CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY CIPN

Colores

Hello,

You have just opened a guidebook on chemotherapy-induced peripheral neuropathy.
We are delighted that you have found it.

This guidebook has been compiled as a collaboration. We at the patient organisation Colores have called upon medical specialists from different fields to be a part of writing this guidebook. Most importantly, we have received practical, first-hand knowledge from patients suffering from neuropathy who have also taken part in the making of this guidebook.

We hope that this guide will provide answers to your questions.

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Below are greetings to you from the patients that took part in the compilation of this guidebook.

"Understanding that my symptoms are real and not imagined, and the fact that I am not the only one suffering from these symptoms, made things easier."

“Doing things requires more concentration than before, but I can manage this”

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INTRODUCTION

Cancer treatment has evolved, and the lifetime expectancy of cancer patients has improved. However, some cancer treatments, namely cytostatic i.e. chemotherapy drugs, can cause peripheral neuropathy, in which damage to the peripheral nervous system occurs as a result of chemotherapy. What is meant by chemotherapy-induced peripheral neuropathy (CIPN) are the side effects which manifest in the peripheral nervous system induced by cancer treatment. CIPN can deteriorate the quality of life significantly. For the majority, the CIPN symptoms disappear or diminish with time, but for some, they are permanent.

In a questionnaire conducted by the cancer-patient organisations' network, 55% of those who responded (262 in total) reported that chemotherapy-induced peripheral neuropathy causes at least some problems in their everyday life, while 20% stated that neuropathy causes significant problems in their everyday life. The majority of the people who responded suffered from more than one symptom. The most common symptoms were numbness, sensory dysfunctions and prickling sensations. More than 30% also reported muscle weakness, sensitisation to touch, balance issues or disturbances in the autonomic nervous system. The majority experienced more than one of the aforementioned symptoms.
Therefore, you are not alone in being affected by chemotherapy-induced peripheral neuropathy. This guidebook will explain what causes CIPN and how it can be treated and alleviated.

WHAT IS CIPN?

Chemotherapy-induced peripheral neuropathy (CIPN) is damage or a malfunction in the peripheral nervous system caused by the nerve toxicity of chemotherapy drugs. In CIPN, the damage occurs in the peripheral nervous system, not in the brain or spinal cord. Anomalies occur especially in the sensory nerves, but there can also be damage in the motor or autonomic nervous systems. Furthermore, there are thin nerve fibres in the human body that transmit pain and heat sensations, for example.

The most common chemotherapy substances that cause neuropathy:

TAXANES	VINCA ALKALOIDS
Docetaxel	Vincristine
Paclitaxel	Vinblastine

PLATINUM DERIVATIVES	OTHERS
Cisplatin	Eribulin
Carboplatin	Bortezomib
Oxaliplatin	Thalidomide

HOW CIPN MANIFESTS ITSELF

Chemotherapy-induced peripheral neuropathy can be divided into two main groups: Painful sensory neuropathy and sensory-motor neuropathy.

Painful neuropathy affecting thin pain nerve fibres (A and C nerve fibres) may also be associated with sensory disturbances and a feeling of numbness due to damage to sensory nerve fibres. Sensory neuropathy can also manifest itself only as numbness or loss of sensation.

Sensory-motor neuropathy involves both sensory and motor nerve damage. Sensory-motor neuropathy may also include damage to the autonomic (involuntary) nervous system. Sensory-motor neuropathy can also occur with no damage or dysfunction in the autonomic nervous system. The manifestation of symptoms in a multiple nerve area, as is common in CIPN, is called polyneuropathy.

The sensory symptoms of CIPN usually start from the toes and fingertips, progressing upwards to the knees and elbows in stocking and glove distribution. The symptoms of neuropathy can also occur in hands only or feet only. Symptoms of neuropathy are more common in the lower extremities. The sensory symptoms of CIPN include numbness, nerve pain (continuous or spontaneous, electric shock-like, burning) and becoming sensitive to external stimulants, such as touch or cold. Nerve pain can be constant or episodic and is often at its worst at rest. The sensory symptoms of CIPN can also manifest as irregular sensations in the sole of the foot.

One of the sensory symptoms of CIPN is sensitisation to external stimulants. The skin may also be sensitive with no external stimulant. Oxaliplatin typically causes sensitivity to cold. For some, chemotherapy-induced peripheral neuropathy can manifest itself as itching.

The sensory symptoms of CIPN may also include proprioceptive dysfunctions. Proprioception is an unconscious sensation transmitting information regarding body posture to the brain as we sit or stand. Proprioceptive endings are mostly located in the joints, but also on the skin. The disturbance of proprioception as a result of chemotherapy can lead to problems in balance in particular. Balance problems can be regarded as powerlessness, but examination will determine whether a proprioceptive dysfunction or powerlessness is the issue. The symptom can also be a combination of various factors. The symptoms of CIPN can therefore vary considerably between individuals, depending on which nerve fibres have been damaged.

HOW CIPN CAN AFFECT YOUR LIFE

Chemotherapy-induced peripheral neuropathy can cause fine motor problems as sensation decreases. Without a sufficient sense of touch, the fingers become clumsy, and this can be seen, for example, in difficulty buttoning a shirt or doing other things that require dexterity. If the proprioception of the joints has been disturbed, it can lead to difficulties in walking. If this kind of sensory deficiency occurs with disturbance of the sense of touch and fine touch, it can even lead to sensory ataxia,

in which the sensory control of the lower extremities is severely declined, and walking can be staggering.

If the symptom is sensitisation instead of numbness, mechanical hypersensitisation may cause pain when walking. Especially in neuropathy caused by oxaliplatin, it is common that the cold sensitivity of the skin increases, and the symptoms become worse in the cold, for instance, in the cold section of the supermarket. Raynaud's disease, i.e. restricted blood flow to the fingers, can also occur.

The pain caused by polyneuropathy is often at its worst at nighttime. The pain is commonly localised from the ankles down and can slowly proceed below the knees. The "restless legs" syndrome may also be an additional difficulty in trying to fall asleep, as the shaking and twitching legs seem to have a life of their own.

MOTOR SYMPTOMS OF CIPN

Vinca alkaloids, in particular, can sometimes cause weakness of the tips of the extremities and rarely muscle paralysis. As the tips of the extremities become weak, the foot (or wrist) hangs powerlessly, and walking becomes shuffling as the foot drags (foot drop).

AUTONOMIC SYMPTOMS OF CIPN

If the neurotoxicity of chemotherapy targets the autonomic, i.e. involuntary nerves, disturbances of the functions regulated by the autonomic nervous system may occur. The symptoms of these disturbances depend on whether the sympathetic or parasympathetic system has been damaged. The autonomic nervous system is in charge of the neural regulation of the automatic functions of the body, such as the abdominal tract, endocrine endocrine glands (sweating, secretion of saliva), heart (regulating heart rate) and blood pressure. Possibly the most common CIPN symptom of the autonomic nervous system is constipation. Low blood pressure (orthostatic hypotonia) and related dizziness and falling down, sweating disorders (most commonly exhaustion of sweat), dryness of the mouth and eyes and erectile dysfunctions in men can also be symptoms of the autonomic nervous system.

PREVALENCE OF CIPN

Chemotherapy-induced peripheral neuropathy occurs in more than 70% of patients in the first month after treatment has ended. For many, the symptoms are reversible and three months after the end of treatment, the prevalence of CIPN is about 60% and continues to decrease so that six months after the end of treatment, only about 30% display CIPN symptoms. For some, the CIPN symptoms are permanent.

Certain factors increase the risk of chemotherapy-induced peripheral neuropathy. However, the risk factors can vary between different medicines. In the case of a pre-existing polyneuropathy caused by some other factor, the risk of developing chemotherapy-induced neuropathy is elevated. In cases like these, the symptoms may be more difficult. Furthermore, previous treatment with neurotoxic drugs increases the risk. Diabetes mellitus is associated with polyneuropathy as a comorbidity, and diabetes also increases the risk of developing chemotherapy-induced neuropathy. Smoking, excessive alcohol consumption and renal failure also enhance the risk of CIPN. A cumulative dose of a drug also increases the risk of CIPN. The risk increases with the dosage. Genetic factors (hereditary polyneuropathy and certain predisposing genes)

have also been found to elevate the individual's risk of developing chemotherapy-induced peripheral neuropathy. In the case of an underlying deficiency of folic acid and/or vitamin B12, the risk of CIPN is increased. Some people develop polyneuropathy with age, and old age is another risk factor for developing CIPN.

A study investigating treatment with oxaliplatin found that symptoms induced by exposure to cold (cold-induced pain) that remain for more than four days after the third treatment cycle may predict a difficult case of neuropathy.

Different chemotherapy drugs cause different neuropathic symptoms on various time frames. In the case of some, especially the platinum derivatives, it is common for the symptoms to develop only after the treatment has ended. This is what is meant by the "delay in the onset of symptoms" portrayed in the following table.

In the table below, the various characteristics of different chemotherapy drugs are displayed. All the substances in the table cause dysfunctions of superficial sensation (touch, sensations of heat and pain).

Disturbances in deep sensation, which may affect sensory-motor functions, are caused specifically by the platinum derivative drugs (cisplatin, carboplatin and oxaliplatin). Nerve pain, i.e. neuropathic pain, is caused specifically by cisplatin, vincristine and especially bortezomib, which is used to treat haematological cancers. Regarding sensory-motor functions, vincristine and paclitaxel cause the most dysfunctions, mainly weakness symptoms, or even paralysis in the peripheral parts of the body. Autonomic symptoms are most commonly caused by vincristine, while cisplatin is the second most common cause. The other chemotherapy drugs are rarely the cause of autonomic symptoms. The worst drugs inducing neuropathy are oxaliplatin and paclitaxel.

It is typical, especially with platinum derivatives, that neuropathy symptoms begin as late as six months after treatment has finished. Correspondingly, the symptoms may continue for a long time after treatment has ended. This does not usually occur in connection with other chemotherapy drugs.

Table: The typical symptoms of chronic chemotherapy-induced peripheral neuropathy

Chemotherapy drug	Dysfunctions of superficial sensation, touch, heat sensation, pain sensation	Dysfunctions of deep sensation, vibration perception, motor sensation, ataxia	Neuropathic pain, nerve pain	Dysfunctions of motor neurons, motor dysfunctions	Dysfunctions of the autonomic nervous system	Delay in the onset/ length of symptoms
Cisplatin	++	+++	++	-	+	+++
Carboplatin	+	++	-	-	-/+	+++
Oxaliplatin	++	+++	+	-	-/+	+++
Paclitaxel	++	++	+	++	-/+	-/+

Markings; - does not occur, -/+ uncertain, + rare, ++ common, +++ very common

Chemotherapy drug	Dysfunctions of superficial sensation, touch, heat sensation, pain sensation	Dysfunctions of deep sensation, vibration perception, motor sensation, ataxia	Neuropathic pain, nerve pain	Dysfunctions of motor neurons, motor dysfunctions	Dysfunctions of the autonomic nervous system	Delay in the onset/ length of symptoms
Docetaxel	++	+	+	+	-/+	-/+
Vincristine	++	+	++	++	+++	+
Ixabepilone	+++	+	-/+	+	-	-
Bortezomib	+++	+	+++	+	-/+	-
Thalidomide	++	+	+	+	-	-

Markings; - does not occur, -/+ uncertain, + rare, ++ common, +++ very common

CIPN AND PLATINIUM DERIVATIVES

The platinum derivative compounds display some specific qualities. The known risk factors of neuropathy do not seem to be relevant when it comes to cisplatin.

With the use of platinum derivatives, Lhermitte's symptom may also occur, meaning an electric shock-like sensation when bending the neck and head down and forward.

Related to the use of platinum derivative compounds are also cold-induced, acute symptoms in the throat, mouth and face area as well as in the hands. For most, these symptoms are temporary. The symptoms may also include spasms of the jaw, cramps which may cause difficulty in speaking. The symptoms are harmless.

The platinum derivative compounds can also cause disturbances of taste and smell, which are also reversible and will pass after treatment has ceased.

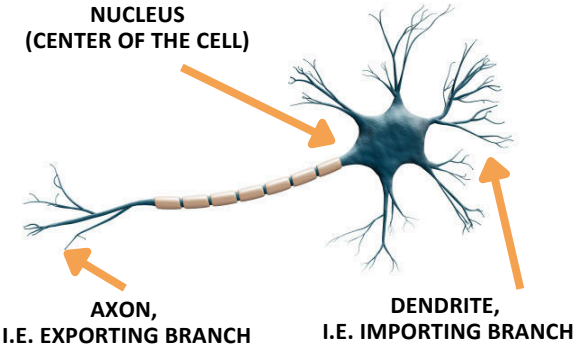
Damage of the hearing and balancing nerves may also occur, causing problems with hearing and balance.

The delay in the onset of symptoms caused by platinum derivative compounds may cause the symptoms to continue for another 2-6 months after treatment has ended. Oxaliplatin-induced neuropathy is completely reversed in about 40% of the cases in 6-8 months after treatment has ceased, however, for about 35% the chemotherapy-induced neuropathy symptoms persist for as long as 5 to 6 years after the end of treatment.

Combination therapy may induce more severe neuropathic symptoms. In combination therapy with 5-fluorouracil and oxaliplatin (FOLFOX treatment), 92% develop sensory chemotherapy-induced peripheral neuropathy affecting sensory nerves. These symptoms last an average of 9 months but may persist even longer.

MECHANISMS

The nerve cells of the human peripheral nervous system contain the nucleus, i.e. the centre of the cell, the importing branch, i.e. dendrites, and the exporting branch, i.e. axons. Axons vary in thickness and also the myelin sheath surrounding them can be thicker, thinner or completely missing. The function of the myelin sheath is to accelerate the progression of the nerve cell's message, the electric signal. The thicker the nerve fibre and myelin sheath, the quicker the nerve signal progresses.



The signal transmitted by the exporting branch of the nerve cell, i.e. the axon, is transferred from the end of the axon to the importing branch of the next nerve cell. A muscle may also be at the end of the axon, in which case the nerve is connected to the muscle with a neuromuscular junction. In neuromuscular junctions, the electric signal of the nerve cell is converted into chemical form and transported to the muscle cell. As a result of the signal, the muscle contracts. The functioning of nerves requires a lot of energy.

The axons, i.e. the exportation branch of the nerve cells, transmitting signals to tissues, are the most common target for the toxicity effects and damage caused by chemotherapy. The thin nerve fibres which have no myelin sheath at all are particularly susceptible to the toxicity of chemotherapy.

In rare cases, the damage also occurs on the myelin sheath surrounding the nerve cells.

The function of the thin nerve fibres, which are easily damaged by chemotherapy drugs, is to transmit pain, cold and heat sensations as well as sensations from the internal organs via the nerve fibres which transmit information from the skin. The thin nerve fibres also transmit the sensation of itchiness. The exporting thin nerve cells transmit information to the autonomic nervous system. This explains the dysfunctions of the autonomic nervous system caused by chemotherapy. The thin nerve fibres of the skin can be seen to have reduced in a skin sample by a person suffering from chemotherapy-induced peripheral neuropathy.

The nerve nodes located near the spine, i.e. spinal ganglia, are command centres of the nerve cells and transmit pain sensations to the brain through the spinal cord among other things. These are affected especially by platinum derivatives. Platinum may also accumulate in the nerve nodes.

In the sensory nerve, information is transferred along the peripheral nerve to the correct point of each skin area in the spinal cord and travels further to the sensory cortex of the brain, where the actual sensation of touch takes place.

The neural damage caused by chemotherapy happens on many levels. In the skin area, destruction of the nerve endings occurs. Furthermore, as the connection between the skin and the deep parts of the skin is lost and disturbed, sodium channels begin to form. The sodium channels transmit spontaneous nerve signals, which can be sensed as pain or other unpleasant sensations.

The damaging of both the sensory and pain nerves can cause a normal touch to be perceived as unpleasant and also, sensations of pain become stronger.

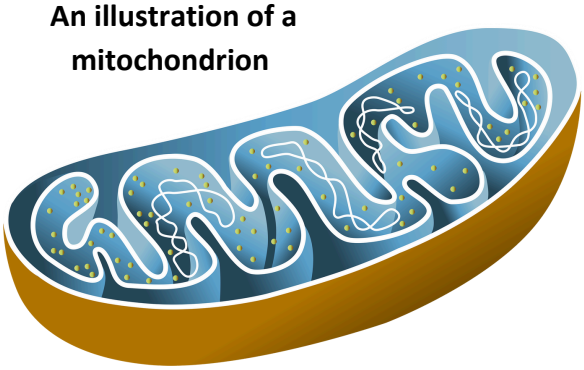
Dysfunctions of the pain pathways are not necessarily limited to the peripheral nervous system but in addition to CIPN, changes can occur in the central nervous system.

At the cellular level, the mechanisms of chemotherapy-induced peripheral neuropathy are mitochondrial damage, nitro-oxidative stress and inflammation. Mitochondria are intracellular organelles, small power plants that produce the energy the cells require. Through so-called cellular respiration, mitochondria convert energy from food into ATP (adenosine triphosphate), the "energy currency" used by cells. Without ATP, the cell cannot function. In the nerve cells, mitochondria produce more than 90% of the energy, or ATP, to maintain normal cellular functions. Functioning of the nerves consumes a lot of energy. Transporting the signal from the nucleus through the exportation branch, axon, transmitting the signal to the next nerve cell at the end of the nerve and transforming the electric signal to transmit it in a chemical form into the muscle cell; in the neuromuscular junction everything requires a lot of energy, or ATP.

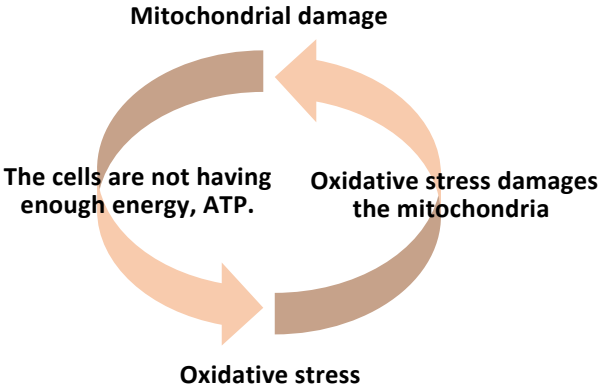
The disturbance of the functioning of the mitochondria and the consequent insufficient production of ATP is considered a central cause for chemotherapy-induced peripheral neuropathy.

Sensory nerves run out of energy, especially when the mitochondria of axons are destroyed.

An illustration of a mitochondrion



Oxidative stress is partly a consequence of mitochondrial damage. Oxidative stress refers to an imbalance in the oxidation-reduction state of cells. In oxidative stress, the oxidising factors are too strong, or the reducing factors, i.e. the antioxidative systems, work ineffectively. Reactive oxygen radicals are compounds formed from oxygen that contain an unpaired electron. The reactive oxygen radicals facilitate oxidative stress and oxidising effects. This creates a vicious cycle in which mitochondrial function further deteriorates.



PREVENTION OF CIPN

At present, there is no medicinal way to prevent the development of chemotherapy-induced peripheral neuropathy. Several substances have been studied, but so far there is no evidence of the efficacy of any treatment. The area is still being widely researched.

MEDICINAL TREATMENT OF CIPN NERVE PAIN

The nerve pain caused by chemotherapy can be treated with drugs. However, non-steroidal anti-inflammatory drugs are usually not beneficial. The strongest scientific evidence regarding efficacy in treating nerve pain is from serotonin and norepinephrine reuptake inhibitors (SNRIs). Of these, Duloxetine and Venlafaxine, for example, are used to treat neuropathic pain caused by chemotherapy.

Other medicinal treatments and their combinations can also be tried. Other oral medicines used to treat polyneuropathy include nortriptyline, amitriptyline, tramadol, gabapentin, pregabalin and lidocaine as a local anaesthetic. Medication is always continuous and not for occasional pain. However, no medication will help with symptoms of numbness.

NON-MEDICINAL TREATMENT OF CIPN

For some, a treatment called TNS (Transcutaneous Nerve Stimulation Therapy) used in physical therapy has proved effective in treating neuropathic pain. In TNS, electrodes are placed on the skin, on the area of pain, which transmit a light current that can be sensed as vibrations. This is based on a gate control theory, in which the vibration signal as the faster signal overrides the pain signal in the spinal cord.

Acupuncture has also been tried and studied, but as of yet, there is no conclusive research evidence.

In the case of increased sensitivity of the superficial nerve in a limited area, some may benefit from a capsaicin patch, which falls somewhere between medicinal and non-medicinal treatment. The capsaicin patch can be used as an individual treatment or in combination with other medicines. As a result of exposure to capsaicin, the pain receptors of the skin become less sensitive to various stimuli. The sensitivity of the nerves will be restored after the treatment has ended.

Lymphatic treatment will not help with pain symptoms, but in the case of swelling making the symptoms worse, lymphatic treatment may reduce the swelling. When lymphatic swelling is being treated with lymphatic therapy, the treatment should always include compression bandages, and in neuropathy treatment, the compress bandages should be made with possibly two layers of gypsum padding and one low-elasticity compression bandage. Furthermore, when using medicinal support socks, the pressure should be classed as 1 (recommendation by käypähoito.fi, 2021, compression treatment)

SIGNIFICANCE OF DIET

There is not enough evidence to suggest that any foods or supplements studied at the moment could prevent or alleviate chemotherapy-induced peripheral neuropathy. Many compounds vital to the functioning of the nervous system and metabolism have been studied. As an exception, if a cancer patient has been diagnosed with vitamin B12 deficiency, it should be treated, as it may be a factor in developing neuropathy.

Even though none of the compounds studied has proved clearly beneficial as a supplement, it is likely useful if an individual is able to follow a diverse diet providing enough energy and protein during cancer treatment. One should try to eat fruits and vegetables to ensure sufficient intake of vitamins, trace elements and other compounds beneficial to health. The intake of essential fatty acids and fat-soluble vitamins should be procured by consuming soft fats such as rapeseed oil, oily fish and nuts. Hard fats, processed meat products and alcohol should be avoided.

EXERCISE IN THE TREATMENT OF NEUROPATHY

Exercise can help with peripheral neuropathic pain induced by chemotherapy, as it reduces chronic inflammation. Chronic inflammation appears to play a role in the aetiology and treatment of chemotherapy-induced peripheral neuropathic pain. Exercising changes the sensations of hands, feet and other body parts in the brain. The changes that occur with exercise may also help with general sensitisation related to neuropathic pain, which is a fairly common characteristic of chemotherapy-induced peripheral neuropathic pain, regardless of the specific cause of the neuropathy.

In recent years, several studies on the beneficial effects of exercise on neuropathic symptoms related to cancer treatment have been conducted. Exercise has been found to reduce pain and sensory dysfunctions, such as numbness, loss of sensation or sensitisation of the lower and upper extremities, as well as weakening of balance. The research recommends endurance exercise (walking), strengthening the muscles of the lower extremities and balance exercises. Physical activity and good muscle strength are connected to less severe neuropathic symptoms. For patients receiving taxane, platinum and vinca alkaloids, especially geriatric patients, progressive resistance elastic band training for muscle strength, as well as walking, are recommended as a home exercise program.

For neuropathic symptoms in the upper extremities, versatile training is recommended, including grip strength training for approximately 40-60% of maximum strength, fine motor finger exercises and tactile exercises, such as touching various surfaces.

EXERCISE PROGRAM FOR CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

Exercises for the foot and the sole of the foot

Starting position. Exercise for improving the small muscles of the sole.
Lift your big toe from the surface.
If needed, you can hold the other toes
on the surface with your hand and try to lift the big toe only.
Repeat 5 times.
Keep your big toe on the surface and lift your other toes off the surface. If needed, you can hold the big toe on the surface with your hand and try to lift the other toes only. Repeat 5 times.

Starting position. Place a towel or a corresponding light cloth under your toes.
Exercise for strengthening the small muscles in the sole.
Curl your toes and with each curl,
gather the towel so that it becomes shorter.

Exercises for the foot and the sole of the foot


Massage the sole of your foot with a tennis ball, for example.
Roll the ball from the ball of the foot to the heel and back.

Grab a soft ball and press the ball towards the ground with the ball of your foot, complete as a pumping exercise, you can pump the entire area of the sole by pressing the ball.
Exercise for improving the lymphatic and blood circulation.


Slide your foot from side to side, taking turns in sliding the outer side and inner side of the foot against the surface. Slide your foot lightly against the floor.
Exercise for improving the mobility of the ankle and the ball of the foot.
Execute the move with both legs.


Exercise for abdominal and back muscles.
Sit in the front of a chair and keep your back straight.
Lean forward without rounding your back. As you lean forward, you will feel tension in your abdominal muscles and as you stretch back in the starting position, the abductor muscles in your back are activated.
Complete the move calmly. Repeat 10–15 times.


Complete the exercise sitting in a chair.
Stretch the knee keeping the ankle bent.
As you stretch your knee, you will feel your thigh muscle activate, keep the knee stretched for 5 seconds and lower your leg calmly to the floor, then repeat with the other leg.
Repeat 10–15 times with both legs.

Exercises for muscle strength


Exercise for the extensor muscles of the hip and abdominal muscles.
Starting position.
Take turns lifting your thighs off the chair keeping your back as straight as possible during the exercise.
Repeat 10-15 times.


Starting position, stand in front of a chair.
Exercise for strengthening the entire body.
Sit calmly on the chair and stand up. Repeat 10-15 times.
Note! Place the chair against the wall to prevent it from sliding from under you during the exercise.

Starting position. Grab the backrest of a chair. Exercise for thigh muscles. Squat holding on to the backrest and stand up. Repeat 10-15 times.

Starting position, grab the backrest of a chair. Exercise for the gluteal muscles. Stretch your leg backward keeping your upper body still. The range of the movement is small. Repeat with both legs 10-15 times.

Exercises for muscle strength


Grab the backrest of a chair and stand on your toes. Lower yourself from the toes to the heels. Repeat 10-15 times. The exercise strengthens the muscles around your ankle and shin.


Starting position. Stand at an arm's length facing the wall and press your palms wide apart against the wall. Push-up against the wall. During the exercise, keep your body in control, do not arch your back. Repeat 15-20 times.


Exercise for the biceps sitting down or standing up. Grab dumbbells suitable to you or fill up a ½ litre water bottle. Keep your wrist straight and your upper arm in place next to your body during the exercise, the only movement coming from your elbow joint. Repeat 10-15 times with both arms.

Exercises for improving balance


Stand on one leg. Execute the move with both legs.
Practise staying in the position.
Have a chair nearby in case you need support.


Stand in a walking position.
Apply your weight in turn to the front leg and then to the back leg.
Repeat 10-15 times on both sides.


Exercise for improving balance. Lift your knee up and touch it with the opposite hand. Complete the move calmly on each side keeping control of your position.
Repeat 10 times.

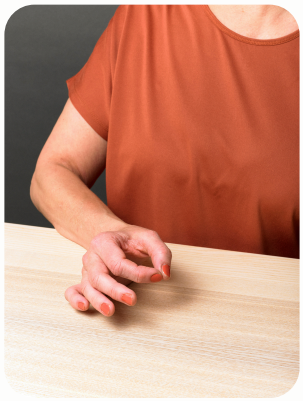
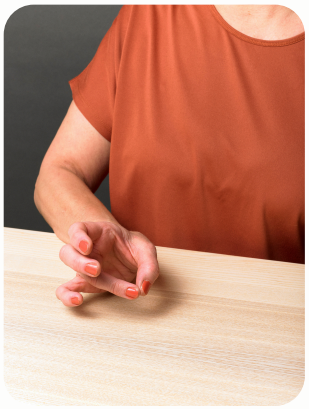
Exercises for improving balance



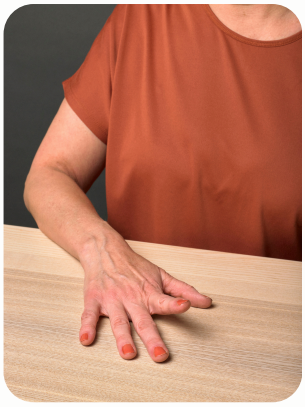
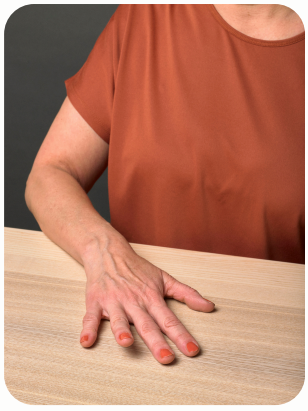

Place three markers on the floor: one to the front,
one to the side and one to the back.
Touch the markers with your foot.
Repeat with the other leg.
If needed, have support nearby.

Draw a horizontal number eight with your thumb and
trace the movement with your eyes.
Try to keep your head still.
Draw the number eight in both directions, alternating between arms.

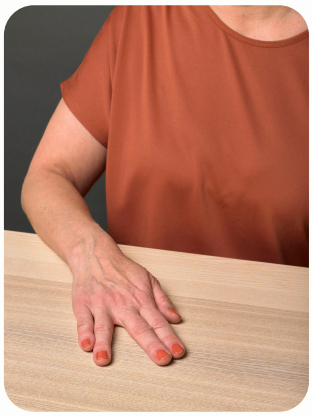
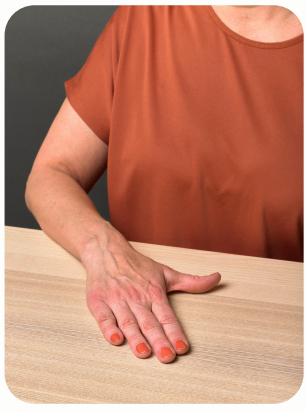
Exercises for upper extremities

Fine motor exercise.
Touch each finger in turn with your thumb.
Repeat 5-10 times.

Place your hand on a surface and lift each finger off the surface in turn.
Try to keep the other fingers on the surface.
Repeat 5-10 times.

Place your hand on a surface and part your fingers
alternating between fingers.
Repeat 5-10 times.

Exercises for upper extremities

Tactile exercise for the hand. There are various materials, such as a rustling plastic bag, soft wadding, stones and water in the picture. You can choose different materials at home and feel them. Do not, however, choose sharp items so as not to hurt yourself.

Fine motor exercise.
Take a buttoned shirt and button it.

Exercise for improving the muscles in the forearm and grip strength. Grab a soft ball or make a tight bunch out of a pair of socks, for instance. Squeeze the ball with pumping movements.
Repeat 5-15 times with both hands.

SOURCES:

Neurologist Aki Hietaharju's video lecture on chemotherapy-induced peripheral neuropathy (Information on chemotherapy-induced peripheral neuropathy (colores.fi))

Diet:

Katarzyna Szklener 1, Sebastian Szklener 2, Adam Michalski 3, Klaudia Żak 3, Weronika Kuryło 3, Konrad Rejdak 2, Sławomir Mańdziuk 1 Dietary Supplements in Chemotherapy-Induced Peripheral Neuropathy: A New Hope? Nutrients 2022 Jan 31;14(3):625.

Jennifer M. Mongiovi1,2,, Gary R. Zirpoli3 , Rikki Cannioto2 , Lara E. Sucheston-Campbell4 , Dawn L. Hershman5 , Joseph M. Unger6 , Halle C. F. Moore7 , James A. Stewart8 , Claudine Isaacs9 , Timothy J. Hobday10, Muhammad Salim11, Gabriel N. Hortobagyi12, Julie R. Gralow13, G. Thomas Budd7 , Kathy S. Albain14, Christine B. Ambrosone2 and Susan E. McCann2,15, Associations between self-reported diet during treatment and chemotherapyinduced peripheral neuropathy in a cooperative group trial (S0221) Breast Cancer Research (2018) 20:146

Jiri Grim 1 , Alena Ticha 2,3,*, Radomir Hyspler 2,3, Martin Valis 4 and Zdenek Zadak 2, Selected Risk Nutritional Factors for Chemotherapy-Induced Polyneuropathy, Nutrients 2017, 9

Exercise:

Holschneider DP, Yang J, Guo Y, Maarek JM, Reorganization of functional brain maps after exercise training: Importanse of cerebellar- thalamic- cortical pathway. 2007. Brain research. Volume 1184. pages. 96-107.

Kleckner IR, Zhang J, Touroutoglou A, Chanes L, Xia C, Simmons WK, Quigley KS, Dickerson BC, Barrett LF. 2017. Evidence for a large- Scale brain system supporting allostasis and interoception in humans. Nature human behaviour. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5624222/pdf/nihms852367.pdf>

Costigan M, Scholz J, Woolf CJ. 2009. Neuropathic pain. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2768555/pdf/nihms-110677.pdf>

Seretny M, Currie GL, Sena ES, Ramnarine S, Grant R, MacLeod MR, Colvin LA, Fallon M. 2014. Incidence, prevalence and predictors of chemotherapy-induced peripheral neuropathy: a systematic review and meta- anlysis. Pain. Dec; 155 (12): 2461-2470.

Cathcart-Rake EJ, Hilliker DR, Loprinzi CL. 2016. Scrambler therapy in the treatment of chronic chemotherapy-induced peripheral neuropathy. ,

Ian R. Kleckner, Charles Kamen, Jennifer S. Gewandter, Nimish A. Mohile, Charles E. Heckler, Eva Culakova, Chunkit Fung, Michelle C. Janelsins , Matthew Asare, Po-Ju Lin, Pavan S. Reddy, Jeffrey Giguere, Jeffrey Berenberg, Shelli R. Kesler, and Karen M. Mustian. 2018 Effects of exercise during chemotherapy on chemotherapy-induced peripheral neuropathy: a multicenter, randomized controlled trial. Support care cancer. 2018. Apr. 26(4): 1019-1028.

Dhawan, Shelly. Anderws, Rachel. Kumar, Lailit. Wadhwa, Sanjay. Shukla, Garima. 2020. A Randomized controlled trial to assess the effectiveness of balancing exercises on chemotherapy- induced peripheral neuropathic pain and quality of life among cancer patients. Cancer nurse. Jul/Aug. 43 (4) 269-280.

Ikio, Yuta. Sagari, Akira. Nakashima, Akira. Matsuda, Daiki. Sawai, Terumitsu. Higashi, Toshio. 2022. Efficasy of combined hand exercise intervention in patients with chemotherapy-induced peripheral neuropathy: a pilot randomized controlled trial. Support care cancer. Jun. 30(6) 4981-4992.

Eight-week, multimodal exercise counteracts a progress of chemotherapy-induced peripheral neuropathy and improves balance and strength in metastasized colorectal cancer patients: a randomized controlled trial Philipp Zimmer 1 2, Sina Trebing 3, Ursula Timmers-Trebing 4, Alexander Schenk 3, Rainer Paust 5, Wilhelm Bloch 3, Roland Rudolph 6, Fiona Streckmann 3 7 8, Freerk T Baumann 9 2018 Feb;26(2):615-624. Support Care Cancer

It's never too late - balance and endurance training improves functional performance, quality of life, and alleviates neuropathic symtoms in cancer survivors suffering from chemotherapy-induced peripheral neuropathy: results of a randomized controlled trial

S Kneis 1, A Wehrle 2, J Müller 1 3, C Maurer 4, G Ihorst 5, A Gollhofer 6, H Bertz 7 BMC Cancer 2019 May 2;19(1):414.

A Randomized Controlled Trial to Assess the Effectiveness of Muscle Strengthening and Balancing Exercises on Chemotherapy-Induced Peripheral Neuropathic Pain and Quality of Life Among Cancer Patients Shelly Dhawan 1, Rachel Andrews, Lalit Kumar, Sanjay Wadhwa, Garima Shukla Cancer Nurs 2020 Jul/Aug;43(4):269-280.

Effects of exercise during chemotherapy on chemotherapy-induced peripheral neuropathy: a multicenter, randomized controlled trial Ian R Kleckner 1 2, Charles Kamen 3, Jennifer S Gewandter 3, Nimish A Mohile 3, Charles E Heckler 3, Eva Culakova 3, Chunkit Fung 3, Michelle C Janelsins 3, Matthew Asare 3, Po-Ju Lin 3, Pavan S Reddy 4, Jeffrey Giguere 5, Jeffrey Berenberg 6, Shelli R Kesler 7, Karen M Mustian 3 Support Care Cancer 2018 Apr;26(4):1019-1028.
doi: 10.1007/s00520-017-4013-0. Epub 2017 Dec 14.

Ian R. Kleckner, Charles Kamen, Jennifer S. Gewandter, Nimish A. Mohile, Charles E. Heckler, Eva Culakova, Chunkit Fung, Michelle C. Janelsins , Matthew Asare, Po-Ju Lin, Pavan S. Reddy, Jeffrey Giguere, Jeffrey Berenberg, Shelli R. Kesler, and Karen M. Mustian. 2018 Effects of exercise during chemotherapy on chemotherapy-induced peripheral neuropathy: a multicenter, randomized controlled trial. Support care cancer. 2018. Apr. 26(4): 1019-1028.

Preventive effect of sensorimotor exercise and resistance training on chemotherapy-induced peripheral neuropathy: a randomised-controlled trial Jana Müller 1 2 3, Markus Weiler 4, Andreas Schneeweiss 2 5, Georg Martin Haag 6, Karen Steindorf 7, Wolfgang Wick 2 4, Joachim Wiskemann 8

Br J Cancer. 2021 Sep;125(7):955-965. doi: 10.1038/s41416-021-01471-1. Epub 2021 Jul 5.

Impact of Somatic Yoga and Meditation on Fall Risk, Function, and Quality of Life for Chemotherapy- Induced Peripheral Neuropathy Syndrome in Cancer Survivors Mary Lou Galantino 1 2 3, Robyn Tiger 4, Jennifer Brooks 5, Shera Jang 1, Kim Wilson 1 Integr Cancer Ther. 2019 Jan-Dec;18:1534735419850627. doi: 10.1177/1534735419850627.

Effects of foam pad balance exercises on cancer patients undergoing chemotherapy: A randomized control trial Chanatsupang Saraboon 1, Akkradate Siriphorn 2 J Bodyw Mov Ther. 2021 Oct;28:164-171. doi: 10.1016/j.jbmt.2021.07.013. Epub 2021 Aug 8.

Efficacy of combined hand exercise intervention in patients with chemotherapy-induced peripheral neuropathy: a pilot randomized controlled trial Yuta Ikio 1 2, Akira Sagari 3, Akira Nakashima 2, Daiki Matsuda 1 2, Terumitsu Sawai 2, Toshio Higashi 4 Support Care Cancer . 2022 Jun;30(6):4981-4992. doi: 10.1007/s00520-022-06846-5. Epub 2022 Feb 21

New quotes:

Bae EH, Greenwald MK, Schwartz AG. Chemotherapy-Induced Peripheral Neuropathy: Mechanisms and
Therapeutic Avenues. Neurotherapeutics. 2021 Oct;18(4):2384-2396. doi: 10.1007/s13311-021-01142-2.
Epub 2021 Oct 21. PMID: 34676514; PMCID: PMC8804039.

Zhang S. Chemotherapy-induced peripheral neuropathy and rehabilitation: A review. Semin Oncol. 2021
Jun;48(3):193-207. doi: 10.1053/j.seminoncol.2021.09.004. Epub 2021 Sep 22. PMID: 34607709.