve root inflammation or disc chemical sensitization.

Spondylarthrosis is a form of osteoarthrosis, a degenerative disorder that affects different structures of the spinal cord – bones, joints, ligaments, muscles, vertebrae and intervertebral discs and leads to a narrowing of the spinal canal. With aging degenerative changes occur in the intervertebral discs and ligaments. The dehydrated disc thins out and becomes more fragile and loses its capacity to absorb and distribute tension uniformly to annulus fibrosus and vertebral body. Fibrous changes develop, the pressure in the back of annulus fibrosus increases due to physiological lordosis. The increased pressure leads to the formation of fissures in the back of annulus fibrosus. A decrease in disc height disturbs the articulation of apophyseal joints and vertebral bodies, which leads to loading of joints and limits their mobility. Hypertrophy of articular joint facets,

degenerative arthropathy, joint space narrowing, subchondrial sclerosis and bone formations occur causing *stenosis of the vertebral* and intervertebral canal. In osteoporosis, the size of vertebrae decreases thus additionally narrowing the spinal canal. The spinal canal configuration changes, progressively narrowing the lateral recesses where the nerve roots lie before exiting through the intervertebral foramens. Changes in the lateral recessus is more marked in the lumbar region. Such degenerative changes (spondylosis) are diffuse, bilateral and have different manifestation in different spinal segments. In most cases, the structure of annulus fibrosus remains injured but intact. Changes occur in ligaments, most commonly hypertrophy of the yellow ligament. Over the years, degenerative changes lead to fibrous ankylosis and stabilization of spinal segments.

Disc herniation follows degenerative changes in 20% of patients. Various trivial motions such as bending or coughing may cause prolapse of nucleus pulposus, which pushes the weakened annulus fibrosus outwards. In more severe cases, partial rupture of annulus fibrosus occurs and nucleus pulposus may protrude through the fissures. Herniation can occur forward to the vertebral body with the formation of Schmorl's nodes. These three types of disc herniation are associated with a different degree of spinal roots injury caused by the solid fragments of annulus and nucleus. Typically, only nuclear fragments protrude through fissures of annulus, laterally on the left or right (medially less often) and compress one or more nerve roots. One disc herniation can affect a few nerve roots, with the corresponding clinical manifestation. Larger protrusions can compress the nerve roots to the articular apophyses or the lamina of vertebral arch. Protruded nucleus is resorbed and decreases in size but causes chronic irritation of nerve roots and subsequent arthrosis and osteophytosis.

Soft tissues injury (muscles and ligaments) as a result of bending, turning, heavy lifting, prolonged sitting in an uncomfortable position is one the most frequent causes of low back and neck pain. In such cases, apophyseal joints between two vertebrae are displaced which damages the joint capsules and surrounding soft tissues. One of the most common causes (25%) of neck pain is the whiplash injury.

In many cases, causes of pain are not clear, it is not possible to make a precise diagnosis and treatment is non-specific. They are divided into:

structural: degenerative disorders, spinal stenosis, hereditary anomalies, myofascial syndrome, traumatic injuries and fractures, kyphoscoliosis, spondylolisthesis, Scheuermann's disease, achondroplasia.

non-structural (not related to the spinal cord): neoplasms (primary, metastatic), infections, osteomyelitis, paraspinal and epidural abscess, septic, tuberculous or ankylosing spondylitis, adhesive arachnoiditis, rheumatoid arthritis, spondyloarthropathias, Reiter's syndrome, internal diseases, prostatitis, endometritis, abdominal aortic aneurysm, pancreatitis, peptic ulcer,

cholecystitis, renal and endocrine diseases, acromegaly, hyperparathyroidism, hyperthyroidism, metabolic bone diseases, osteoporosis and Paget‘s disease.

Back pain is most commonly due to *structural causes*. It is not always possible to specify them in terms of anatomy as most patients present with similar symptoms. This requires that the general practitioner refer the patient to a number of tests and to a neurologist and other specialists.

Timely diagnosing of *non-structural causes* of back pain is particularly important. In case of evidence of such injuries, the general practitioner must urgently refer the patient to a neurologist.

Factors contributing to back pain are: medical: (respiratory diseases, trauma, pregnancy, menstruation), occupational (prolonged sitting, driving, casual employment), family-related or personal (family problems, small children, job dissatisfaction, depression, anxiety, alcohol abuse, smoking with cough).

Back pain is mixed (nociceptive and neuropathic). Several types of pain manifest at the same time: local, radicular and muscle spasm pain.

The **local pain** is nociceptive and results from a pathological process damaging the structures containing nociceptors (periosteum, ligaments, fascia, intervertebral joint capsule, muscles, annulus fibrosus and tendons). It is constant and burning but may intensify provisionally. Although it is diffuse it is experienced around the affected area. Percussion of the affected area intensifies the pain.

The **radicular** or sciatic pain is neuropathic. It arises both from mechanical compression of nerve roots in foramen intervertebrale, lateral recess or spinal canal, and from the activity of inflammatory neuromediators (cytokines and chemokines), originating from the degenerated intervertebral disc. It is acute and severe, with distal radiation from the spine to the limb in the relevant dermatome. It overlays the dull reflected pain. Intensifies when coughing, sneezing and stretching or compressing the nerve root, for which different methods are used (Lasegue, Wasserman, Neri's symptom, etc.). It is accompanied by pain in specific points (Valleux’s) along the nerve, paraesthesias and negative sensory and motor symptoms.

The pain caused by the **protective spasm** of paravertebral muscles that protects the affected areas from movement is nociceptive and dull. It is paroxysmally increasing, disturbs the normal posture and accompanied the local pain. Muscles are painful to pressure, especially at the level of the vertebra affected. Bending forward, aside and back intensifies the pain.

Clinical Course

Back pain is divided into acute and chronic, depending on their duration. Pain of specific aetiology tend to occur acutely and subside relatively faster, while pain of other aetiology tends to occur subacutely and have a chronic course. Pain with acute onset can also become chronic.

Predominantly Acute Onset Back Pain

The acute idiopathic low back pain, also referred to as ‘lumbago’ is the most common (80% of cases). It occurs in patients aged between 25 and 50, and is twice more common in men than in women.

It is caused by paravertebral muscles and ligaments stretching due to lifting weights from uncomfortable position, sudden movement or falling down. There is no correlation between the severity of pain and physical exertion. The pain is nociceptive.

Pain is sharp, posture is impaired due to spasm of the sacrospinal muscles. The pain increases with sitting or standing up from a sitting or lying position and is relieved when lying on one's back with flexed knees and thighs. No neurological symptoms are found except for a pain upon palpation on both sides, paravertebral muscles spasm and restricted bending forward.

Pain can be quickly relieved by treatment. If not treated correctly, it may become chronic, which will lead to degenerative changes in the intervertebral joints and vertebraesa.

Acute idiopathic neck pain is equivalent to idiopathic low back pain. The onset is acute, upon standing up or with a sudden movement of the head. The pain is sharp, making the movement of the head difficult; therefore, the head remains tilted. Besides pain and a marked spasm of the neck muscles, no negative neurological symptoms are identified. Symptoms resolve spontaneously in 7-10 days although in some cases pain may become chronic.

Lumbar disc herniation is the cause of acute, chronic and recurrent low back and leg pain in 5-8% of the patients with low back pain. The lumbar herniated disc most often occurs around the age of 30-40 when the composition of nucleus pulposus is still gelatinous. Men are affected more often than women. Most often the disc between L5-S1 is affected, and in descending order L4-L5, L3-L4 and L2-L3.

A fully developed syndrome manifests as spontaneous low back pain (moderate or severe, knife-like pain), deep in the gluteal region, laterally and under the sacroiliac joint, and in the posterior lateral thigh region radiating to the posterior side of the inlower leg and foot (sciatica), back stiffness and defformation and a combination of paraesthesia, reduced tendon reflexes and muscle weakness. In case of severe pain, the patient may stay in bed avoiding even the slightest movements, as coughing and sneezing aggravate the pain. Sitting or standing up from a sitting position, going up and down stairs are particularly painful. Pain and numbness are induced by different techniques. The posture is impaired (sciatic scoliosis) with bending forward and sideways (the side is determined by the relation between the disc and the nerve root). The analgesic posture is also associated with reflex contracture of paraspinal muscles, which is visible or palpaple. The

injured leg is slightly flexed at the knee, so that the foot does not touch the floor, and the body weight is distributed to it for a short time while walking, so the patient limps.

Radicular damage symptoms include foot or leg paraesthesia (hyper-, hypo- or dermatome anaesthesia are more rare), weight loss or loss of the knee jerk reflex or the Achilles reflex, decreased muscle tone of flank and lower leg muscles, and asthenia more rarely. Large central protrusion manifests with bilateral symptoms and may be accompanied by sphincter dysfunction, cauda equina syndrome and elevation in CSF protein.

A disc prolapse at L_5-S_1 affects the **S_1** root, presenting with spontaneous and palpation pain in the central gluteal region (around the sacroiliac joint), back of the thigh and lower leg to the heel, and IV and V toes. Lassegue's sign is positive. Paraesthesias and sensory disorders are localized in the lower leg and the two last toes. The loss of the Achilles reflex is an early symptom. Muscle weakness includes the plantar flexors of the toes and foot (difficult toe walking), abductors of toes and flexors of the lower leg.

A disc prolapse at L_4-L_5 affects the **L_5** root with spontaneous and induced pain in the lateral gluteal region to the femoral head, posterior lateral thigh region, lateral side of the lower leg to the external malleolus, dorsal surface of the foot, and I, II, and occasionally III toe. Lassegue's sign is positive. Paraesthesias are experienced in all or only distal regions. Weakness includes dorsal flexors of I toe and foot (difficult walking on heels). The Achilles reflex is preserved, decreased or lost, the knee reflex is always weakened or absent.

Less common injury at **L_3** (L_2-L_3 prolapse) and at **L_4** (L_3-L_4 prolapse) causes pain and sensory disorders in the front of the thigh and knee, and the anterior medial lower leg (L_4). The knee jerk reflex is weakened or absent. The injury to L_3 leads to weakness of mm. quadriceps and iliopsoas, and the injury at L_4 weakens m. tibialis anterior.

Injury at **L_1** (thigh-pit pain) and **L_2** (lateral thigh pain) is considerably more rare.

A more medially located disc protrusion at level L_4-L_5 can affect not only L_5, but also the sacral (S_1, S_2, S_3) roots. The medial compression manifests with bilateral leg pain and pelvic floor disorders. Protrusion with a more lateral location can affect an upper nerve root. Symptoms are not always fully developed. Low back pain may not be accompanied by leg pain ("sciatia") or the low back pain disappears and pain, sensory and motor leg disorders remain. The disease may commence with leg pain only from the very beginning.

Cervical disc herniation, in contrast to lumbar disc herniation, is not a prevailing cause for nerve root damage. Herniation of the lower cervical discs is a common cause for pain in the neck, shoulder and arm. The onset is acute following a different in grade trauma (sudden hyperextension of the neck, manual therapy, water jumps, car accident, etc.). Sometimes an acute pain onset occurs upon awakening, not related to visible causes, and difficult to account for by pre-existing vertebral

changes. Most often the C7 (in 70%) is affected, more rarely - C6 (20%), and most rarely - C5 and C8 (10%).

Clinically, it progresses with pain (nociceptive and neuropathic), excitatory (paraesthesia) and defficiency sensory and motor disorders located in the area innervated by the damaged nerve root. Head movements are restricted, pain is aggravated by neck movements, particularly by hyperextension and flexion, coughing and sneezing, due to the cervical muscles spasm. The restriction affects mostly the extension and rotation of the head towards the side of pain.

The *medial disc protrusion* can lead to spinal cord compression or even complete spinal cord injury, and paramedially – to partial spinal cord injury with the corresponding clinical presentations. As there is no pain, the syndrome can immitate amyotrophic lateral sclerosis or combined systemic atrophy. It is important to identify the presence of pelvic floor disorders and level of sensory disorders.

Thoracic disc herniation with thoracic pain is relatively uncommon (0.5% of patients with disc disorders). In 75% of patients the four last thoracic vertebrae are affected, mostly T_{11}-T_{12}. It is commonly caused by traumas and high falls on feet. In milder cases, pain radiates along the respective intercostal nerve (intercostal neuralgia), there can be no spontaneous pain in the vertebral region, and may simulate visceral pain. In contrast to pleural pain, it is not intensified with deep aspiration. Pain typically aggravates at night. Paravertebral pain and increased muscle tone are identified on palpation. Spinal cord compression can cause paraesthesia, loss of superficial and deep sensation below the level of injury, paraplegia and pelvic floor disorders.

Whiplash associated disorders occur in 60% of people injured in car accidents. Whiplash occurs *when* the head moves suddenly when a car gets rear-ended.

Clinically, symptoms start within 12 to 24 hours after the trauma, following muscle bleeding and oedema. It develops with neck pain, reflected pain in the head or upper extremities. Less frequent are the back pain and pain between the shoulder blades, dizziness and paraesthesia. The injury to ligament and bone structures causes sharp pain that intensifies with the slightest head movement. Cervical flexor muscle spasm occurs (m. sternocleidomastoideus, mm. scaleni, m. colli longus). 10% of patients report pain radiation to the arm. These symptoms are poorly defined anatomically and are not due to root damage but to reflected pain from the intervertebral disc, muscles, ligaments and apophyseal joints. Subjective perception of insensibility may develop in the region innervated by the ulnar nerve as a result of spasm of m. scalenus anterior and brachial plexus compression. Longitudinal ligament rupture and intervertebral disc herniation accompanied by radicular pain are rare. Scapular muscle dysfunction leads to pain in the back, shoulder and arms. The temporomandibular joint can also be damaged. Most patients recover within a few months.

Soft tissue injury causes in some patients (elderly and females) psychosomatic reactions that make symptoms chronic. In 20% of patients pain remains chronic due to apophyseal joints damage.

Neurological examinations do not reveal anomalies, except for tenderness on palpation and limited movements in the cervical region. In most patients, neuroimaging methods do not reveal pathological changes.

Fractures of laminas, articular processes and occipital condyles occur very rarely in the upper cervical segment. There could be also neurological symptoms of nerve root or spinal cord compression or impaired circulation in the anterior spinal artery.

Back Pain with predominantly subacute onset and chronic course

Lumbar spondylosis manifested with intervertebral disc degeneration, without protrusion, affects elderly patients (about 60 years old). Although it narrows the vertebral canal, it does not entail negative neurological symptoms and nerve root injury syndromes, in the absence of co-existing disc disease. Low back pain is diffuse, moderate and constant, without remissions, accompanied by spinal stiffness and restricted spinal mobility. No good correlation exists between the radiographic osteophyte changes, disc space narrowing, subluxation of the joints and neurological symptoms. The most probable cause of pain is articular facet hypertrophy.

Spinal stenosis due to spondylosis in patients with a narrowed spinal canal also causes nerve root compression. Spondylosis is most commonly found in the region of the inferior articular facet of L_5 and narrows the lateral recess in the superior edge of the vertebra compressing L_5 and more rarely, the S_1 nerve root. It manifests with pain in one or both legs when getting up and walking, which is alleviated when lying down and bending forward, and various sensory, reflex and motor nerve root disorders. The radicular pain syndrome may be accompanied by articular capsule pain. In the presence of apophyseal joint hypertrophy, the nerve root could be pressed to the floor of the intervertebral canal from the superior or inferior articular process. Spondylosis may lead to compression of cauda equina roots between the posterior facet of the vertebral body and ligamentum flavum posterolaterally.

Spondylotic caudal radiculopathy presents as claudicatio intermittens and manifests with pain, numbness and legs weakness when walking, which subside with rest. It is the lumbar equivalent of spondylotic cervical myelopathy.

Congenital spinal canal stenosis due to abnormalities of vertebrae is rare.

Congenital abnormalities are common in the lumbar region and though rarely themselves the source of pain, they may predispose an individual to discogenic or spondylotic complications by virtue of altering the mechanics and alignment of the vertebrae or size of the spinal canal. A common anomaly is a lack of fusion of the laminae of one or several of the lumbar vertebrae or of

the sacrum (spina bifida), frequently accompanied by malformation and asymmetry of intervertebral joins or dysraphism. Sacralisation of L_5 (fusion of the vertebra to the sacrum) or lumbarisation of S_1 (looks like sixth lumbar vertebra) are relatively rare.

Spondylolysis is a genetic abnormality with bone defect in the vertebral pars interarticularis. In the more common bilateral form in young individuals, sm the vertebral body, pedicles, and superior articular facets move anteriorly and cause spondylolisthesis. Initially the disease may be asymptomatic but later low back pain (L_5, and more rarely L_4) occurs. Development of spondyloptosis is also associated with nerve root symptoms: paraesthesias, sensory and reflex impairment and muscle weakness.

Spondylolisthesis (usually at L_4) may develop without spondylolisis in middle-aged and elderly women as a result of degenerative changes. It manifests with low back pain, which is hard to differentiate from pain of other aetiology.

Cervical spondylosis is one of the most common causes of pain in the neck, back of the head, shoulders and arms, unilaterally or bilaterally. It is accompanied by stiffness and limited spinal mobility, articular crepitus caused by head movement, and headache that is undistinguishable from the tension headache. No negative neurological symptoms are identified if there is no coexisting disc disease. It is frequently asymptomatic; however, as disease progresses, the narrowed intervertebral canal causes nerve root irritation and gradual onset of radicular pain that is precipitated by slight trauma accompanied by sensory and motor symptoms. It is most severe with extension of the head and turning it to the side of the pain. In the presence of a narrowed spinal canal, disease progression may cause spinal cord compression with myelopathy. In other cases, spinal arteries compression may result in ischemic myelopathy. A disc herniation causes sharp and severe pain, which is not well localized, aggravates with movements and is accompanied by muscle spasm. Occasionally, long before the occurrence of radicular pain, the patient experiences poorly localized pain in the interscapular area accompanied by muscle spasm.

The C5 and C6 nerve roots are most often affected because these are the most mobile vertebrae, placed under unfavourable angle and subject to the most intense degeneration.

Myofascial pain is the primary source (20%) of back pain. It is caused by repetitive microtrauma of muscles due to poor working posture, stress, anxiety, etc. Pain is local and associated with increased tone of the painful muscle. Typical are the pain-generating local trigger zones that are revealed as induration of the adjacent muscle on palpation.

Chronic idiopathic back pain is due to mistreatment of acute idiopathic pain, poor working posture, weak muscles, chronic overload of the back and other factors leading to degenerative changes in spinal muscles and ligaments.

The pain is moderate and, if not caused by an attack, its onset is gradual and unclear. In that case it is moderate or a sensation of discomfort and tiredness in the low back predominates, which is increased by any physical activity. An examination identifies moderate tenderness on palpation and increased paravertebral muscle tone, without negative neurological symptoms. Pain-inducing techniques are negative, and the low back mobility is preserved. Repeated back movements associated with hyperflexion and extension intensify the paravertebral muscle pain and tone.

Psychosomatic back pain is caused by anxiety and depression that lead to chronic paravertebral muscle spasm. It is more common in the cervical region but it can also occur in the lumbosacral region. Clinically, it presents as diffuse spasm and paravertebral muscles pain. In order to accept such cause, any other possible organic cause must be ruled out. On the other hand, pain precipitated by organic causes can become chronic due to psychogenic factors. Antidepressant effectiveness in the treatment of pain is of diagnostic significance.

Brachial Plexitis

The injury of nerve roots that form the brachial plexus at the level of the intervertebral canal results in shooting or burning pain in the back of the neck radiating to shoulders, on the outer arm, to the elbow and wrist. It develops with sensory (hypoesthesia or anaesthesia), motor (muscle weakness and hypotrophies) and reflex symptoms. Sometimes, the radicular pain is the only symptom and slight paresis of m. triceps brachii may not be noticeable due to compensation by other muscles. In acute disc protrusion due to trauma or strong movement, the pain is more severe and radiates up and down the arm. Neurological deficit occurs.

Differential diagnosis is made by a Pancoast tumour of the pulmonary apex, myofascial syndrome and thoracic outlet syndrome. *Extraarticular pain syndromes* include capsulitis, tendinitis, rotators injury, bursitis and periarthritis mimicking joint pain.

Fibromyalgia

This chronic pain syndrome is characterized by diffuse pain, tender points, tiredness, headache, irritable bladder, sleep disturbance, memory impairments and muscle stiffness. Most patients (75%) have long-standing myofascial syndrome before development of generalized pain in fibromyalgia. Both syndromes present with trigger zones that precipitate referred pain on palpation. The risk of development of fibromyalgia is higher in patients with other long-standing (over 6 years) pain syndromes, such as the whiplash syndrome, chronic back pain and inflammatory rheumatic diseases, such as systemic lupus, rheumatoid and psoriatic arthritis. The risk is also higher for physically inactive people, particularly with age.

The *prevalence* is about 2% of population and increases with age. Women are predominantly affected (up to 90%). Prevalence in women reaches up to 3.4%, and in men it is only 0.5%.

The syndrome's *pathophysiology* is associated with the emotional trauma, genetic factors and deficit of serotonin and noradrenalin, elevated levels of substance P and nerve growth factor, and disturbed circulation to the muscles. Muscular ischemia causes peripheral sensitisation with subsequent increased nociceptive afferentation to the central nervous system, which leads to impaired processing of somatosensory afferent activity on the central level – central sensitisation and neuropathic pain.

The disease *onset* is between 25-60 years of age. It is triggered by different factors: psychological or physical trauma, posttraumatic stress disorder, infections, endocrine disorders, etc. Primary clinical symptoms are muscle sensitivity (mechanical allodynia) and chronic diffuse and migrating pain. Fibromyalgic tender points are symmetric and scattered all over the body. They are typically localized in muscles, ligaments and tendons. When pressed, they do not cause referred pain and are not associated with muscle spasm in contrast to myofascial trigger points. In 20-40% of patients true myofascial trigger points are detected. Their formation is acute – after whiplash injury or muscle overload or gradually, after chronic extremity overuse, poor posture, sleep disturbances and poor motion activity. Body areas where the pain is the most pronounced change within hours and days. The pain is dull, burning and is often experienced as pressure. It is mainly localized in muscles, however some patients report of joint pain and superficial pain. Most affected are the cervical, brachial and lumbar muscles – m. sternocleidomastoideus, m. trapezius, m. masseter, m. temporalis, m. levator scapulae, m. gluteus maximus and minimus, and m. quadratus lumborum. Rest pain aggravate with physical activity (particulatly in a static posture), psychic tension, insomnia, cold, noise, weather changes, infections, stress, strong light and crowded places. They are relieved by heat, massage and physical exercise with muscle stretch. Temporomandibular joint pain, tension headache and low back pain frequently occur.

Most patients (70%) experience morning stiffness similar to that reported by patients with rheumatoid arthritis. They complain of diffuse swelling of hands and feet. The muscle spasm and shortening due to trigger points cause joint dysfunction and mobility disorders. Osteochondrosis and radiculopathy are also common.

There is diffusely increased tenderness (multimodal and pressure allodynia), hyperalgesia, dysaesthesia and paraesthesias. Patients with more advanced disease present with cognitive deterioration such as memory impairment, impaired concentration, stress intolerance and difficulty in performing multiple tasks at the same time. 80% of patients report fatigue and weakness.

There is a number of „functional somatic syndromes". Irritable bowel and bladder syndromes are common.

Diagnosis is made in the presence of diffuse pain and pressure allodynia in 3 or more anatomical locations and sensitivity in more than 11 of 18 fibromyalgia-specific tender points. These symptoms must last for more than three months and other causes of pain must be ruled out.

The *differential diagnosis* includes chronic inflammatory and neoplastic diseases, thyroid dysfunction, inflammatory and metabolic myopathies that must be ruled out by suitable tests. The chronic fatigue syndrome has much in common with fibromyalgia and, according to some authors, it is one and the same syndrome. However, in the chronic fatigue syndrome there is no diffuse pain and allodynia present.

Prognosis is better at a young age. 24% of patients have remissions, while other present with chronic disease.

Diagnostic Methods in Back Pain

1. The disease history gives information about the type and duration of employment, trauma, other diseases, weight loss, urinary problems, previous pain attacks and treatment received, underwent surgical operations, onset, causes of occurrence, character and distribution of pain and further development, description of other symptoms (stiffness, paraesthesias). It is necessary to establish the presence of „Yellow flags" that increase the risk of chronic pain (table 4).

It is important to determine the *character* (table 2), *duration, frequency* and the aggravating and relieving *factors* of pain (table 1). Progressively increasing pain is indicative of spinal tumour, chronic pain with exacerbations and remissions are suspicious of spondyloarthropathy, and pain radiating down the lower extremity is indicative of nerve root irritation.

2. The neurological examination provides an opportunity to detect induced pain, stiffness, limitation of movements, deformities and neurological deficit.

Pain-inducing techniques make it possible to identify its aetiology. The absence of positive response to the pain-inducing techniques is indicative of the presence of psychogenic or muscle factors of pain. Pain aggravation by external and internal rotation (Patrick's test) of the hip is indicative of hip joint pathology.

Neurological deficit with involvement of the anterior nerve root manifests itself with weakened tendon reflexes, muscular hypotonia, weakness, atrophy, fasciculations and sensory disturbance.

Sciatic pain radiates along the back of the thighs and causes numbness on the back of the hip, posterior lateral lower leg and radiates to the lateral malleolus. It is most commonly caused by

disc prolapse but also may be attributable to spinal stenosis, neuropathy or neuritis, trauma, bursitis and osteoarthritis.

Cauda equina syndrome is suspected with a history of bladder (retention is the most common, incontinence is more rare) and sphincter disorders, saddle anaesthesia, muscle weakness in lower extremities or gait impairment.

Spinal cord compression syndrome manifests itself with pelvic floor, conductive sensory and pyramid signs.

3. Neuroimaging methods are not indicated for routine diagnosis in the absence of „red flags". There is a poor correlation between symptoms, neuroimaging methods and pathology. Most patients do not manifest the pathological changes that cause the pain. 15-45% of asymptomatic patients present with degenerative changes in the spine that increase with age. The MRI scan is the most sensitive method for assessing the spinal cord, and the CT scan – for spinal bone structures.

2. EMG study is absolutely indicated in the presence of negative neurological symptoms:

- muscle activity and F-wave to localize the nerve root affected.
- Conduction velocity of sensory and motor fibres to identify axon degeneration in the peripheral nerve.
- Second response to the flexor reflex to determine the pain threshold.

3. Detection of trigger points all over the body:

- Algometry – pain threshold below 4 kg.
- Thumb pressure – pressure pain threshold before nail whitening.

4. Laboratory methods to test serum and urine are used in the following situations:

- Pain lasting for more than 4 – 6 weeks: complete blood count, serum calcium and phosphor levels and alkaline phosphatase to rule out a systemic or bone disease.
- Temperature: complete blood count and erythrocyte sedimentation rate, and if there is clinical evidence, also tuberculin test and Brucella agglutination test to rule out an inflammatory process.
- Men under 40 years, chronic low back pain and morning stiffness – complete blood count with differential, rheumatoid factor and HLA-B27 antigen to rule out ankylosing spondylitis, and Chlamydia antibodies to rule out Reiter's syndrome.
- Men above 60 years – urea test, alkaline and acid phosphatase, specific prostatic antigen, to rule out a tumour.

5. Other tests:

- **Osteodensitometry** for osteoporosis – in women above 40.
- **Mammography** to rule out a tumour – in women above 40.

6. Consultations by other specialists

- **endocrinologist** for thyrotoxicosis or hyperparathyroidism.
- **urologist** to rule out a prostate tumour – men above 60.
- **neurosurgeon** for patients diagnosed with disc herniation or spondylosis suspicious for spinal stenosis with neurologic deficit who did not respond to conservative treatment for a period of 2 months.

General practitioner should:

1. Collect anamnestic evidence of the type, side, radiation, episodes, aggravating and relieving factors of pain.
2. Test reflex action, muscle strength, sensation and growth symptoms to identify neurological impairment.
3. Refer the patient for emergency consultation by a neurologist, if there is anamnestic and clinical evidence of sciatica, disc prolapse, negative neurological symptoms, uncontrollable pain and progressive neurologic deficit.
4. Schedule a consultation by the respective specialists for arthritis, gynaecological, renal, endocrine, gastrointestinal diseases, bone disorders and osteoporosis.

Differential Diagnosis of Back Pain

The differential diagnosis is intended to rule out pain originating from other organs and to identify evidence of serious spinal cord pathology (referred to as „red flags") that necessitate specific and more extensive studies. The next step in diagnosing is to detect nerve root injury.

1. Traumatic injuries are a common cause of back pain. Vertebral fractures are the result of flexion injuries in car accidents or high falls. They can affect the body, pedicles, lamina or spinous processes of one or several vertebrae, as well as may cause dislocations or complete spinal cord injury at a certain level. A fracture may also result from a minimal trauma in the presence of myeloma, metastatic carcinoma, osteoporosis, osteomalacia, hyperparathyroidism or hyperthyroidism that injured the vertebra.

2. Ankylosing spondylitis (Bekhterev's disease) could be misdiagnosed for a long time as disc disease. At the onset of disease, the morning spinal stiffness prevails over the pain, which is not aggravated by physical activity.

3. Reiter's syndrome can also precipitate low back pain caused by due to the sacroiliitis or lumbar spondyloarthropathy.

4. Spondyloarthropathies may be caused by infectious agents such as Treponema pallidum, Salmonella, Shigella, Escherichia colli, Mycoplasma pneumoniae.

5. Inflammatory diseases such as septic or tuberculous spondylitis and post-puncture spinal epidural abscess cause diffuse back pain which is not relieved by rest, accompanied by paravertebral muscle hypertonia and fever.

6. Adhesive arachnoiditis after spinal anaesthesia or operative interventions can cause chronic back pain.

7. Endocrine diseases such as hyperparathyroidism, hyperthyroidism and acromegaly lead to increased bone calcium uptake followed by osteoporosis. Acromegaly may also cause narrowing of the spinal canal.

8. Metabolic bone diseases such as osteoporosis and Paget's disease cause back pain.

- *Osteoporosis* is a systemic metabolic skeletal disease characterized by decreased bone mass and microarchitectural deterioration of bone tissue. Primary osteoporosis is the most frequent – postmenopausal and senile osteoporosis. Secondary osteoporosis is less frequent and results from endocrine (hyperparathyroidism, hyperthyroidism, hypogonadism, hyperglucocorticism), gastrointestinal (gastric or intestinal resection, Crohn's disease, malabsorption, pancreatic insufficiency, liver disease), blood, rheumatic and genetic diseases (Turner and Kleinfelter syndromes), or is drug-induced (glucocorticoids, heparin, thyroid hormones, antiepileptic agents). Lifestyle, adequate nutrition, calcium intake, physical activity, hormonal state are also of significant importance. Smoking, alcohol and coffee abuse along with low calcium intake contribute to the development of osteoporosis. Spinal vertebrae are the predominant location of osteoporosis. In osteoporosis, the bone trabeculae of spongious bone become thinner and are more brittle, which results in vertebral body microfractures. Vertebrae typically become biconcave and wedge-shaped. Bone mass loss in osteoporosis is asymptomatic in most cases. Occasionally, compression fractures in the thoracic and lumbar region cause sharp radicular pain accompanied by muscle weakness in lower extremities. The sharp pain lasts for 2-3 weeks; then it may subside or remain as chronic back pain. Chronic pain as a result of osteoporotic fractures is caused by the increase in the mechanical tension in lumbar vertebrae and by paravertebral muscles spasm. Minimal trauma spinal fractures in patients with osteoporosis precipitate neurologic impairment.

- *Paget's disease* affects about 3% of people above 40 years of age. It is of unknown aetiology and is progressive. The disease starts in one bone then spreads to multiple bones, mostly the tibia, skull and vertebrae. Bone alteration includes destructive and reparative changes. Deossification of the cortical bone leads to microfractures. They are later followed by osteosclerotic changes in the bone. These changes in the vertebras result in lowering of the anterior part of the vertebrae and thoracic kyphosis. There is chronic back pain which is not relieved by rest and often worsens at night. It may be accompanied by typical radicular pain.

9. Scheuermann's disease is a juvenile epiphyseal disease of the spine which causes back pain upon loading.

10. Achondroplasia is a hereditary disease of unknown aetiology that causes dysfunction of the endochondral ossification. The patients' appearance is typical: massive head, prominent forehead, short arms and legs. The typical marked lumbar lordosis, shortened vertebral bodies and vertebral degeneration lead to spinal stenosis. Commonly, around the age of 40, there is low back pain accompanied by sensory and motor symptoms in lower extremities. Spastic paraparesis with pelvic floor disorders may also occur when spinal compression is located in the thoracic region.

11. Hip joint arthrosis (coxarthrosis), knee joint arthrosis (gonarthrosis) and periarthritis of the hip joint can cause serious differential diagnostic problems.

12. Lumbosacral plexitis, as well as traumatic, compression and diabetic sciatic or femoral neuropathies and meralgia paresthetica must be considered in the differential diagnosis.

13. Vascular diseases of lower extremities, mostly occlusion of the common or internal iliac artery, and thrombosis of the abdominal aorta may cause low back pain radiating towards the hip. The pain is deep, constant, poorly localized and is accompanied by numbness in the leg. Changes in the leg temperature are detected, there is no femoral and dorsalis pedis pulse, possible intermittent claudication.

14. Primary or metastatic tumours haemangioma, osteoma, sarcoma, reticulosarcoma, myeloma, neurofibroma, meningioma and metastatic carcinoma should always be considered in the differential diagnosis. Tumours located in the small pelvis, and particularly retroperitoneally, compress the lumbosacral plexus and cause low back pain, sometimes accompanied by sciatic radiation of pain.

15. Pregnancy and menstruation (20% of women) may cause back pain. During the second half of gestation, hormonal changes cause softening of fibrous tissues of the spine and pelvis followed by ligament tension and low back pain. They also allow for changes in herniated discs. Those changes are particularly distinct in multiparas. Endometriosis can affect the lumbosacral plexus and precipitate low back pain and sciatica.

16. Pain in some **internal diseases** radiates to the spine. Small pelvic pain (urological and gynaecological diseases) spreads to the sacral region, from the lower abdomen (intestines) to $L_2 - L_4$ vertebra, and from the upper abdomen (stomach, pancreas and retroperitoneal space) to lower thoracic and first lumbar vertebrae.

Complex Regional Pain Syndrome

It is a rare peripheral nerve neuralgia.

It is **classified** as a complex regional pain syndrome type I (reflex sympathetic dystrophy)

and complex regional pain syndrome type II (causalgia). Both syndromes are different in terms of aetiology, clinical symptomatology and response to treatment.

The **incidence** is 5 per 100,000 patients at risk. Women are affected 4 times more often than men.

The **aetiology** *of causalgia* is associated with a traumatic lesion of large proximal nerve trunks caused by a knife, bullet, machine parts, sharp stones or other objects, with incomplete interruption of a peripheral nerve. In 10% of cases, the disease is idiopathic and is not preceded by a clear cause.

Reflex sympathetic dystrophy occurs without peripheral nerve injury caused by minor leg injuries: postoperative inflammation, infection, burning, injury, freezing, joint degeneration, trauma, splinting and plastering, etc. that lead to prolonged limb swelling with peripheral nerve compression. Half of the conditions develop after upper limb trauma (n. medianus or n. ulnaris), more rarely, lower limb (n. ischiadicus or n. peroneus), wrist, knee or ankle trauma. In 30% of patients it occurs after a wrist fracture. A common reason is the surgical intervention for: knee joint arthroscopy (4%), carpal tunnel syndrome (5%), ankle (13%) and total knee arthroplasty (13%). It is less common after myocardial infarction or stroke.

The **pathogenesis** is associated with reorganization of the central autonomous control. Early sympathetic symptoms (oedema, vasodilation, trophic changes and increased temperature) are caused by neurogenic inflammation. The central release of neuropeptides causes nociceptive sensitization and leads to hyperhidrosis and motor impairment such as dystonia. Substance P and tumour necrosis factor-α activate the osteoclasts and cause osteoporosis. In chronic forms, the skin is cool, vasoconstriction develops. Sympathetic pain decreases over time due to decrease in the inflammatory component.

Sensory disorders in the limb affected go beyond the anatomical area of innervation and are quickly restored. They are caused by a change in the cortical processing of touch information as a result of the chronic pain.

The **clinical features** of the two syndromes are characterized by four key symptoms in the distal parts of the limbs: pain, swelling, skin discolouration and stiffness. They do not correlate with the degree of injury. Sensory, motor, autonomic and trophic symptoms change over time when passing into the chronic stage. The more severe the acute phase, the greater the likelihood of chronification.

The main and most common symptom is *spontaneous limb pain* at rest, more pronounced in fingers, palm or foot. It is constant, moderately severe, burning or lightning, deep, more rarely superficial. It is aggravated by touch, heat, cold, noise and emotions due to hyperalgesia. It is mostly intensified by a limb movement that stimulates the joint mechanoreceptors, and therefore the

patient does not move the limb and keeps it from any contact. The patient cannot even bear the contact with clothes, however often covers the limb with a towel damped with ice water wishing to relieve the pain. The pain radiates to extensive areas beyond the affected nerve.

Paraesthesias are reported more rarely but the patient may have the feeling of 'foreign' limb. Hyperesthesia and allodynia are more common. Hyperalgesia and allodynia are secondary phenomena associated with the central processing of nociceptive information.

Autonomic disorders in the acute phase manifest with distal oedema, warm, glossy and red skin in affected limbs. The swelling is the area of initial trauma, on the back of hands and feet, more rarely in knees. Initially, it is soft and limited, later hardens and can affect the entire limb. The swelling intensifies at the end of the day and disappears when in chronic phase. It is accompanied by sudomotor and vasomotor, and later trophic disorders that decrease in the chronic stage. In acute stages (the first 6 months) the skin temperature is increased in the affected limb due to vasodilatation, the skin is red and appears hyperaemic. In some cases, the skin temperature changes every day. In the chronic phase, vasodilation is replaced by vasoconstriction, the skin temperature drops on the injured side, skin turns pale or bluish and appears thin and glossy. In cold forms, the skin temperature is low since the onset, it may not change over time and remain lower through the years, and the skin colour remains bluish. The swelling and trophic changes are less pronounced. Both forms present with hyperhidrosis and rarely, hypohydrosis. The skin of the affected limb is wet and warm, or cool, glossy and smooth, flaky and discoloured.

Muscle stiffness is due to limb swelling and lack of motion due to severe pain. Disease progression is associated with ligament fibrosis and joint adhesion that limit mobility.

Trophic changes at the onset of disease occur as plus symptoms – increased nail and hair growth, and periarticular patchy osteoporosis. They abate with time and gradually turn negative – decreased nail and hair growth, skin atrophy, which becomes tight and glossy, and immobilization osteoporosis. In more severe cases, there could be subcutaneous tissue atrophy, thinning finger pads (pencil-sharpened appearance) and muscle hypotrophy with fibroses and muscle contractures.

Muscle weakness in the affected limb is available in a large proportion of patients. In the acute phase, it is associated with sparing the limb due to pain, and the chronic stage manifests with energy deficiency in affected muscles. The range of limb motion is decreased in the acute phase due to swelling and muscle spasm. The range of motion is limited in the chronic phase due to contractures and fibroses of palmar and plantar aponeuroses.

The disease may not develop through the phases described. The areas affected can expand from the distal to proximal parts of limbs, involve nonadjacent regions (70%) or mirror regions in the other limb.

In some patients intense postural tremor in the affected extremity and, more rarely,

myoclonus and focal dystonia are present. The cold form is more commonly accompanied by dystonia due to insufficiency of GABAergic inhibitory neuronal circuits.

The ***reflex sympathetic dystrophy*** runs in three phases. Patients do not develop all possible symptoms in the course of disease. The acute phase starts within a few days after the injury and lasts for a couple of weeks. It is characterized by spontaneous burning pain that spreads along the peripheral nerves or blood vessels. Pain is worsened by cold but is not affected by emotions. There could be hyperpathia, hypoesthesia or hyperesthesia and dysesthesia. The limb skin is warm, dry and red, or cold, bluish, oedematous and sweaty. Nail and hair growth are increased. Limb movements are limited. The second, dystrophic phase starts 3-6 months after the injury. During that phase, the pain is burning and radiating above and below the lesion, there is hyperesthesia and hyperalgesia. Nail dystrophy occur and the hair growth is slowed down. Joints become stiff, thickened, with decreased range of motion. Slight muscle atrophy, oedema and osteoporosis are identified. The third, atrophic phase, that occurs 6 months after the injury, manifests with pain, decreased skin temperature, trophic changes represented by smooth and glossy skin, joint stiffness and locking with muscle contractures, decreased or excessive sweating, bone demineralization with muscle atrophy and decreased muscle strength.

Causalgia develops with severe, constant and burning pain. Symptoms occur several hours or 1-2 weeks after injury and affect the proximal parts of the limb. The pain persists for more than 5-6 weeks, which is the time that is necessary for tissue recovery. It worsens at night, by emotional or environmental stimuli. It can also present with paroxysms of deep pain.

Diagnosis is made according to IASP criteria in the presence of specific symptoms. Except for the constant pain, which is not proportionate to any of its causes, the patient should report at least one symptom of at least 3 of 4 categories:

1. hyperalgesia, hyperesthesia;

2. asymmetry of skin temperature, change or asymmetry of skin colour;

3. asymmetry of sweating, oedema;

4. decreased range of motion, dystonia, tremor, muscle weakness, trophic changes in hair and nails.

The study must identify at least one manifestation of at least 2 of 4 categories:

1. Hyperalgesia on pricking, pain on touch, hyperalgesia or allodynia on pressure;

2. Asymmetry of skin temperature, change or asymmetry of skin colour;

3. Asymmetry of sweating, oedema;

4. Decreased range of motion, dystonia, tremor, muscle weakness, trophic changes in hair and nails.

The last requirement is that there is no other diagnosis to better explain symptoms. In order

to diagnose complex regional pain syndrome typeII it is necessary to clinically and neurophysiologically identify peripheral nerve lesion.

There are no **tests** to prove disease.

Infrared thermography detects temperature differences, which exceed 1^0 in both forms. Patients have a positive ice water test.

Conventional radiography can, within 4-8 weeks after the onset, visualize the development of patchy osteoporosis in juxta-articular bones. In later stages, osteoporosis becomes diffuse.

Three-phase bone scintigraphy with technetium-99m is an early predictor of osteoporosis. The isotope uptake is increased in the periarticular region which is indicative of increased bone metabolism.

MRI scan allows for differentiation of other diseases.

EMG study allows for identifying peripheral nerve damage.

Differential diagnosis includes localized infection in the limb that may simulate the hot form or arterial occlusion simulating the cold form.

General practitioner, in the presence of anamnestic and clinical evidence of complex regional pain syndrome, should refer the patient for an emergency consultation by a neurologist.

Neurologist should make a diagnosis based on the clinical criteria and tests performed.

Entrapment Neuropathies

They are focal lesions caused by compression of peripheral nerves when they run through bone-fibrous anatomic canals, under ligaments, retinaculums, fibrous muscle formations or, on pressure, through the skin in certain parts where the nerve runs superficially. External pressure is exerted by crutches, plaster or other hard objects.

The course of disease is a combination of nociceptive and neuropathic pain. Nerve trunks are a source of local nociceptive pain (nerve trunk hyperalgesia) spreading to adjacent regions but not radiating along the nerve. Such pain is caused on palpation of the ulnar nerve in the cubital canal. The associated referred pain phenomenon is common.

Entrapment of n. medianus can occur in the distal and proximal part of the nerve.

Carpal tunnel syndrome is the most common distal compression neuropathy. The prevalence is 2-3% of population, with middle-aged women being affected 3 times more often. The nerve injury is due to entrapment of n. medianus in the carpal tunnel in the wrist region, and local ischemia. The increased pressure inhibits venous drainage and nerve blood supply. When the critical level of hypoxia is reached, nerve pain fibres become hyperexcitable and generate spontaneous impulses.

Pathological processes that lead to compression are divided into 3 groups. The first group is associated with processes involving the canal walls and narrowing its space. The group includes wrist injuries (carpal bones dislocation), hypertrophic arthropathy and thickening of flexor retinaculum. Constitutionally, a narrower canal promotes syndrome development, particularly in occupations relating to repeated movements of wrist and arm. The second group of causes is associated with factors directly relating to the canal contents. It includes tendon and bursal disorders, hypertrophic neuropathies, lipomas, xanthomas and ganglions. The causes in the third group are idiopathic: myeloma, Raynaud's disease, renal insufficiency, amyloidosis, gout, diabetes mellitus, hypo- and hyperthyroidism, myxoedema, Graves's syndrome, acromegaly, hypophysis hyperactivity, obesity, pregnancy (soft tissue swelling), venous shunt for haemodialysis and many other systemic diseases. Repeated hand operations aggravate the symptom over time due to thickening of the synovial sheath of tendons that run through the canal along with the nerve.

Clinically, the onset is gradual, with episodes of painful numbness in one or both wrists. The symptoms are localized in the area of nerve innervation – thumb, forefinger, long finger and radial half of the fourth finger. Most typical are positive sensory symptoms in the form of acroparesthesias. Pain and paraesthesias are most intense at night and wake the patient up from his sleep. Symptoms are induced by reading newspaper, repeated wrist and finger flexion, driving and sewing. The disease progression is associated with burning pain. Tinnel's sign and Phalen's manoeuvre are used to induce neuropathic pain and they could be negative.

The second important symptom in 40% of patients is the referred nociceptive pain, which may be experienced at the onset of disease. It is deep, poorly localized in the wrist region, intensifies by repeated movements and spreads to the proximal side of the limb, predominantly to the elbow, and rarely reaches the shoulder. It spreads over the media parts of the limb and may be stronger than the neuropathic pain.

Sensory disorders of function loss are rarely identified, in distal finger tips innervated by n. medianus. The sensation in the palm region is not affected because the sensory nerve branches set off before the carpal tunnel.

Autonomic trophic changes in finger tips and hypohidrosis are rarely found. Some patients also have Raynaud's syndrome present due to involvement of sympathetic nerve fibres.

The positive motor disorders such as spontaneous fasciculations in the muscles innervated by n. medianus are rare. Hypotrophy develops after loss of sensation in patients with axonal damage and neuropathic pain. The manifestation of motor symptoms is indicative of more severe damage and usually requires surgical decompression. Pain-free thenar hypotrophy is less common. The muscles innervated by n. medianus distally of the carpal tunnel are affected: mm. abductor pollicis brevis, opponens pollicis, flexor pollicis brevis and lumbricales of the forefinger and middle finger.

The *differential diagnosis* includes nerve injury in the cubital region.

EMG study reveals decreased conduction in the distal nerve segment and decreased motor response amplitude (in axon degeneration).

Entrapment of n. medianus in proximal parts of the limb can occur in three different locations around the elbow, and rarely in the axilla, as a result of improper crutch use.

Pronator syndrome occurs in excessive forearm pronation (tennis) or in the presence of muscle hypertrophy and tendon ligaments that cause nerve compression. It develops after trauma, elbow joint dislocation and bleeding in the forearm region. It may occur due to compression in three different locations. Most often, it is between the two heads of m. pronator teres, proximally to the branching of n. interosseus anterior, at the nerve entry into the forearm.

Patients complains of diffuse pains in the forearm, thumb and forefinger insensitivity. The nociceptive pain is deep, in the proximal side of m. pronator teres, in the area of compression. It is aggravated by excessive forearm pronation with fingers flexion and when carrying heavy objects with the forearm. Paraesthesias along n. medianus occur. Writing is painful. There is referred pain in the proximal side of the limb, most commonly in the middle and back arm, and sometimes in the shoulder. There are positive and negative sensory neuropathic symptoms in the region innervated by n. medianus, which are not clearly defined and are hardly differentiated from the carpal tunnel syndrome. There is no pain aggravation at night and the Tinnel's sign is positive in the proximal end of m. pronator teres but not in the carpal tunnel.

Muscle weakness and hand clumsiness occur when making pinching or circle-like motions. The proximal nerve injury is distinguished from the distal injury (carpal tunnel syndrome) by the characteristic weakness of m. flexor digitorum and m. flexor pollicis longus. It is detected by the so-called circle test – if the patient is able to make a circle by opposing the tip of the thumb to the tip of the forefinger, they are unable to flex both distal phalanges. The forefinger remains hyperextended in the distal interphalangeal joint due to weakness of m. flexor digitorum profundus, and the thumb, due to weakness of m. flexor pollicis longus. If compression is under the aponeurosis of m. biceps, there is typical weakness of m. pronator when attempting pronation. Weakness in other muscles develops depending on the degree of compression. Long flexor muscles of fingers and thumb can be affected, as well as m. abductor pollicis brevis.

EMG study is not capable of detecting the location of lesion.

Entrapment of n. ulnaris is mostly proximal, in the cubital region, and more rare in the wrist.

Ulnar nerve entrapment at the elbow (cubital tunnel syndrome) is the second most common entrapment neuropathy of n. ulnaris in the fibrous bone canal. Degenerative arthritis at the elbow joint that leads to ulnar neuropathy is referred to as late ulnar paralysis. It may occur years after a

traumatic joint injury and has a progressive course. Predisposing factors are diabetes, hereditary neuropathies, narrow ulnar bone canal or a hypermobile nerve which easily dislocates out of the canal. In many cases, it may occur without a tangible cause.

Clinically, the syndrome can develop with different sensory and motor disorders. Patients report deep nociceptive pain in the medial cubital region. It spreads to the internal proximal side of the arm, axilla and medial proximal third of the forearm. The pressure on the nerve or flexion of the elbow joint causes pain that is different from the pain in Tinnel's sign.

Positive sensory symptoms are expressed as spontaneous tingling in the region of the hypothenar eminence, medial side of IV and V finger. Tinnel's sign at the level of the elbow is very common. Negative sensory symptoms manifest with impaired sense of touch in the ulnar part of the hand, at the ulnar region of IV and the entire V finger on the dorsal and ventral side. Autonomic symptoms (anhidrosis) are also likely to be present.

Positive motor symptoms manifest as continuous fasciculations in the hypothenar eminence. Negative motor symptoms are present in the region innervated by n. ulnaris. The weakness in m. flexor carpi ulnaris and m. flexor digitorum profundus is typical for the proximal nerve compression. Weakness is observed in finger abduction and adduction. Hypotrophies of the hypothenar eminence and mm. interossei are also present. The typical claw hand is due to hypotrophy of mm. lumbricales of IV and V finger with preserved long extensor muscles. The injury to m. adductor pollicis is manifested as weakness when opposing the thumb to the forefinger. To compensate, the m. flexor pollicis longus (innervated by n. medianus) is contracted involuntary and the terminal phalange of the thumb is markedly flexed (Froment's sign). The weakness of the ulnar flexors of the forearm is much less manifested than the weakness of the intrinsic hand muscles.

EMG study shows the location of nerve injury.

Guyon's syndrome, due to nerve compression in the Guyon's canal at the wrist, is the second more common cause of ulnar neuropathy. It is commonly due to repeated external pressure exertion caused by various tools, bicycle handlebars, overly tight watch bands, fast gain in weight or use of crutches and walking sticks. It can be caused by gangliomas in the canal, acute or chronic hypothenar occupational injury (electricians twisting cables) and carpal bones fracture.

There are three variants of clinical course of nerve compression at the wrist. Symptoms vary from purely motor to purely sensory depending on the location of compression in the canal. The deep motor branch only is more often affected than the sensory branch innervating the fingers. Therefore, there is only nociceptive but not neuropathic pain and hypotrophy of m. interosseus dorsalis I. The compression of the nerve in the proximal side of the canal further causes disorders in the digital sensory branch. Pain may radiate to fingers and forearm. The rarest compression in the

distal part of the canal presents with only sensory disorders in the ulnar side of the wrist. Thrombosis of the ulnar artery that also runs through the canal causes Raynaud's syndrome.

Nerve entrapment at the forearm, above the Guyon's canal is rare. It is caused by a fracture and manifests as compression at the wrist. If the lesion is located proximally of the dorsal sensory cutaneous branch, the sensation in the dorsal part of the wrist will be impaired. Dysesthesias are also possible. The injury to the dorsal sensory branch is usually due to a trauma.

Entrapment of n. radialis may occur above and under the elbow.

Compression above the elbow is caused by compression of the upper arm by somebody else's head while sleeping, by crutches or by opposing to the chair or bench edge. It occurs often after alcohol consumption or during anaesthesia, hence the patient is insensitive to the numbness in the arm caused by pressure. Compressions caused by muscle overload, fibrous myopathy, drug injections, thickening of the epineurium, tumour and humeral fracture are more rare. Patients recover spontaneously in about 10 weeks. The clinical course manifests all the symptoms of distal (under the elbow) compression accompanied by additional paresis of m. triceps brachii.

Entrapment at and under the elbow level is associated with the syndrome of n. interosseus posterior. That deep motor nerve runs through the Frohse's arch (between the superficial and deep head of the supinator) that narrows with wrist supination and extension. It is a rare condition that is associated with a fracture of the upper third or dislocation of the head of radius and fracture of the ulnar bone. It may occur in a similar way to Saturday night palsy with improper arm position during sleep and alcohol consumption. It is less common in lipomas, neurofibromas and rheumatoid arthritis. The idiopathic form occurs with the compression in the Frohse's arch, as a result of repeated pronation, supination and extension of the elbow or application of tourniquets.

The sensory branch of the radial nerve dislocates distally to the elbow before running into the arcade, therefore the compression in that region is associated with purely motor symptoms. The wrist and finger extensors and m. brachioradialis are affected, which results in deep pain in the forearm, wrist drop and sensory disorders. Patients are unable to extend their fingers in metacarpophalangeal joints and deviate their wrists ulnary.

Superficial sensory radial nerve in chronic compression at the wrist is a result of overly tight watch bands, bracelets or cuffs and it leads to neuropathic pain referred to as cheiralgia paresthetica. It may also result from a fracture of the radius or intravenous infusions.

Patients complain of local pain in the lateral distal part of the forearm, with no nerve trunk hyperalgesia. Positive sensory symptoms manifest with dysesthesia and paraesthesia triggered by wrist movements. The Tinnel's sign is positive and indicates the location of injury. Negative sensory changes manifest with impaired sense of touch in the dorsal lateral side of the hand, dorsal side of I and II finger to the proximal interphalangeal joint and radial side of III finger.

Digital nerves are rarely compressed, when wearing tight rings for a long time. There is neuropathic burning pain and spontaneous numbness in the area of one digital nerve (one finger half). The Tinnel's sign indicates the accurate localization of the damage. So-called "*Bowler's thumb"* occurs in cricket and bowling players and is caused by constant irritation of the digital nerves of the thumb. Perineural fibrosis and painful nodules formation develop. So called *"Harp player's thumb"* is caused by playing stringed musical instruments. It is characterized by painful nodule formation and hypersensitivity to touch.

Thoracic outlet syndrome is rare, it is seen in younger and middle-aged women. The onset is spontaneous or induced by shoulder or neck trauma leading to muscle spasm. It is due to compression of the subclavian artery and vein and brachial plexus. It is divided into vascular (arterial or venous) and neurogenic that usually occur separately.

Arterial syndrome occurs with the compression of subclavian artery and presents with mural thrombosis and atheromatous degeneration, arterial stenosis and emboli formation in the limb. It manifests with ulcerations of the fingertips, pale, cold and shivering arm, missing pulse.

Venous syndrome is caused by occlusion of subclavian or axillar vein. It develops as a result of repeated compression of the vein between the first rib and the clavicle caused by the thickened m. scalenus anterior. It differs from the arterial syndrome by the diffusely swollen, bluish arm, with swollen veins of the thorax and shoulder. Numbness in the hand occurs as a result of peripheral nerves ischemia.

Neurogenic syndrome is rare because compression is transient and rarely results in neurological symptoms. In the presence of supernumerary rib, larger processi transversi, connective tissue between processi transversi and tuberculum of mm. scaleni, and in myofascial syndrome, with spasm of m. scalenus anterior, the inferior trunk of the plexus (C_8 and T_1) may be compressed.

Patients complain of unilateral, spontaneous, constant and dull pain in the front and back of the shoulder that radiates to the lateral side of the forearm and wrist. It may also radiate to the occipital region of the head and cause headache. It is aggravated by physical activity and lifting of the affected arm. If intensified at night, it is necessary to differentiate it from the carpal canal syndrome. In some cases, the pain is paroxysmal but becomes more frequent and intense over time. Sensory disorders and numbness occur before motor disorders caused by injury to C_8 and T_1 roots. They are more marked at the wrist (T_1) than at the arm (C_8). Hypoesthesia and paraesthesias include the entire IV and V finger, ulnar side of the wrist and the medial side of the forearm. There is hypotrophy and weakness of the internal muscles of the wrist innervated by n. ulnaris, thenar, and particularly of the innervated by n. medianus m. abductor pollicis brevis. Muscle spasm is identified in the neck and shoulder.

Adson and Roos' manoeuvres are positive due to contraction of m. scalenius, narrowing of the interscalenous space and raising of the first rib.

EMG findings are normal.

Costoclavicular syndrome is caused by improper posture or trauma with compression of the neurovascular brachial trunk between the first rib and the clavicle. It manifests with pain, paraesthesia and numbness in the arm and hand at night or early in the morning. The syndrome is confirmed by pulling the shoulders downwards and backwards (chest rise and shoulder retraction), in which symptoms are aggravated and the radial pulse is diminished. It is due to compression of the subclavicular artery between the clavicula and the first rib.

Syndrome of m. pectoralis minor (hyperadduction syndrome) occurs as a result of compression between m. pectoralis minor and the thorax. It is caused by myofascial syndrome that leads to shortening of the muscle or improper body posture. Symptoms are transient (they occur at night or early in the morning), they are not objectively identified and resemble costoclavicular syndrome but more commonly affect the ulnar and medial side of the arm.

Diagnosis is made by inducing the symptoms and suppressing the radial pulse with arm abduction above the head rotating outwards and backwards. M. pectoralis minor is extended and the adjacent neurovascular bundle is compressed in this position.

Neuralgic amyotrophy develops after influenza, typhus, smallpox and other infectious diseases or after serum injection. It is characterized by acute pain in the shoulder that is likely to spread to the arm, back and neck. The right arm is more commonly affected but the pain is bilateral in 25% of cases. Pain is increased by arm movements and at night. It is relieved by resting the limb, in adduction and flexion in the elbow. Proximal weakness in the shoulder and arm occurs affecting the muscles innervated by n. axillaris and n. suprascapularis. Sensory disorders are not commonly observed.

Waxman's sign is a flexion-adduction sign that induces pain through abduction and external rotation at the shoulder followed by extension in the elbow.

EMG findings reveal peripheral nerve damage.

Serum sickness neuropathy develops after application of heterologous serum, typhoid or paratyphoid vaccination or after application of medications that form complexes with serum proteins. There is no correlation between the quantity of serum applied and the severity of symptoms or development of neuropathy. The pathogenesis is associated with precipitation of immune complexes that results in vasculitis and perivascular oedema with peripheral nerve swelling. The swelling leads to peripheral nerve compression at the foramina they pass through. Neuropathy affects the brachial plexus. Sudden pain is experienced in the shoulder or upper arm. There are also serum sickness-specific symptoms: lymph node enlargement, joint pain, myalgia and

albuminuria. Muscular weakness develops at the shoulder and quickly progresses to paresis and severe muscular atrophy. Tendon reflexes disappear, vasomotor changes occur. Sensory disorders are poorly marked and radial muscles are less commonly affected.

This condition must be differentiated from myalgic and arthritic pain in serum sickness that affects muscles and joints.

Entrapment of n. axillaris is associated with fractures of the surgical neck of the humerus, at lower dislocation of the shoulder or at external rotation and abduction of the arm. It develops with paresis of m. deltoideus and limited abduction of the arm. Hypoesthesia in the external upper arm is found.

Entrapment of n. suprascapularis occurs under the upper transversal scapular ligament caused by lipomas or trauma in the shoulder area that involves the nerve, surrounding tissues or the ligament. It is seen in volleyball players, basketball players, gymnasts, in heavy lifting and carrying a backpack. It manifests with poorly localized pain in the shoulder that is stronger in the posterior and lateral sides. Weakness of m. supraspinatus and m. infraspinatus is present. No sensory disorders are detected, as the nerve is a purely motor nerve.

EMG findings reveal nerve lesion.

Entrapment of n. musculocutaneus occurs in strong extension of the forearm, intensive physical exercise, repeated pronation and supination of the forearm (screw driving) and hyperextension with arm pronation (falling or tennis playing).

The clinical course presents with weakness of m. biceps brachii, pain in the anterior lateral side of the elbow and dysesthesia in the radial side of the forearm. The sensory part of the nerve may be electively injured, distally from the motor part, due to compression at the lateral side of the aponeurosis of m. biceps. It may be injured spontaneously during venous manipulation or as a result of carrying a weighty bag on a bent elbow.

Entrapment of n. accessorius may occur spontaneously, after sports-related incidents or surgical manipulations in the posterior triangle of the neck – lymph node biopsy. The clinical course presents with weakness of m. trapezius and sternocleidomastoideus, pain and instability in the shoulder. Abduction of the arm is impaired, the superior angle of scapula is more lateral than the inferior one. This impairment is increased during arm flexion.

Entrapment of n. thoracicus longus occurs during anaesthesia when the patient is in the Trendelenburg position, with poorly positioned shoulder support pressing them down. It may occur when carrying heavy objects on the shoulder and lymph node biopsy at the base of the neck. It leads to shoulder instability, difficult arm raising and lateral dislocation of the inferior angle of scapula in relation to the superior angle. It is intensified during resisted arm extension. The pain is localized at the shoulder and spreads to the neck and arm.

Entrapment of n. ischiadicus most commonly occurs as the nerve exits the pelvis in the sciatic foramen. Injuries are caused by femoral fractures and dislocation, penetrating injuries, complications during hip surgery, prolonged pressure on the hip in comatose states, primary and metastatic tumours (lymphomas) and more rarely by spontaneous or anticoagulation-induced haematomas. A deep intramuscular injection may damage the nerve directly or cause muscular fibrosis that is to eventually compress it. Endometriomas may compress the nerve in the sciatic foramen. Lesions in the upper third of the hip affect both the fibular and tibial components but the fibular component of the nerve is always more affected. Lesions in the middle hip equally affect the both components of the nerve.

The clinical signs include hip pain, paraesthesia in the posterior part of the leg, hypoesthesia in the lateral side of the leg and foot, foot drop and impaired hip extension. If the fibular component is affected electively, the lesion clinically resembles nerve injury at the caput fibulae level.

Entrapment of n. peroneus communis at caput fibulae level, in a costo-fibrous canal between the fibular bone and m. peroneus longus, is due to compression of the nerve in bedridden and comatose patients or during general anaesthesia. It may be also injured during prolonged squatting position, sitting with crossed legs, at ankle twist and overstretching or be caused by tumours, ganglions and cysts of the knee joint.

Clinical signs include foot drop (due to weakness of m. tibialis anterior) and deep pain in the lateral upper third of the leg or in fossa poplitea. There are also sensory disorders present in the region innervated by the nerve.

N. peroneus profundus may be compressed due to muscular swelling in the anterior compartment of the leg – anterior tibial compartment syndrome. It may be caused by excessive exercise, trauma and reperfusion after arterial occlusion.

The progression is associated with severe pain in the anterior compartment of the lower leg and motor disorders.

Entrapment of n. peroneus superficialis caused by high and tight shoes is rare. Patients have no local pain at the compression location but experience paraesthesia that is aggravated with walking. The Tinnel's sign indicates the compression location. Hypoesthesia to touch is detected.

Entrapment of n. tibialis posterior may occur in fossa poplitea as a result of chronic compression by an aneurism of a. poplitea. It manifests with positive and negative sensory disorders in the foot.

Tarsal tunnel syndrome is more common. Compression of n. tibialis posterior occurs after traumas, fractures and dislocations of the ankle joint, wearing tight plaster casts, skates, ski shoes or shoes, tenosynovitis, osteophytes, tumours, chronic thrombophlebitis, gout, hyperlipidaemia and metabolic diseases that cause swelling, such as diabetes, hypothyroidism and rheumatoid arthritis. It

is seen in sprinters, especially after strenuous exercise and long hiking. Patients complain of constant, deep, burning or constricting pain and shivering above and behind the medial malleolus, heel, foot and its fornix. The region is tender on palpation. Positive symptoms manifest with spontaneous numbness in the foot. Negative sensory symptoms are presented by hypoesthesia to touch and pain in the plantar side of the foot. Symptoms are aggravated at night, by prolonged standing and walking, and are alleviated by movements in the ankle joint in contrast to those experienced in plantar fasciitis. Tinnel and Phalen's signs behind and under the medial malleolus are positive. The percussion of flexor retinaculum or dorsal flexion and twisting of the foot cause electric-like pain. There can be motor symptoms related to weakness of phalanges that impair the extension phase of the foot during walking.

EMG findings reveal denervation of m. abductor hallucis and prolonged distal motor latency.

Entrapment of n. femoralis may occur above the inguinal ligament (between m. psoas and iliac muscles) which causes impairment of those muscles function. Lesions under the inguinal ligament only affect some of the nerve functions because, a few centimetres after its entry under the ligament, the nerve splits into cutaneous branches for sensory innervation of the anterior side of the hip and into motor branches. The nerve may be damaged by hematomas or abscesses in the iliac muscles. In such cases, the patient lies with his hip flexed, abducted and externally rotated in order to alleviate the nerve compression. Injuries may also occur during anaesthesia in patients lying in a lithotomy position when the nerve is compressed under the inguinal ligament. The forced leg extension or hyperextension of the hip over the side of the bed in comatose patients can overstretch and damage the nerve. Penetrating punctured traumas, catheterization of the femoral artery and surgical interventions with lateral dislocation of m. psoas may also cause nerve injury.

Entrapment of n. saphenous occurs at 10 cm above the medial femoral epicondyle at the exit of the nerve from the subsartorial fascia. The pain occurs in the medial side of the leg to the inner side of the foot and the big toe. It is increased with limb movements, imitates knee joint injury or claudicatio intermittens. The prepatellar nerve branch may be separately injured after a trauma (medial meniscectomy) or spontaneously. Burning pain and hypoesthesia under the knee appear. Paraesthesias and dysesthesias during knee tension.

Entrapment of n. cutaneus femori lateralis in the hip is referred to as meralgia paresthetica. The nerve runs through a tunnel formed by a small slit in the lateral end of the inguinal ligament. It is susceptible to compression to spina iliaca, where it passes between the bone, ligament and the insertion of m. sartorius. The syndrome occurs in conditions related to abdominal growth: pregnancy, fast gain weight and liver diseases. It may be due to a direct trauma, tight jeans

or belt, keeping a wallet in the front pocket, etc. More rarely, it may be caused by retroperitoneal malignant rumour and abdominal surgeries.

The clinical signs include burning neuropathic pain and dysesthesia in the lateral side of the hip, which are worsened during prolonged sitting and walking. Painful dysesthesia disappears as soon as the hip is flexed. Local nociceptive pain in the compression area is rare. Negative sensory symptoms manifest with hypoesthesia to touch and pain in the lateral side of the hip. They are most severe 2-3 cm under the inguinal region and never spread under the knee. Marked dynamic mechanic allodynia is identified. The Tinnel's sign is negative. Prognosis is good, in most cases it disappears spontaneously with the cause of compression removed.

Plantar digital nerves can be compressed between the heads of adjacent metatarsal bones or when passing through the deep metatarsal ligaments. Compression often occurs in the area of the common plantar digital nerve, before its bifurcation into n.n. digitales proprii. This occurs most often in the third and fourth metatarsal space and leads to **Morton's neuralgia**. The syndrome is common and affects mainly women. Patients complain of local pain in the distal plantar third of the foot when walking. The pain becomes constant over time and spreads to the entire foot. It is worsened with wearing high heels. Palpation identifies local sensitivity and the movement of II and IV metatarsal bone to each other causes severe local pain. The pain is worsened upon pressing the toes to each other and with simultaneous compression of the area under the toes. The Tinnel's sign is negative. Negative sensory symptoms manifest with hypoesthesia to touch and pain in two adjacent toes, most frequently the third and fourth toe. Positive sensory symptoms are present as neuralgic electric-like pain between affected toes. There is also constant burning which is hard to tolerate by patients.

Sural nerve is rarely compressed in the anatomic fibrous arcade that duplicates its aponeurosis. It develops in athletes and with prolonged compression in the posterior inferior side of the calf. Pain is experiences in the lateral side of the ankle and foot. There are no sensory disorders, just local Tinnel's sign.

Joplin's neurinoma is caused by compression of the digital nerve at the medial side of the big toe when wearing tight shoes. It manifests with local pain and sensory symptoms in the medial side of the big toe, sometimes bilaterally.

Diagnostic methods in entrapment neuropathies

Tinnel's sign may be provoked along the myelinated and non-myelinated primary afferent nerve fibres. Percussion on the nerve trunk generates ectopic impulses in the axon due to increased mechanosensitivity and membrane hyperexcitability at the level of compressed axons. This results in dysesthesia in the skin innervation region of the affected nerve.

In **Phalen's test**, flexion of the wrist for 60 s causes numbness radiating to the wrist due to venous congestion. Alternatively, the test is performed with a tourniquet on the arm with applied pressure of 60 mm Hg. The test is sensitive and can be used to monitor the therapeutic effect.

In **Addson's test**, with the abduction and elevation of the arm over the head and turning the head to it, with the neck stretched and a deep breath taken, the radial pulse in the elevated arm is suppressed. The existing neurological symptoms are aggravated. The pulse amplitude may also decrease in healthy individuals, however there are no neurological symptoms.

Roos test is associated with aggravation of symptoms during external rotation at 90 degrees of arm abduction accompanied by palm opening and closing for 3 minutes. The moderate pressure on fossa supraclavicularis for 15 s aggravates the symptoms. There could be a difference in the blood pressure readings between the two arms.

EMG findings reveal the location and degree of injury. There could be decreased velocity of conduction in the peripheral nerves due to focal demyelination or decreased amplitude of the sensory action and compound muscle potential as a result of axonal injury.

Differential diagnosis in entrapment neuropathies

Thoracic tunnel syndrome must be differentiated from cervical disc disease, apophyseal joint syndrome, carpal tunnel syndrome, arthropathy, pericapsulitis, Pancoast's tumour, aneurism of the subclavian artery and neuralgic amyotrophy. Entrapment of the neurovascular trunk is suspected in case of neck pain and neurological symptoms in the upper limb that are aggravated with arms and neck placed in a specific position.

It is most difficult to make a differential diagnosis with lateral disc herniation C_5-C_6, which causes pain, sensory disorders and paraesthesia in the shoulder, trapezius muscle, radial side of the forearm and thumb. The pain radiates to the elbow and along the dorsal side of the forearm down to the index finger and third finger. There are sensory disorders and paraesthesia in the region of II and III finger. Tenderness on palpation in the region of m. triceps brachii and paravertebrally is detected.

Entrapment neuropathies of the upper extremities must be differentiated from radiculopathy of C_5 and C_6, C_6 and C_7 or C_8 and T_1 root. The compression of n. suprascapularis must be differentiated from subacromial bursitis, rotator cuff syndrome and brachial plexitis.

General practitioner, in the presence of anamnestic and clinical evidence of entrapment neuropathy, should refer the patient for an urgent consultation by a neurologist.

Neurologist should make a diagnosis based on the clinical criteria and tests performed.

Polyneuropathies

Neuropathies affect axons and myelinated sheath or Schwann's cells. Axons are more commonly affected with the longest and thickest nerve fibres being injured first. Degeneration starts from the distal parts of axons and progresses proximally. That mechanism is referred to as "dying-back" and it is a result of metabolic disorders in cell bodies or axons. Axonopathies are symmetric and are typical for toxic and metabolic disorders of peripheral nerves. In rare circumstances, axons are preserved but segmental demyelination is in place. It develops between Ranvier's nodules and more often due to autoimmune attack on peripheral nerves and roots (Guillain-Barre syndrome). Limbs can be affected distally and proximally, symmetrically. Neuropathies rarely develop as a consequence to impaired development or abnormal metabolism of Schwann's cells. The clinical course of polyneuropathies varies depending on their aetiology.

Polyneuropathies affect predominantly one of the nerve fibres types. They may affect mainly sensory fibres of large diameter (that conduct vibration and proprioception) and motor nerve fibres of mean diameter. Sensory fibres of small diameter (that conduct pain and temperature) could also be affected whether or not together with autonomic nerve fibres. Pain is a typical symptom in small fibre neuropathies.

Multiple mononeuropathy is caused by ischemia of the peripheral nerves due to vasculitis of small and medium blood vessels. It may be the first manifestation of systemic vasculitis. Irrespective of aetiology, it starts with sharp pain and numbness in the affected limb. Negative sensory and motor symptoms occur two days later.

Neuropathy is acute if symptoms develop for less than 3 weeks. The symptoms of subacute neuropathy develop within several weeks to months, while the symptoms of chronic neuropathy develop for more than 6 months.

Painful small fibre neuropathies

These is a subtype of sensory neuropathies which affect mainly the fine myelinated Aδ and non-myelinated C nerve fibres.

The **prevalence** is about 3% of the population with an increased frequency between the ages of 45 and 70.

Aetiology is mostly related to diabetes. It is also observed in inflammatory, hereditary sensory and autonomic, and hereditary sensory neuropathies, vasculitis, sarcoidosis, systemic lupus, Sjogren disease, Fabry disease, AIDS, erythromelalgia, some viral infections and cytomegalovirus polyradiculoneuritis. Idiopathic neuropathy is due to autoimmune and neurodegenerative mechanisms.

The **clinical profile** is common, irrespective of the cause. Small fibre neuropathy is the cause of 90% of cases with burning (restless) legs syndrome. Predominant symptoms are pain and

painful paraesthesia in contrast to the symptoms of thick myelinated fibres. Sensory and autonomic functions, and to some extent the thick nerve fibres may be impaired along with motor symptoms development.

Diabetic neuropathies

Neuropathies are the most common microvascular complication of diabetes. 70% of men and 50% of women have neuropathy 12 years after the onset of diabetes. Predisposing factors are the longer disease duration, poor glycaemic control, smoking, obesity, cardiovascular risk factors and type 2 diabetes. Pain is reported by a small number of patients (10%), with diabetic neuropathy of the fine nerve fibres. The normalization of blood sugar leads to resolution of symptoms in most cases, due to regeneration of nerve fibres. Pain also disappears with progressive degeneration of fibres.

Pathogenesis is multifactor and is related to metabolic and vascular factors leading to progressive loss of autonomic and somatic nerve fibres. The severity of neuropathy correlates with the degree of hyperglycaemia. The resulting paranodal demyelination and axonal injury lead to onset of clinical signs.

Classification divides painful diabetic neuropathies into generalized and focal. Diabetic focal (or multifocal) neuropathies are subdivided into cranial, of the extremities, proximal and radiculoneuropathies of the body. Generalized symmetric polyneuropathies are subdivided into acute and chronic sensomotor conditions.

Cranial neuropathies are rare (1%). They mostly affect n. oculomotorius and n. abducens more rarely. They are spontaneously recovered in several months.

Focal neuropathies of the extremities are divided into compression- and ischemia-induced neuropathies. Entrapment neuropathies in diabetic patients will not improve without treatment. These most commonly affect n. medianus, n. radialis, n. femoralis, n. peroneus communis and n. cutaneus femori lateralis (meralgia paresthetica). Ischemic neuropathies have a sudden onset, manifest with unilateral nociceptive pain and resolve spontaneously within a few months.

Proximal neuropathies occur in elderly patients with type 2 diabetes. They manifest with severe neuropathic pain in one or both lower extremities in the hip area. It is aggravated at night and causes sleep disturbances. There are also asymmetric, proximal motor disorders that manifest with weakness and hypotrophies of thigh muscles. No sensory disorders are identified. This condition must be differentiated from the chronic inflammatory demyelinating neuropathy, which is responsive to immunomodulation. They have the tendency to recover slowly (within 1 year) and incompletely.

Radiculoneuropathies of the body are rare and predominantly affect middle-aged and elderly men with a long history of diabetes. The main clinical manifestation is burning or piercing pain that increases at night and is accompanied by skin dermatomal hyperesthesia. The pain is localized in the lumbar region or abdominal wall, unilaterally and more rarely, bilaterally. Motor disorders in the lumbar and hip area are less common. Symptoms tend to resolve within 6 months.

Acute sensory neuropathy is a variant of symmetric polyneuropathy. It is caused by inadequate diabetes control with glycaemic variability, irrespective of the direction, which results in nerve ischemia. This condition may develop after an episode of ketoacidosis.

The onset is acute, with severe neuropathic pain that increases at night. The pain is constant, burning and intensifies distally from the hip or knee. Marked hyperesthesia and deep pain are common and are accompanied by sudden and sharp electric-like pain. An examination may reveal depressed knee-jerk reflexes, distal hypoesthesia and allodynia.

Chronic distal sensomotor neuropathy is the most common type. It is often identified yet with the diagnosis of type 2 diabetes. In the course of diabetes, the number of patients increases to 40% of all diabetic patients. It initially affects the thin myelinated and non-myelinated nerve fibres, with thick myelinated fibres being affected later in the disease course. Therefore, the impairment of the pain and temperature sensation predominates over the impairment of the sense of touch, proprioception and motor activity. That allows the patient to use effectively their anaesthetised limbs. The absence of protective sensory information results in limb overload, injury, infections, plantar ulceration, painless bone fractures and Charcot joints in the legs. Trophic disorders and diabetic foot develop. Neuropathy manifests with strictly individual symptoms in each patient that remain unchanged in the course of the disease. Many patients experience positive (pain, hyperesthesia) and negative sensory and motor symptoms. Intensity of symptoms depends on the length of the nerve injured, hence they predominate in the lower extremities. More severe injuries also affect fingers. Negative symptoms include numbness, distal hypoesthesia for all sensory modalities (including impaired vibration sensation) and motor disorders in lower extremities. Hypoesthesia is symmetric, in the shape of socks but it may ascend proximally. Pain is burning, deep (as if coming from the bones) accompanied by numbness and electric-like shock sensations (burning paresthesias) and increases at night. The impaired proprioception (impaired joint position sense and vibration sensation) leads to unsteady gait. Autonomic symptoms appear early in the course of disease along with sensory disorders. Some of the first sensory symptoms are impairment of vascular and sudomotor innervation of the legs with clinical signs of anhidrosis and absence of piloerection. Peripheral oedema may develop. Tendon reflexes are preserved, Achilles reflexes are absent; in more severe cases, knee jerk reflexes are also depressed. Muscle weakness is rare,

however hypotrophies of small arms and legs muscles is observed occasionally. Marked motor disorders or asymmetry of symptoms question the diagnosis.

The disease is contingent on the hyperglycaemic control but independent of the temporary fluctuations it progresses over time.

Peripheral neuropathies due to vitamin deficiencies

Alcohol and malnutrition as a result of gastrointestinal diseases, poor diet, conditions after major surgery or other cause, with resulting vitamin deficiency, lead to painful neuropathy.

9% of alcoholics are affected, mostly women.

It is due to a deficiency of B group vitamins, thiamine, pyridoxine, pantothenic acid, cyanocobalamin and niacin. This leads to axonal degeneration with myelin and axonal destruction. The longest and thickest peripheral nerves of lower extremities are progressively and symmetrically affected (70%), as those of upper extremities are less affected. Disease progression involves the posterior and anterior nerve roots.

The *clinical signs* at onset are dysesthesia, burning feet syndrome, severe pain in the feet, and progressive loss of sensation, autonomic symptoms and muscle weakness. Motor disorders vary from loss of Achilles reflexes to wrist or foot drop. Foot paraesthesia is aggravated by touch. The involvement of sympathetic postganglionic fibres causes excessive sweating of the volar surfaces of palms and feet. Trophic skin changes in the feet, oedema, pigmentations and glossy skin develop.

Neuropathies due to Infectious Diseases

HIV infection and AIDS cause inflammatory, infectious, infiltrative, vasculitic, degenerative and toxic (drug-induced) painful neuropathies.

Distal symmetric sensory polyneuropathy is the most common and affects 30% of patients with AIDS. This condition is rarely identified at the early stage of HIV infection but becomes more frequent with deterioration of the immunological status and correlates with disease severity.

Clinically, it manifests with pain and symmetric distal sensory disorders in the toes and feet. They spread proximally over weeks and months. Marked allodynia, dysesthesia and hyperpathia make waling painful. Patients sleep with uncovered feet to avoid contact with blankets. Upper limbs are usually unaffected. An examination reveals hypoesthesia for pain and temperature, decreased vibration sensation, with minimum impairment of motor functions. Achilles reflexes are preserved while knee jerk reflexes are increased due to concomitant myelopathy.

Painful inflammatory neuropathy is immune-mediated, with segmental demyelination and acute or subacute progression. It may occur during the period of seroconversion or later in the course of disease. It is similar to the Guillain-Barre syndrome but, by contrast, both protein and

cells are increased unlike the protein-cell dissociation in CSF. The clinical symptoms manifest within a few days to weeks – pain and paraesthesia in the legs progressing distally to proximally. Pain is experienced deep in the muscles of the back and thighs, and worsens at night. It is accompanied by muscle weakness and depression of tendon reflexes. Spontaneous recovery to different extent occurs for weeks to months. Few patients die from respiratory complications.

EMG findings show primary demyelination and conduction block.

Polyneuropathies in malignancies

Paraneoplastic neuropathies are sensorimotor or purely sensory and painful. Clinical manifestations precede the tumour diagnosis by months or even a year. Early symptoms are pain and dysaesthesia in the distal part of the limbs, body and face. Symptoms spread proximally. Acute or subacute loss of all sensory modalities occurs, with loss of deep sensibility that may be asymmetric. The kinaesthetic sense is severely impaired leading to severe disability irrespective of the preserved muscle strength. Tendon reflexes are depressed or absent. Dementia, cerebellar dysfunction, myelopathy and dysautonomia are identified.

The CSF analysis reveals pleocytosis and increased protein levels. Anti-neuronal antibodies are detected in the serum. EMG findings reveal normal motor fibre conduction and sensory fibres damage.

Specific Pain Neuropathies

This group includes neuropathies in which the damage to fine afferent nociceptive nerve fibres is due to a specific cause.

Clinically, it manifests with pain in the distal part of the limbs that is worsening in the evening and at night. It is experienced superficially in the skin and may be diffuse and constant (burning) or more severe, paroxysmal, localized and sharp (electric-like). There may be additional positive and negative distal sensory symptoms of the socks or gloves pattern. It may be also accompanied by motor and autonomic symptoms. A neurological examination will show distal hypoesthesia to touch, pain and temperature. In some cases, sensory symptoms are more marked, with loss of deep sensitivity and marked motor and autonomic symptoms. It can manifest with symptoms that are typical for the specific neuropathy-inducing disease.

Hereditary sensory and autonomic neuropathies (HSAN) are different types. The first type is the *autosomal-dominant sensory and autonomic neuropathy* (HSAN type I according to Dick's classification). It predominantly affects the fine and, to a smaller extent, thick nerve fibres. This relatively rare type is most commonly associated with burning pain, typically in feet, at the early stage of disease. It manifests clinically after 20 years of age with spontaneous pain and

progressive impairment of pain and temperature sensation. Other sensory modalities are also impaired. Mild autonomic symptoms (impaired sweating function in the distal parts of the limbs, pelvic floor disorders) and slight distal weakness of limbs with muscle hypotrophies with ulceration occur. Upper limbs are less affected. Cellulite, osteomyelitis and arthropathy with foot deformity develop.

EMG findings reveal impairment of sensory fibres in peripheral nerves.

The second type is the *autosomal recessive sensory neuropathy* (HSAN type II) or Riley-Day syndrome. It manifests at birth and affects all sensory modalities. Autonomic symptoms and slight distal muscle weakness in the limbs are likely to occur.

EMG findings reveal impairment of sensory and, to a small extent, motor fibres.

Diagnostic Methods in Painful Neuropathies

1. Medical history reveals complaints of spontaneous sharp pain (burning, prickling or deep), paraesthesia and dysesthesia in toes and dorsal part of the feet. The sharp pain is short-term, piercing electric-like pain. Paraesthesia and dysesthesia are more typical in diabetic and alcoholic neuropathies. Patients have a feeling of coldness in their feet or tight skin, they are hypersensitive to temperature stimuli (cold and heat). Pain and dysesthesia are increased at rest and especially at night, and disturb patients' sleep. Allodynia leads to intolerance to blankets, socks and shoes. Disease begins from lower extremities and may spread to arms over time, however, as neuropathy progresses, pain disappears. Some patients experience lower leg muscle cramps.

2. A neurological examination shows evidence of fine fibres involvement. Sensory disorders are characteristic and may affect one or all sensory modalities. Distal hypoesthesia to pain and temperature is found in the lower limbs, and pain continues even after the stimuli are removed. Hyperpathia is a common symptom. Qualitative sensory disorders occur, with tactile stimuli feeling like burning. Autonomic symptoms are also identified, mostly sweating disturbances, constipation or diarrhoea, incontinence and impotency. Xerostomia and xerophthalmia, orthostatic hypotension and excessive sweating are less common. The functions mediated by cholinergic and cutaneous vasomotor fibres are more affected than those mediated by adrenergic fibres. Proprioception is rarely impaired, tendon reflexes are normal or depressed.

Exclusion criteria are the presence of considerable dysfunction of thick fibres which manifests with decreased proprioception in the toes, loss of vibration sensation in lower extremities, distal muscle weakness and hypotrophies or generalized areflexia. The vibration sensation may be decreased at the toes but it should be normal at the ankle level. If it is impaired at a higher level, it is indicative of injury to thick nerve fibres.

1. Standard EMG study does not reveal deviations but the sympathetic skin response may show fine nerve fibres impairment. The detection of slowed conduction velocity in motor fibres is an exclusion criterion.

2. Cardiovascular autonomic function tests can reveal subclinical disorders.

3. Skin biopsy with assessment of intraepidermal nerve fibres is a method for evaluating the extent of loss of fine nerve fibres.

4. Laboratory tests of blood sugar, electrophoresis, antinuclear antibodies and other blood tests depending on the suspected underlying disease.

Differential Diagnosis of Painful Neuropathies

In differential diagnosis of peripheral nervous system diseases, it is important to detect the anatomical localization of symptoms, their progression over time and pathophysiological characteristics.

Differential diagnosis includes the search for the underlying cause of neuropathy. If not such cause found, it is considered to be idiopathic neuropathy, which is typical for elderly patients and has a benign course. Pain is not typical for a specific type of neuropathy, so the differential diagnosis is based on other symptoms.

General practitioner, in the presence of anamnestic and clinical evidence of painful neuropathy, should refer the patient for an urgent consultation by a neurologist.

Neurologist should make a diagnosis based on the clinical criteria and tests performed.

Central Neuropathic Pain

It occurs after injury to the spinothalamic tract in the cerebrospinal axis. It is predominantly caused by an injury, spinal cord diseases, stroke and multiple sclerosis.

Spinal Neuropathic Pain

Spinal Cord Injury Pain

The most common cause of spinal cord injuries is trauma. It leads to loss of motor, sensory, sexual, pelvic floor functions and pain. 60-80% of patients experience chronic pain and 40% of patients report severe pain. Pain occurs a year and a half after the injury on the average.

Pain is subdivided into several types that develop with different clinical symptoms: nociceptive (musculoskeletal, visceral) and two types of neuropathic pain (at and below the level of the injury). Musculoskeletal pain is the most common (58%), followed by neuropathic pain at the level of the injury (42%) and below the level of the injury (34%).

Musculoskeletal pain is caused by structure damage and instability of the spine and its stabilizing structures – ligaments, muscles, intervertebral discs and joints, without spinal cord injury. Pain originates from normally innervated structures, rostrally of the level of spinal injury. Pain is contingent on the activity and posture and, although not radicular, it may radiate along the body or towards the limbs. Another type of musculoskeletal pain is due to the muscle spasm in patients with incomplete injury. It occurs most often (72%) after chronic overuse of the arm and shoulder in paraplegics who use wheelchairs.

Visceral pain occurs in the presence of coexisting visceral injury. It predominantly affects the bladder and causes urinary tract infections. Nociceptive pain appears, that is of changed quality depending on the level of injury. Pain is dull, of unclear localization in the abdominal region.

Neuropathic pain above the level of the injury is due to complex regional pain syndrome or entrapment of peripheral nerves. Patients are predisposed to such injuries due to overuse of their upper limbs when using crutches and wheelchairs.

Neuropathic pain at the level of the injury is lightning or burning pain with segmental or dermatome radiation. It is detected in two segments above or below the level of the injury. Due to the specific spread, it is referred to as encircling, radicular, segmental pain or pain in the transitional, border or marginal zone. It is often accompanied by allodynia or hyperesthesia in the respective dermatomes. This condition is due to nerve root damage caused by trauma, secondary by the disc or apophyseal joints due to spinal cord instability or spinal cord injury. Pain that is caused by nerve roots damage is unilateral and increased by spinal cord movement.

Spinal cord damage leads to bilateral neuropathic pain. In order this pain to be generated there needs to be critical amount of tissue along the spinal cord involved. It is increased by activation of neurons around the damage and spreading of pain and abnormal sensations at the level of the injury.

Syringomyelia should be considered in patients with delayed development of segmental pain after the injury, particularly with the level of sensory loss going up. Typical cases manifest with loss of pain and temperature sensation but all sensory and motor functions may be impaired, and allodynia and hyperalgesia are likely to occur. An injury to cauda equina causes considerable deafferentation of the spinal cord resulting in neuronal activity and pain. Damaged roots of cauda equina generate spontaneous activity that feels like pain. Arachnoiditis may occur limiting the normal movement of nerve roots and leading to their mechanical irritation with every movement. Peripheral stimuli lead to abnormal activity in the region of axonal injury and burning pain in lower lumbar and sacral dermatomes.

Neuropathic pain below the level of the injury occurs sometime after the injury. It is also referred to as a central dysesthesia syndrome, central, phantom or deafferentation pain. It is the

most common (30%) chronic spinal cord injury pain. It is due to decreased afferentation to supraspinal structures (thalamus) that is incoming through the spinothalamic and other ascending pathways from structures below the level of the injury and the activation of supraspinal structures by abnormal activity generated above the location of the injury.

Pain is bilateral, spontaneous or induced, in the anaesthetic region, caudally from the level of the injury and exhibits characteristics of neuropathic pain. It is constant burning, pulsating or lightning pain, with twitching and tingling sensation and may be accompanied by hyperalgesia. It fluctuates depending on the mood, activity, presence of infections and other factors. This pain is not contingent on the posture and movements but may be caused by sudden noise or shaking of the body.

Phantom sensations after spinal cord injury are a form of impairment of sensory functions. They are detected in 90% of patients in the sensory disorders area. They vary from paraesthesia and dysesthesia to complex phantom sensations that include positional sense, movement and functional illusions such as micturition and orgasm. These complex phantom sensations are experienced by 60% of patients and resolve after several weeks or months following injury.

Pain in syringomyelia

A spinal cord injury and involvement of the spinothalamic pathway cause neuropathic pain. It is unilateral, located in the arm, shoulder, neck and thorax in the cervical-thoracic pain or in lower limbs in dorsal-lumbar form. Pain in the posttraumatic form occurs within months or years.

Pain is spontaneous accompanied by allodynia, hyperalgesia, dysesthesia and paraesthesia. It occurs spontaneously and more often is constant burning (superficial or deep) pain, and more rarely is lightning paroxysmal pain. Several types of pain are often experienced in the same anatomic locations. This pain is aggravated by cough, physical exertion and Valsalva's sign due to dynamic changes in CSF at the syrinx. It is intensified by psychological factors such as emotions, anxiety and stress.

Induced pain (mechanical and temperature allodynia and hyperalgesia) begins or continues after the stimulus is removed. It radiates beyond the point of stimulation and is increased by repeated stimuli. Hyperpathia, paraesthesias and dysesthesias are common.

Sensory disorders in the affected area take the form of unilateral or bilateral thermoalgesic deficit, with segmental distribution in the region of the neck, shoulders, body, arms and face. Sensory disorders (pain and temperature hypoesthesia) in the face manifest as concentric circles around the nose due to injury to the nucleus of n. trigeminus. They are located ipsilaterally to the cavity and vary from slight hypoesthesia and hypoalgesia to complete anaesthesia and analgesia. Vibration, mechanical, and temperature and, to a smaller extent, pain thresholds are elevated.

Proprioceptive and tactile sensations are affected in 50% of patients. Other signs of dorsal column involvement, such as graphesthesia and movement direction impairment could be present.

Cavity enlargement frontally causes segmental areflexia, muscle weakness and hypotrophies, mostly in arms as a result of impairment of the anterior horn. The proximal cavity enlargement impairs the medulla oblongata and cranial nerves (mostly IX and XII). Pyramid signs may also occur.

Central Pain

Central pain syndrome after brain injury is most common after stroke. Each lesion, from the brainstem to the cortex, including in the superior and inferior region of medulla oblongata, pons, midbrain, infrathalamic region, thalamus, capsula interna (posterior limb), subcortical structures and cortical areas that receive somatosensory afferentation, may cause neuropathic pain. Similarly to spinal cord pain, it has three key characteristics: it is constant, neuropathic in character and there is induced pain present (allodynia and hyperpathia).

Central Post-Stroke Pain

It was described by Dejerine and Roussy as a „thalamic pain syndrome" after stroke. It develops in 25% of patients with lesion in the posterolateroventral thalamic nucleus. Accompanying hemiparesis is observed in cases where the lesion extends laterally or dorsally beyond the thalamus and involves capsula interna and other subcortical structures. Lesions may be located in different regions in the brain. There is no difference in the incidence of neuropathic pain caused by stokes or haemorrhages. The lesion size is also insignificant.

The *incidence* of post-stroke pain is up to 2%.

Pain rarely occurs immediately after stroke, it usually takes latent period of up to several years. Burning pain appears within 3 months after stroke in 60% of patients, and within 2 years in the rest of patients.

Clinically, it manifests with neuropathic pain in one of the body halves that is collateral to the side of the injury and not always involving the face. Depending on the injury location, symptoms may be more marked in the face or limbs. It may only involve one limb or a part of it (hand or foot). Infarctions in the lower part of the brainstem cause crossed pain in the ipsilateral side of the face and contralateral part of the body, which is similar in terms of distribution of sensory disorders to Wallenberg syndrome. That localization of pain is due to the injury of the ipsilateral afferent trigeminal bundle, spinal trigeminal nucleus and crossed spinothalamic tract. A lateral lesion in medulla oblongata results in localized pain around the ipsilateral eye.

Pain is superficial, burning and deep, constant or paroxysmal. Paroxysmal pain may be allodynic in character and may occur independently of the constant pain caused by touch, movement or temperature stimulation. Pain intensity varies from mild to severe, and is most severe in lesions in the thalamic area. Its intensity fluctuates during the day as well as in response to emotional factors.

Central neuropathic pain is not necessarily accompanied by other symptoms of central nervous system injury, except for sensory symptoms. They include elevated pain and temperature thresholds, hypo- or hyperesthesia, hyperalgesia, allodynia, hyperpathia, paraesthesias, dysaesthesias, sensation radiation, etc. Sensations conducted through fine afferent fibres are most impaired. They vary from slight hypoesthesia to one modality, mostly pain or temperature sense modality, to complete loss of sensation to all modalities. There are also great variations in the combination of symptoms. Some patients may experience paradox reactions to temperature stimuli, with reversed perception of the stimulus (cold as hot, and vice versa). Hyperesthesia to different temperatures (allodynia to cold and hot) is common. Allodynia is also found in 70% of patients. Tactile allodynia is the most common and allodynia to cold and skin movement are less common.

It is often accompanied by autonomic symptoms (vasoconstriction with extremity coldness), mild hemiparesis and choreoathetoid movements in affected limbs.

Pain in Multiple Sclerosis

Acute (20% of patients) and chronic (50%) pain syndromes are often the first symptoms of the disease. They are most often localized in lower extremities. Every patient may experience more than one type of pain. It may be superficial or deep, burning, lightning or piercing pain. The pain is precipitated by touch, physical exertion, walking, standing, changes in the ambient temperature, overstrain, depression or stress. It is alleviated by rest, temperature change, physical activity and change of posture.

Acute pain syndromes include trigeminal neuralgia, Lhermitte's symptom, painful tonic epileptic seizures, paroxysmal pain in the limbs and pain in optic neuritis.

Chronic pain syndromes include central pain, dysesthesia, painful spasms in limbs and back pain.

Central neuropathic pain (in 30%) is due to demyelinating lesion in the spinothalamic tract. It may be the first symptom of disease or may occur during remission. It is predominantly localized in the lower extremities.

Other pain syndromes include therapy-induced visceral and neuropathic pain, headache and other nociceptive pain. Muscle and joint pain in the limbs (shoulder most commonly) may

result from the abnormal posture, joint fixation, and overuse of extremities or uncomfortable adaptive aids.

Pain in Parkinson's Disease

Most patients (up to 75%) have sensory symptoms, of which pain is the most common. This is determined by the involvement of the striatonigral dopaminergic system in pain mechanisms. Pain syndromes are subdivided into motor and non-motor associated symptoms. A source of pain may be autonomic disturbances, restless legs syndrome and depression in Parkinson's disease.

Pain that is *not related to motor symptoms* is seen on the contralateral side and is bilateral, but more intense on the side of more marked motor symptoms. Some patients experience genital, oral or abdominal pain. Burning oral pain is similar to the pain in the burning mouth syndrome which is associated with decreased dopaminergic inhibition. Pain is persisting or intermittent, diffuse, cramp-like or burning. Dopaminergic and opioidergic system related to basal ganglia are involved in pain occurrence.

Abdominal pain and dysphagia are common. Painful anismus due to involuntary dystonic anal sphincter spasm is rarer. They result from direct impairment of the gastrointestinal tract (autonomic and enteral nervous system) due to the degenerative process, deferred gastrointestinal passage and painful constipation. Dopaminergic therapy causes cramps and abdominal bloating.

Nociceptive pain *related to motor symptoms* is more common. It may precede the diagnosis by months or years. Joint pain (shoulder or hip) due to rigidly increased muscle tone are the first symptom in 30% of patients. It is often misdiagnosed as radiculopathy or frozen shoulder syndrome. In patients with late Parkinson's disease, rigidly increased muscle tone and akinesia lead to postural disturbances followed by back pain. In patients with degenerative changes in the spine, the combination with pain precipitated by motor symptoms results in severe and chronic pain. Patients with motor fluctuations experience different pain syndromes. Morning dystonia, biphasic dystonia and off-period dystonia are painful.

Restless legs syndrome is associated with unpleasant sensation of pain in the lower extremities. It is caused by impaired supraspinal modulation of pain from basal ganglia via the descending dopaminergic paths.

Pain in Somatization Psychiatric Disorders, and in Dementia

Anxiety and depression lower the threshold of pain and patient's tolerance to that pain. Somatization disorders may cause pain that do not follow the anatomic distribution of peripheral nerves and other structures.

Patients with *dementia* do not experience changes in the pain threshold but have a higher pain tolerance. The motivational and affective aspect of pain is decreased due to degeneration of multiple structures in the medial pain system (mainly amygdala and hippocampus).

General practitioner, in the presence of anamnestic and clinical evidence of central neuropathic pain, should refer the patient for an urgent consultation by a neurologist.

Neurologist should make a diagnosis based on the clinical criteria and tests performed.

Treatment

Nociceptive Pain Treatment

Nociceptive pain responds to NSAIDs and analgesics (opioid and non-opioid).

Opioid analgesics are less effective in for neuropathic than nociceptive pain. They decrease the intensity of spontaneous neuropathic pain by 30%. They are not suitable for long-term therapy in patients with chronic pain as they worsen depression. A combination of opioids with NSAIDs increases the analgesic activity without considerable increase in adverse effects. Three types of opioids are used – μ agonists, κ agonists (mixed agonists/antagonists) and partial μ agonists. According to their pharmacokinetic properties they are subdivided into three categories: very short-acting, short-acting and long-acting agents. They are subdivided into hydrophilic and lipophilic.

Dihydrocodeine tartarate (DHC Continus) is an opioid slow-release analgesic for the treatment of chronic moderate to severe pain. Tablets (2 x 60 mg or 90 mg) are administered at 12 hours and should be swallowed whole.

Oxycodone and oxycodone-combinations are semisynthetic opioids, very similar to morphine. This medication is a combined μ- and κ-receptor agonist, therefore it is more efficient and causes less adverse reactions than morphine in relation to neuropathic pain. Its efficacy is similar to the efficacy of antidepressants and anticonvulsants. It is prescribed as normal and slow-release tablets at an average dose of 40 mg (5-10 mg per intake). Oxycodone has a short half-life and is rapidly eliminated, with high oral bioavailability. Slow-release medications (Oxycontin and oxycodone-combinations) is preferred, which pose a lower risk of abuse and addition. These drugs are administered at 12 hours intervals and should be swallowed whole.

Fentanyl is a synthetic lipophilic opioid that is 80 times more potent analgesic than morphine. It takes effect rapidly but has a shorter duration of activity. It is administered in the form of transdermal patches (Durogesic), in doses from 25 to 100 μg per hour. They provide slow release of the medication for 72 hours. This drug accumulates in the epidermis and adipose tissue under the patch and is slowly absorbed through the skin microcirculation into the systemic circulation. It is necessary to reduce the dosage in low weight and febrile patients due to the low body weight and increased skin circulation, respectively. It is much less efficient compared to other opioids for the

treatment of neuropathic pain. Adverse reactions (constipation and sleepiness) are less pronounced than morphine's side effects, but it often causes insomnia. This drug may be applied at a dose of 25 μg/hour (1 patch per 3 days) in case of severe pain. Minimal effective doses must be used.

Non-opioid analgesics mainly include NSAIDs and some neuropeptide modulators. They are used for the treatment of nociceptive pain. They are less efficient than opioid analgesics. Lower doses of more potent analgesics cause less adverse reactions than high doses of milder analgesics.

Paracetamol (up to 1000 mg/day) is a first-choice medication in mild to moderate nociceptive pain.

Tramadol hydrochloride (50 – 400 mg/day) has a direct opioid (μ-receptor agonist) and indirect non-opioid, monoaminergic activity, as it inhibits presynaptically the noradrenaline reuptake and activates serotonin release. It is administered orally in normal or slow-release tablets and is efficient for the treatment of neuropathic pain. Adverse reactions include nausea, dizziness and constipation. It's addictive potential is low, therefore it is suitable for pain relief.

A combination of Paracetamol (37.5 mg) and Tramadol hydrochloride (325 mg) is beneficial for managing mixed (nociceptive and neuropathic) pain with less adverse reactions.

Non-steroid anti-inflammatory drugs (NSAIDs) are divided into two big groups: salicylic and non-salicylic.

Salicylic (aspirin) are the oldest drugs, predominantly COX1 inhibitors.

Non-salicylic NSAIDs are subdivided into three groups: specific, selective and non-selective COX-2 inhibitors. Selective inhibitors target mainly but not exclusively COX-2. Specific and selective COX-2 have 3 times less gastrointestinal adverse reactions. The long-term use of this group of medications is not recommended due to an increased risk of myocardial infarction and hypertension. Most of NSAIDs inhibit non-specifically both COX-1 and COX-2.

A limitation for the use of NSAIDs is the so-called "ceiling effect", i.e. dose increase above a specified level does not lead to further analgesia. Adverse reactions of NSAIDs connected with the gastrointestinal tract, thrombocyte aggregation and kidneys are associated with the inhibition of prostaglandin synthesis. They are similar in different NSAIDs and are dose-dependent.

NSAIDs are classified according to the chemical class or according to their half-life. Various drugs differ mostly in their pharmacokinetics than in pharmacodynamics. They are subdivided into agents with short elimination half-life (ibuprofen), administered 3-4 times daily, with a longer half-life (naproxen), which are taken 2 times a day and agents with long half-life (piroxicam), which are taken once daily. The selection of a drug is based on the trial and error approach.

A number of groups are distinguished according to the chemical class. The group of propionic acid includes some long-standing NSAIDs. *Ibuprofen* is taken at a daily dose from 1200

to 2400 mg, over 4 applications. *Naproxen* has a longer half-life, therefore it is taken twice a day at doses of 500 mg. Sodium salt is absorbed faster into the gastrointestinal tract. *Ketoprofen* and *Diclofenac* are taken 3 times per day at a dose of 75 mg. Etodolac is a new medication in this group. The group of indoleacetic acid includes *Indomethacin* (200 mg/day q.i.d.) and *Sulindac* (300 mg/day b.i.d.). A key member of the oxicam-NSAIDs is *Piroxicam*. This drug has a long half-life (up to 60 hours) that allows for once-daily dosing of 20 mg but pronounced gastrotoxicity. The group of fenamic acid mainly includes *Meclofenamate* (400 mg/day). Phenylacetic acid-derived *Aceclofenac* (Aflamil 200 mg/day b.i.d.) is a selective COX-2 inhibitor with quick onset, long-term effect and better safety profile in relation to gastrointestinal adverse reactions.

The use of NSAIDs is limited for up to 10 days in minimal effective doses considering the serious gastrointestinal adverse reactions. Both selective and non-selective COX-2 inhibitors increase the risk of acute myocardial infarction but the degree of risk varies between different NSAIDs. Almost all of the NSAIDs used in clinical practice, except for naproxen, entail an increased risk of acute myocardial infarction. The inhibition of thrombocyte aggregation is an important adverse effect considering the fact that a large number of patients are at an age that necessitates the use of antiaggregants in preventing cerebrovascular disease. Therefore, precaution should be taken when starting a therapy with NSAIDs that inhibit the thrombocyte aggregation and prolong the bleeding time. Some NSAIDs decrease the antiaggregant properties of aspirin, directly competing for the thrombocyte COX-1 binding site. It is preferable to use clopidogrel rather than aspirin in patients who need to take antiaggregants and NSAIDs at the same time.

NSAIDs inhibit the effect of antihypertensive drugs which may result in increase in blood pressure. This effect is more marked in patients treated by angiotensin-converting-enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs). Patients treated with calcium channel blockers demonstrate lower response rates. Antihypertensive therapy may require adjustment.

NSAIDs worsen the renal and liver functions, which has to be taken into consideration in elderly and patients with risk factors such as diabetes and arterial hypertension or renal and liver dysfunctions.

In patients with history of gastrointestinal disorders:

- **First-**choice drugs are the *specific* and *selective NSAIDs.*
    - Rofecoxib 25 – 50 mg/day
    - Celecoxib 200 – 400 mg/day
    - Parecoxib 20 mg/day
    - Etoricoxib 30 – 60 mg/day
    - Aceclofenac 200 mg/day

- Meloxicam 7.5 – 15 mg/day
- Nimesulide 100 – 200 mg/day

Selective inhibition of COX-2, although decreasing gastrointestinal adverse reactions, is associated with an increased risk of atherothrombotic vascular complications.

- **Second**-choice drugs are the *non-selective NSAIDs*. Their anti-inflammatory and analgesic activities are more marked than those of specific and selective NSAIDs. Their use in the form of suppositories or intramuscular (intravenous) applications slightly ameliorates the adverse reactions.

In patients without history of gastrointestinal disorders:

- **First-**choice drugs are non-selective NSAIDs. This group includes a large number of drugs. The most commonly used are:
  - Ketoprofen (Bi-Profenid, Profenid LP) at a dose of 200 – 300 mg/day has a strong analgesic and anti-inflammatory activity and easily passes though the blood-brain barrier. Intramuscular and intravenous formulations are even more effective and faster acting.
  - Naproxen 500 – 1250 mg/day is medication of choice in patients with cardiovascular risk factors.
  - Piroxicam 10 – 20 mg/day
  - Ibuprofen 1200 to 2400 mg/day
  - Diclofenac 75 – 150 mg/day
  - Indomethacin 75 – 200 mg/day
- **Second-**choice drugs are the *specific* and *selective NSAIDs.*
- **Third-**choice drugs are the topical NSAIDs in the form of gels or ointments, which are very effective in some cases.

Muscle relaxants are used for the treatment of nociceptive pain caused by muscle spasm. Centrally acting muscle relaxants that have no direct effect on the muscle, neuromuscular synapse or motor nerves are used.

Baclofen (50-60 mg/day) is a first-choice drug in patients with back pain. Being a GABAergic agonist, it decreases the presynaptic release of excitatory amino acids.

Tizanidine (12-24 mg/day) is a second-choice drug in patients with fibromyalgia and back pain. It inhibits polysynaptic spinal mechanisms associated with increased muscle tone and influence the release of excitatory amino acids by interneurons.

Tolperisone (Mydocalm) stabilizes neuronal membranes, inhibits Na^{+} and Ca^{++} neuronal channels and inhibits mono- and polysynaptic spinal reflexes. **It is not administered** in patients with back pain due to unproven efficiency and harmful adverse effects.

Neuropathic Pain Treatment

Contemporary treatment of neuropathic pain is symptom-oriented. Allodynia is relieved by lidocaine, lamotrigine, gabapentin, amitriptyline, oxycodone and oxycodone-combinations. Lightning pain responds to carbamazepine, phenytoin, lamotrigine, valproates and gabapentin. Burning pain responds to amitriptyline and gabapentin, and paraesthesia and dysesthesia are ameliorated by phenytoin. Drugs influence different pathophysiological pain mechanisms and it cannot be expected that one medication will be efficient in all patients. It is still impossible to identify the specific mechanism that causes neuropathic pain in the specific patient. Different mechanisms may cause the same symptoms.

Neuropathic pain is influenced by several major drug groups: antidepressants, anticonvulsants, membrane stabilizers, NMDA antagonists, $alfa_2$ adrenergic agonists and $GABA_B$ agonists. Opioid medications are administered after careful selection of patients and at optimal dose.

The earlier the treatment is started, the greater the chance of better response. If treatment is started within 6 months after the pain onset, 90% of patients respond to it, and if started within 1 year responders are 75%. Pain alleviation by 30% is clinically effective for the patient. The selection of medication is based on the trial and error approach.

Treatment is started with monotherapy at the lowest possible dose of the selected drug. Titration is made slowly in order to avoid adverse reactions. The dose is increased until a clinical effect or adverse reactions is observed. The maximum dosage should be reached before it is assessed as ineffective. If the first-choice drug is not suitable and pain is not relieved within 1 month, the dose is gradually decreased and the drug is discontinued. Treatment with a second drug is started until effect is achieved.

A drug combination that affects different pain mechanisms is used in non-responders to monotherapy. Some drugs have synergic effect, which allows for dose reduction and a better analgesia. The main objective of the combination therapy is the rapid and effective analgesia. A combination of antidepressants and antiepileptic agents is administered, or a combination of different anticonvulsant drugs. An opioid with quick- onset of action (oxycodone and oxycodone-combinations) may be combined with a slow-acting drug. Administration of gabapentin together with morphine increases its effect on μ-opioid receptors, thus achieving pharmacodynamic synergy. Amitriptyline increases morphine plasma levels by inhibition of the liver glucuronidation. That pharmacokinetic synergy allows for decrease in morphine dose. Antidepressants with monoaminergic effect should not be combined with tramadol due to increased risk of serotoninergic syndrome.

Treatment should be administered for at least 6 – 12 months. Then, gradual dose reduction is attempted. If pain returns, treatment should be continued for another 6 months.

There are no fundamental differences in treatment of peripheral and central neuropathic pain. First-choice drugs in peripheral neuropathic pain are anticonvulsants and second-choice drugs are antidepressants. Central pain is relieved primarily by antidepressants and, secondly, by anticonvulsants. Third-choice drugs in both cases are opioids (oxycodone, oxycodone-combinations and Dihydrocodeine Tartarate BP). In cases of severe pain, treatment may start directly with them.

Anticonvulsants relieve the tearing pain originating from the generation of ectopic impulses in the central and peripheral nervous system. Effective anticonvulsants deal with the ion channels and inhibit ectopic impulses through their membrane stabilizing activity. Modulators of voltage-dependent sodium channels (carbamazepine, oxcarbazepine, lamotrigine) and *blockers of voltage-dependent calcium channels* (gabapentin, pregabalin) are used.

Pregabalin (300-600 mg/day) is a first-choice anticonvulsant, and is most efficient for the treatment of neuropathic pain. It is analogue to gabapentin but is more quick-acting, has better bioavailability and linear pharmacokinetics. It is more effective in the treatment of peripheral and central neuropathic pain than gabapentin. It has quick titration and effect (1^{st} week) and sleep disturbances are improved. Adverse reactions (in 11%) include dizziness, sleepiness, dry mouth, peripheral swellings and weight gain. It should be used in lower doses (150-300 mg) in order to avoid adverse effects.

Gabapentin (900 to 1800 m/day) decreases the frequency, severity and duration of pain attacks.

Carbamazepine (200 – 1200 mg/day) and oxcarbazepine (600 – 1800 mg/day) are first-choice drugs only in patients with trigeminal neuralgia.

Antidepressants are effective in the treatment of burning, short tearing pain and skin hyperalgesia but do not relieve phantom pain. Tricyclic and selective serotonin–norepinephrine reuptake inhibitors (SNRI) are used. Treatment is effective if pain is decreased by at least 50% at the end of the first month of treatment. It lasts between 6 months and one year at the minimal effective dose. If there is no response, antidepressants of another class are used for another month. The combination with opioids increases their analgesic effects.

Tricyclic antidepressants are the most efficient but cause adverse effects.

Amitriptyline (12,5 – 75 mg/day) is used most frequently.

Serotonin–norepinephrine reuptake inhibitors antidepressants (SNRI) are as effective as tricyclic antidepressants but cause less adverse reactions.

Duloxetine (30 – 60 mg/day) is effective in the treatment of neuropathic pain and fibromyalgia.

Venlafaxine (75 до 150 mg/day) increases the pain threshold and is effective in the treatment of neuropathic pain and fibromyalgia.

Mirtazapine (30 – 60 mg/day) is also effective in neuropathic pain.

The structural analogue of GABA baclofen (up to 60 mg/day) has a quick and good effect.

Alfa$_2$-adrenoreceptor agonist tizanidine is effective for the treatment of neuropathic pain and pain due to muscle spasm.

Membrane stabilizer lidocaine blocks voltage-dependent sodium channels and inhibits ectopic impulses. It is used topically in the form of 5% solution patches. They are placed over the painful skin area, whereby a small amount of the drug is absorbed and there are no general adverse reactions. It is effective mainly in patients with postherpetic neuralgia.

Topical steroid and non-steroid anti-inflammatory agents that pass through the skin are also used for the treatment of neuropathic pain. Their efficiency is not confirmed by clinical trials.

Physical aids are widely used for the treatment of back pain. These are: massage, manual therapy, transcutaneous electrical nerve stimulation (TENS), short-wave diathermic device, cryotherapy, acupuncture, physical exercise and corsets. Repetitive transcranial magnetic stimulation (rTMS) is also effective for pain alleviation.

Restriction of motor activity or bedrest for up to 5 days depending on pain severity is recommended to patients with acute back pain. During the next 20 days, exertion should be moderate, and the patient should undergo a physical program supervised by a specialist for the next months. If necessary, the patients are advised to lose weight and to change their lifestyle and work.

Specifics in the treatment of some types of pain:

HIV polyneuropathy only responds to NSAIDs and opioids.

Myofascial pain is relieved by inactivation of trigger points in every single muscle. Dry needling is applied (without solution) or injection of isotonic sodium chloride solution with possible addition of 0.5% procaine or 1% lidocaine, sometimes corticosteroid (solumedrol 10-40 mg), which ameliorate the local inflammation. 2-4 ml of the solution is injected in every point. The local injection of 10 U botulin toxin (Botox) in each trigger point has more durable effect.

In occipital neuralgia, occipital nerves blocks are applied with cordicosteroid and/or topical anaesthetic.

Neuropathic pain in radicular compression

1. Corticosteroid anti-inflammatory agents intramuscular or intravenous for 5 – 7 days

- Dexamethasone 4 – 8 mg/day
- Methylprednisolone 40 – 80 mg/day

2. Antioedematous drugs

- Mannitol 10% - 500 ml/day intravenous slow infusion for 5 – 7 days.

3. Neurosurgical treatment. The most commonly used method is vertebral laminectomy with removal of the prolapsed disc. A successful surgical outcome, free from complications and relapses, is observed in 54% of operated patients.

Indications for neurosurgery:

- pain that is not relieved by conservative therapy
- progressive neurological deficits with second root manifestations
- cauda equina syndrome

General practitioner:

1. Applies treatment for nociceptive pain in acute episode of back pain, without evidence of disc prolapse, sciatic radiation of pain or negative neurological symptoms.

2. If pain is not relieved within 7 days, he/she should refer the patient for consultation by a neurologist.

3. In the event of acute episode of back pain, with evidence of disc prolapse, sciatic radiation of pain or negative neurological symptoms, he/she should refer the patient for treatment by a neurologist.

4. In chronic pain, after consultation by a neurologist, physiotherapist, orthopaedist and psychologist, he/she develops an individual multidisciplinary therapeutic program.

5. Neuropathic pain treatment is always carried out by a neurologist.

6. Traction manipulations (extensions) are not recommended due to frequent complications.

Appendices

Table 1. Back pain aggravating and relieving factors

Aggravating	Relieving	Disease
Cough, sneezing, strain	Lying on hard surface	Disc prolapse
Sitting forward	Standing	Spinal tumour
Standing up, walking	Sitting	Spondylolisthesis
Continuous walking, coughing and lying face down	Rest	Spinal stenosis
Turning in bed	N/A	Ankylosing spondylitis Disc prolapse
Movement in all directions	Rest	Tumour, fracture
Rest	Movement	Inflammatory arthropathies

Table 2. Type of back pain

Type of pain	Disease
pulsating	inflammation
deep, turning	tumour, Paget‘s disease
constant, superficial	muscle strain
sharp, piercing	nerve root compression

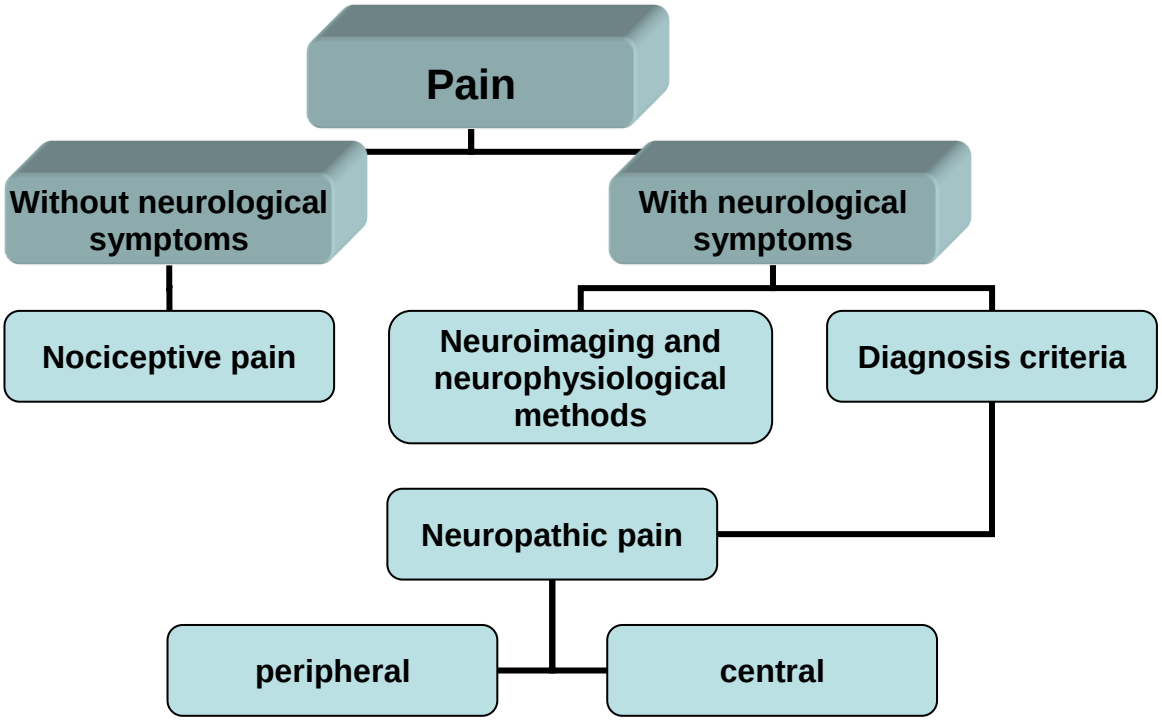
Table 3. Neurological examination in back pain

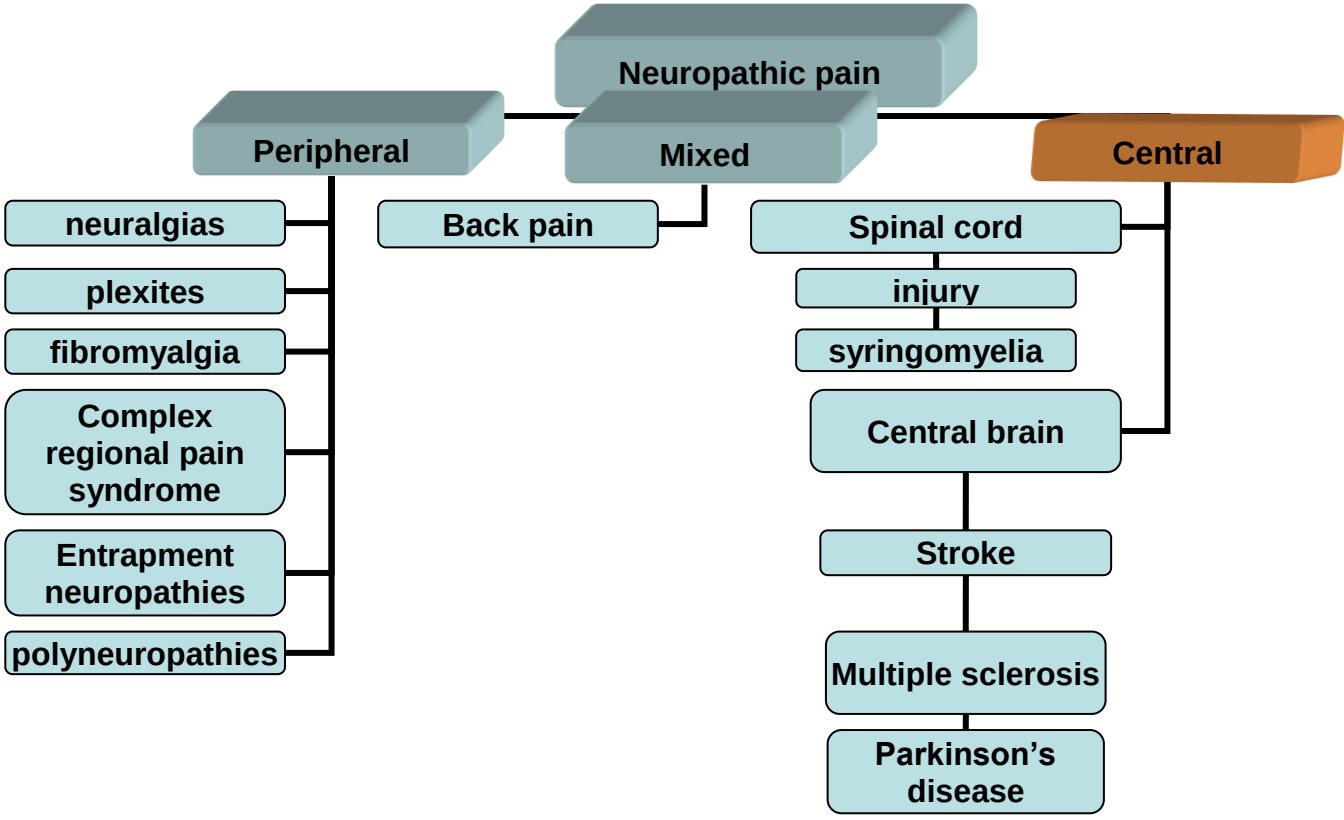
Examination	Finding
Back examination	Scoliosis, kyphosis, skin changes
Gait and turning	Changes in gait
Ability to undress	Mobility
Range of spinal motion	Impaired flexion, extension, rotation and bending aside
Leg length	Difference in legs
Pulse palpation	Vascular occlusion
Palpation in the painful area	Pain, muscle spasm
Growth symptoms	Pain aggravation
Techniques inducing pain in hip and sacroiliac joint	Involvement of the hip or sacroiliac joint Neurological deficit

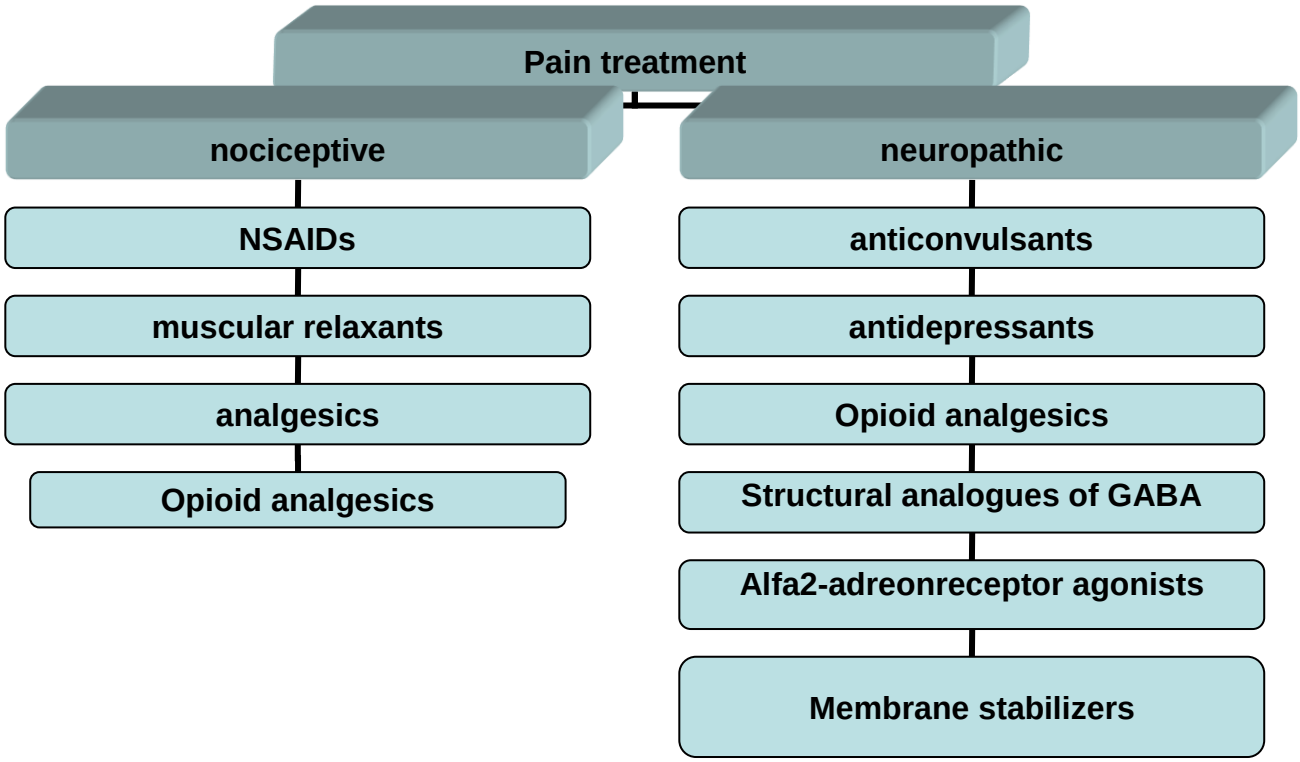
Examination of reflexes and muscle strength Superficial sensation	Neurological deficit

Table 4. Attention calling factors in back pain

Red flags	Yellow flags
disease onset under 20 and above 55 years history of recent serious injury or malignant tumour progressing pain that is not ameliorated at rest thoracic pain long-term use of corticosteroids drug abuse AIDS, immunosuppression or systemic disease unexplained loss of weight or fever neurologic symptoms and structural deformations	fear of disability decreased activity due to pain emotional problems (depression, anxiety, stress, social exclusion)


Pain
Without neurological symptoms
With neurological symptoms
Nociceptive pain
Neuroimaging and neurophysiological methods
Diagnosis criteria
Neuropathic pain
peripheral
central


Neuropathic pain
Peripheral
Mixed
Central
neuralgias
plexites
fibromyalgia
Complex regional pain syndrome
Entrapment neuropathies
polyneuropathies
Back pain
Spinal cord
injury
syringomyelia
Central brain
Stroke
Multiple sclerosis
Parkinson's disease


Pain treatment
nociceptive
neuropathic
NSAIDs
muscular relaxants
analgesics
Opioid analgesics
anticonvulsants
antidepressants
Opioid analgesics
Structural analogues of GABA
Alfa2-adreonreceptor agonists
Membrane stabilizers