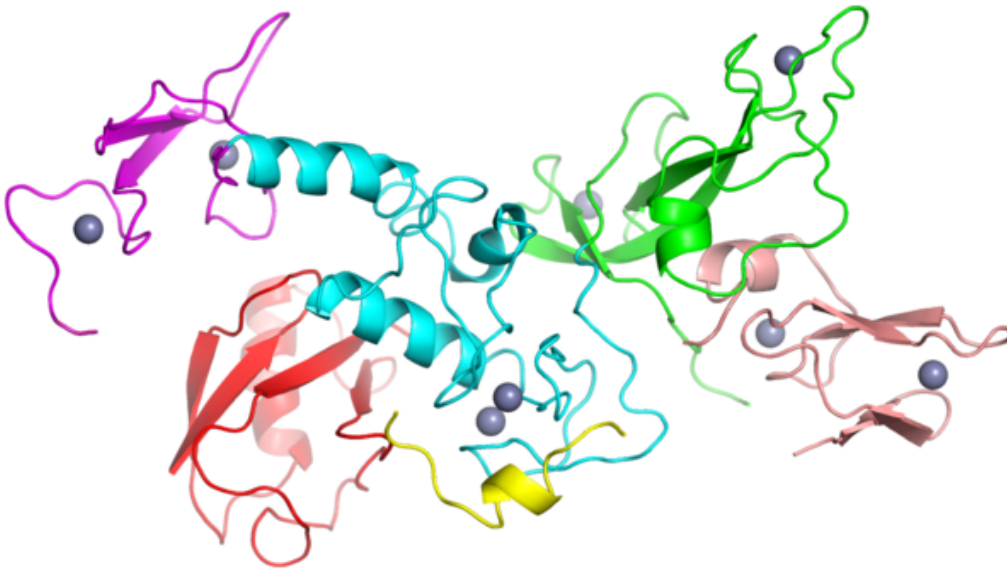


Parkinson's Disease—Symptoms, Stages and Life Expectancy

[See online here](#)

Parkinson's disease is a movement disorder that is characterized by degeneration of dopaminergic neurons of the substantia nigra, which is a part of the basal ganglia. The disease itself mostly has idiopathic causes and is to be distinguished from the symptomatic and the atypical Parkinsonism. The disease has a chronic-progressive course, whereas the life expectancy of those affected generally corresponds to that of the normal population. In this article, you will gain all the exam-relevant facts concerning epidemiology, etiology, pathophysiology, clinic, diagnosis, and therapy of Parkinson's disease.



Definition of Parkinson's Disease

Parkinson's syndrome is characterized by the clinical triad of **rigor**, **tremor**, and **akinesia** as well as possible **postural instability**.

Based on etiology, one can further distinguish between **idiopathic Parkinson's** disease, which is synonymous with **Parkinson's disease**, and **atypical** and **symptomatic parkinsonism**.

Idiopathic Parkinson's disease or Parkinson's disease is considered a diagnosis of exclusion, in the absence of a specific cause.

Symptomatic Parkinsonism, however, is triggered by certain identifiable factors. For example, in the context of intoxication, manganese or lead may cause the disease. Parkinson's syndrome is also triggered by medication, e.g., **neuroleptics**.

Parkinson's syndrome occurring in the context of other **neurodegenerative** diseases is referred to as **atypical Parkinsonism**.

Epidemiology of Parkinson's Disease

The peak of manifestation of Parkinson's disease occurs between ages 40 and 60 years. Both male and female genders are affected almost equally. Prevalence in 60-year-olds is approx. 1% and in 80-year-olds it is approx. 3%.

Etiology of Parkinson's Disease

Etiology of Idiopathic Parkinson's Syndrome

In most cases, no particular cause can be assigned to idiopathic Parkinson's disease. A familial etiology is very rare and is attributed to certain gene loci (Park 1 - Park 11).

Etiology of Symptomatic Parkinson's Syndrome

In the context of symptomatic parkinsonism, there are several possible trigger factors, which can be assigned to different major groups.

The major groups include intoxications, metabolic diseases, inflammations, vascular causes, and medications.

Examples of toxins, which can lead to symptomatic parkinsonism in the context of intoxication are: **manganese**, carbon disulfide, mercury and **MPTP** (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine).

An example of a metabolic disease that can lead to symptomatic parkinsonism is **Wilson's disease**. One aspect is that disturbed copper excretion leads to an accumulation of copper in the body, including the CNS.

Diseases that trigger symptomatic parkinsonism usually affect the brain itself, i.e., Parkinson's syndrome is caused by issues related to **encephalitis**.

A vascular disease, which may trigger symptomatic parkinsonism, is **subcortical arteriosclerotic encephalopathy (SAE)**, which presents itself as progressive atrophy of the brain with simultaneous impairments of cognitive performance.

Medications that modulate dopamine metabolism are possible triggers of symptomatic parkinsonism (see above), for e.g., **dopamine antagonists** such as classical **neuroleptics** and antiemetics including **metoclopramide**.

Other diseases, which possibly trigger symptomatic parkinsonism are **normal pressure hydrocephalus**, intracranial **masses**, and **traumatic brain injuries**.

Pathophysiology of Parkinson's Disease

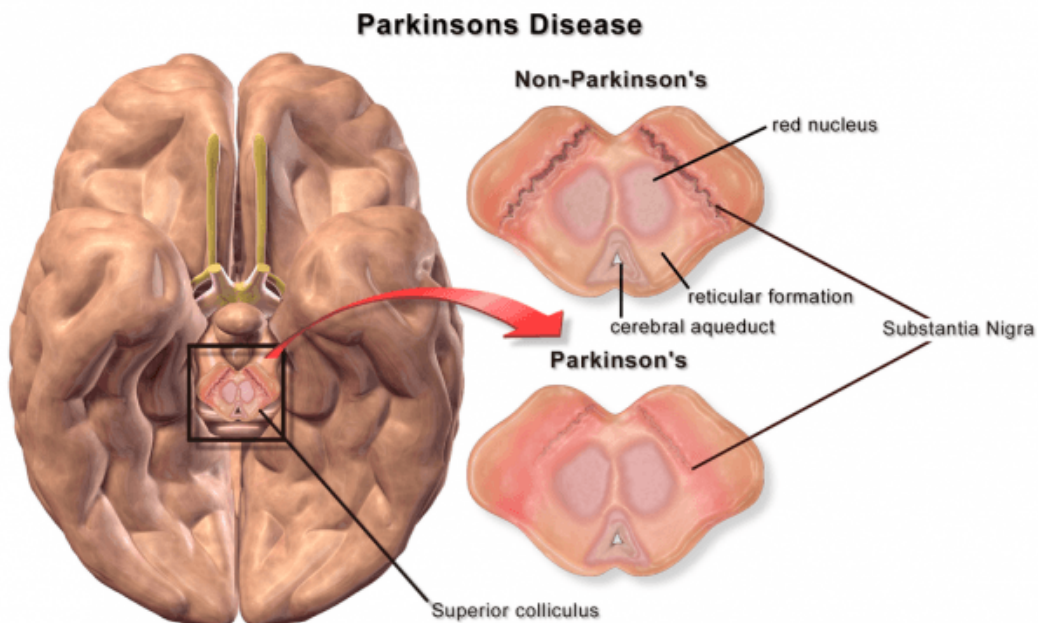


Image: Parkinson's disease. By BruceBlaus, License: CC BY 3.0

In Parkinson's disease, the lesion is located in the compact part of the **substantia nigra**. The decay of **dopaminergic neurons** and thus the loss of inhibitory function of the substantia nigra occurs in the indirect pathway of the **basal ganglia loop**. The disinhibition further activates the indirect pathway and inhibits the thalamus, which results in reduced movement.

Additionally, degenerative changes occur in the area of the dorsal **vagal nuclei** and peripheral **sympathetic ganglia**, resulting in **autonomic dysfunction** disrupting the bladder function (see below).

Typically, the so-called **Lewy bodies** appear in the histopathological specimen. Lewy bodies are usually **eosinophilic hyaline** inclusions and occur in the neurons. They are specifically located in the degenerating neurons of the substantia nigra.

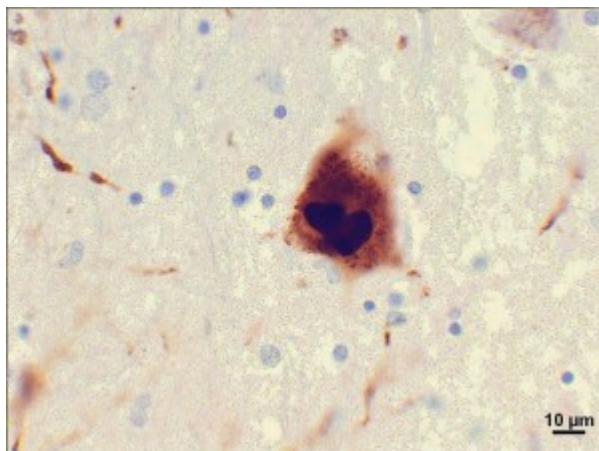


Image: Lewy Bodies. By Suraj Rajan, License: CC BY-SA 3.0

In the neocortex, they are found in **Lewy body dementia**, which is part of cortical dementia.

Clinical Manifestations of Parkinson's Disease

Symptoms of Parkinson's disease



Image: Sir William Richard Gowers, neurologist, researcher, and artist, drew this illustration in 1886 as part of his documentation of Parkinson's Disease. The image appeared in his book, *A Manual of Diseases of the Nervous System*, still used today by medical professionals as a primary reference for this disease. By Beao, License: [Public domain](#)

The typical clinical triad of Parkinson's disease consists of **akinesia**, **rigor**, and **tremor**. Partially, **postural instability** is considered as the core symptom. Typically, the tremor is a **resting tremor**, which initially starts on one side, implying that it manifests **asymmetrically**.

N.B. The one-sided onset of symptoms is a characteristic of Parkinson's disease and occurs in 70% of the cases. The right half of the body is usually more affected. Depending on the most prominent symptom, one can distinguish between **tremor dominant**, **akinetic-rigid**, and **equivalent types**. In the equivalent type Parkinson's

disease, the 3 symptoms of the clinical triad (see above) are roughly equally distinct.

Additionally, the patient's gait provides the 1st clue. In hypo- or akinesia, the patient's gait is marked by small steps and a stooped torso. The arms swing less, usually on one side.

Further symptoms occurring before the onset of classical Parkinson's symptoms include disorders of **REM sleep** and impaired smell either in the form of **hyposmia** or **anosmia**. Pain may involve the shoulder/neck region or the extremities.

N.B. Muscle stiffness and associated pain in the shoulder/neck region are common early symptoms but are not adequate to establish a diagnosis of Parkinson's disease.

As the disease progresses further, vegetative symptoms of **psychopathological** nature such as frontal dementia or **depression** can occur.

The possible **vegetative symptoms** include increased salivation (**hypersalivation**), a mask-like face due to seborrhea, hyperhidrosis, disorders of bladder depletion, obstipation, erectile dysfunction, and disorders of temperature regulation.

Diagnosis of Parkinson's Disease

Parkinson's disease as a clinical diagnosis

In the case of Parkinson's disease, the fact that it is a diagnosis of exclusion should be emphasized. Certain diagnosis can only be made during post-mortem examination on the basis of histopathological diagnostic criteria. These include the detection of **Lewy bodies** and the decay of > 60% of the neurons in the **substantia nigra**.

N.B. Parkinson's disease is a clinical diagnosis based on physical examination, laboratory tests, and instrumental diagnosis.

Possible reversible etiology (due to known factors) of Parkinson's disease (see above) should be excluded.

Physical examination

The most important element in the diagnosis is the physical examination during the course of **anamnesis**. During anamnesis, questions should evaluate the development of the respective symptoms whether or not they are one-sided and the circumstances under which the symptoms occur.

The clinical examination should investigate the presence of classical triad: resting tremors, akinesia, and rigor. Classically, the **resting tremor** has a frequency of 4-7/s and increases during periods of emotional stress or stressful situations.

Rigor is illustrated by the **cogwheel phenomenon** and movement of the extremities. The cogwheel phenomenon is characterized by stretching resistance, which subsides intermittently, followed by recurrence.

Rigor is also characterized by the positive **head fall test**, in which the patient lies on a couch. The patient's head is elevated by the examiner and released suddenly. The head does not fall back onto the couch but is held in its position.

During clinical examination, hypokinesia or **akinesia** presents an increased or decreased turning step count, and the absence of arm swing while walking.

Overall, a positive diagnosis of Parkinson's disease is highly likely after **asymmetric onset**, positive results after the use of **L-DOPA** or **apomorphine** (see below), absence of further neurological deficits, and the presence of (at least) 2 of the following symptoms:

- Rigor
- Resting tremor
- Bradykinesia or akinesia
- Disorders of holding and positioning reflexes (e.g., the tendency for propulsion)

Drug testing for diagnosis of Parkinson's disease

A diagnostic clue suggesting Parkinson's disease is provided by symptom improvement after the application of **L-DOPA** or **apomorphine** (a dopamine agonist, see below). The improvement should occur in 5–15 minutes after the injection of apomorphine.

The L-DOPA test is considered positive if a clinical improvement of approx. 20% is achieved. For a better assessment of clinical improvement, the **Unified Parkinson's Disease Rating Scale (UPDRS)** is used.

Instrumental diagnosis

In the context of an instrumental diagnosis of Parkinson's disease, imaging of the head is performed using MRI, DaTSCAN™ (dopamine-transporter-scintigraphy), SPECT examination (imaging of iodine-benzamide-dopamine-receptor-bond), or transcranial sonography.

MRI is primarily used to exclude other possible reversible causes of Parkinsonism since no specific abnormalities are detected in the MRI of Parkinson's disease.

DaTSCAN™ reveals a decrease in dopamine transporters in Parkinson's disease.

SPECT can be used to distinguish multi-system atrophy (MSA), which represents atypical Parkinsonism. In the case of Parkinson's disease, the dopamine-receptor bond is not affected basically, whereas it is decreased in MSA.

Transcranial sonography provides evidence of hyperechogenic substantia nigra in the majority of patients suffering from Parkinson's disease.

Clinical Assessment Scales of Parkinson's Disease

In addition to the Unified Parkinson's Disease Rating Scale (UPDRS) mentioned above, the **Hoehn and Yahr scale** can also be used, which is used to classify Parkinson's disease into stages 0–5, based on existing symptoms.

| Stage | Symptoms |
|------------|---|
| 0 | No clinical symptoms |
| I | Unilateral symptoms; no or only slight impairments |
| II | Slight, bilateral symptoms; no balance impairments |
| III | Slight to intermediate impairments with slight holding instability; sustained ability to work (depending on the respective job) |
| IV | Full manifestation of the disease including high-degree impairments; unassisted standing and walking |
| V | Patient wheelchair-dependent or bedridden, and dependent on others' assistance |

Differential Diagnosis of Parkinson's Disease

The most important differential diagnosis of Parkinson's disease includes **atypical** and **symptomatic** Parkinsonism and **essential tremors**.

The **atypical Parkinsonism** includes **multi-system atrophy (MSA)**, **progressive supranuclear** (PSP, synonym: Steele-Richardson-Olszewski syndrome), **corticobasal degeneration**, and **Hallervorden-Spatz' disease**.

Atypical Parkinsonism can be distinguished from Parkinson's disease on the basis of the clinical course or the clinical picture. Although the distribution of symptomatic and atypical Parkinsonism is often symmetric, the disease often progresses more quickly over a shorter period of time, and the reaction to **L-DOPA** is often weak.

Further, **irregular tremor**, **myokloni**, and disorders in the **oculomotor system** suggest atypical Parkinsonism.

As an important differential diagnosis of Parkinson's disease, **essential tremor** often occurs **symmetrically** and is mostly limited to the upper extremity. The onset of the disease often starts during youth or early adult age. Essential tremors occur sporadically and show **autosomal dominant inheritance**.

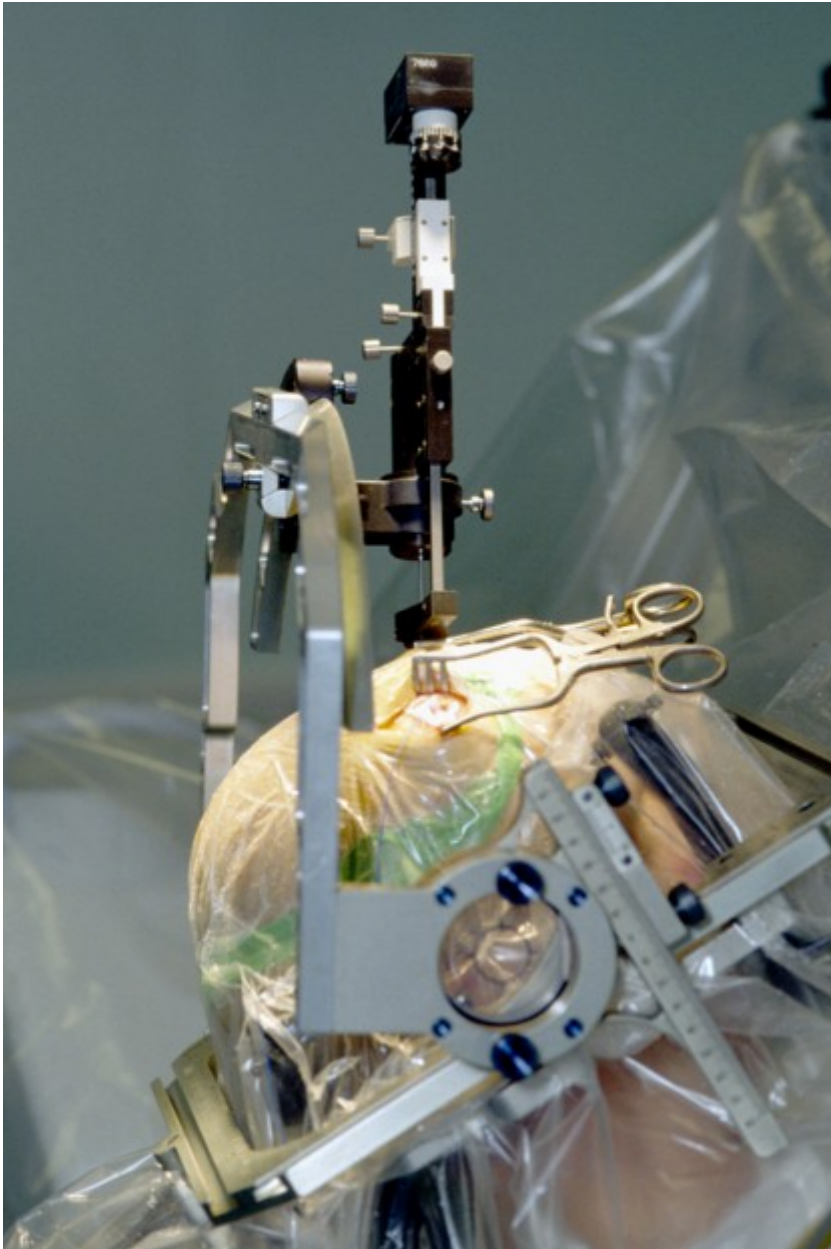
In the course of the disease, no further symptoms that are typical for Parkinsonism, such as rigor or akinesia appear. Further, no resting tremor is observed in Parkinson's disease, but a **postural tremor** is evident.

Characteristically, it improves after the consumption of alcohol and can be treated medically with **beta-blockers** (e.g., propranolol).

Therapy of Parkinson's Disease

Treatment of Parkinson's disease

Therapy of Parkinson's disease can roughly be divided into pharmacological and non-pharmacological types. Non-pharmacological treatment includes **physiotherapy**, speech therapy, and surgical interventions.



[Image](#): Parkinson Surgery. By Thomasbg, [License](#): CC BY-SA 3.0

Surgical interventions for Parkinson's disease include **deep brain stimulation** via implantation of electrodes, which stimulate certain areas of the brain, especially the **nucleus subthalamicus**. Surgical measures should only be considered if pharmacological therapy does not significantly improve the symptoms.

Drug therapy for Parkinson's disease is based on the administration of different doses depending on the patient's reaction. Medications include **anticholinergics**, for e.g., biperiden, **L-DOPA**, **NMDA-antagonists**, or **COMT-inhibitors** (catechol-o-methyltransferase inhibitors).

Overall, drug therapy aims to balance a relatively high level of **acetylcholine** compared with reduced amounts of **dopamine**.

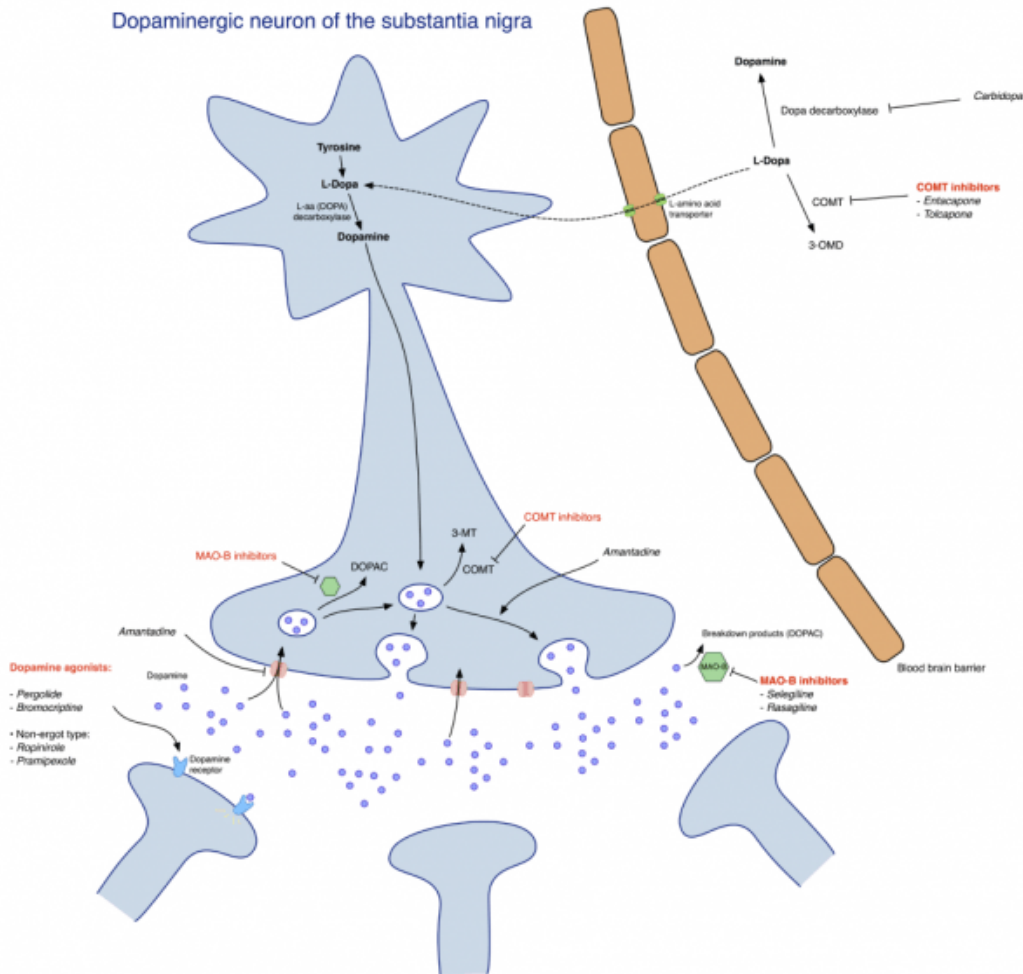


Image: Pharmacological treatment of Parkinson's disease. By Luigi Albert Maria, License: CC BY-SA 3.0

The timing of therapy initiation depends on the biological age of the patient. At an age of **< 70 years**, therapy should be initiated with **dopamine agonists**. In patients aged **> 70 years**, the application of **L-DOPA** is recommended by the 2012 guidelines for Parkinson's disease of the German Society for Neurology.

Overall, the respective therapy regimen is tailored to each individual patient depending on the dominant symptoms.

Anticholinergics such as **biperiden** are mainly used for patients manifesting **vegetative symptoms** and **tremors**. Anticholinergic therapies are contraindicated for patients diagnosed with prostate hyperplasia or glaucoma.

The dosage of **L-DOPA** intensifies symptoms such as **akinesia** and **rigor**. Long-term administration of L-DOPA has a positive effect on the tremor. To avoid peripheral side effects of dopamine such as nausea or a decline in blood pressure, the simultaneous application of a **dopa-decarboxylase inhibitor** (e.g., **benserazide**, carbidopa) is recommended.

In the periphery, carbidopa inhibits the conversion of L-DOPA to dopamine, whereas the conversion in the CNS is not affected since the dopa-decarboxylase inhibitor cannot permeate the blood-brain barrier.

Long-term administration of L-DOPA over several years can lead to loss of its pharmacological effectiveness in as short as 2–3 hours after ingestion (**end of dose akinesia**). Further, the so-called **on-off phenomenon** can occur, suggesting severe fluctuation of symptoms during the course of the day.

Single doses, which are frequently administered and spread out over the course of the day or the application of depot or **controlled-release preparations** should be administered if these effects occur. Additionally, **duodenal infusions** via a percutaneous tube are recommended.

N.B. L-DOPA is recommended for patients > 70 years due to the effects of long-term therapy with L-DOPA.

In patients < 70 years, monotherapy with dopamine agonists is recommended. For example, **pramipexole** or **ropinirole** monotherapies, which are **non-ergot preparations** are preferred to **ergot preparations** since the latter can lead to side effects such as fibrosis of the cardiac valves.

Examples of ergot preparations include **bromocriptine, cabergoline, lisuride, or pergolide**.

N.B. Due to their side effects, ergoline dopamine agonists are not considered as first-line treatment.

Monoaminoxidase-B inhibitors inhibit the further degradation of dopamine, which is thereby available over a longer period of time. Thus, either the dose of L-DOPA can be decreased in combination with a decarboxylase inhibitor or a lower level of symptom fluctuation can be achieved.

The effect of the group of **catechol-o-methyltransferase inhibitors** (e.g., **entacapone, tolcapone**) also depends on the inhibition of dopamine degradation.

Prognosis of Parkinson's Disease

Of the three types of Parkinson's disease, the tremor-dominant type is associated with the best prognosis, showing the most therapeutic efficacy.

Successful therapy for Parkinson's disease results in life expectancy almost equivalent to that of the normal population. On average, care dependency sets in 20 years after the onset of the disease.

References

Burn, D. J. (2009). Dementia in Parkinson's disease. *Non-Motor Symptoms of Parkinson's Disease*, 121-134. doi:10.1093/med/9780199237234.003.0010

Gaig, C., Santamaria, J., & Compta, Y. (2014). Non-motor symptoms in the early motor stages of Parkinson's disease. *Non-motor Symptoms of Parkinson's Disease*, 24-43. doi:10.1093/med/9780199684243.003.0003

Meara, J., & Koller, W. C. (2000). *Parkinson's disease and parkinsonism in the elderly*. Cambridge, U.K: Cambridge University Press.

Stephani, C. (2011). Cognitive and Psychiatric Aspects of Parkinson's Disease. *Symptoms of Parkinson's Disease*. doi:10.5772/21171

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