# Cerebral ischemia

**Cerebral ischemia** is the most common type of stroke. It has an incidence of **180 cases/100,000 population per year** and accounts for **85%** of strokes[1].

### Zona penumbra:

### Zona penumbra (Heart):

### Amaurosis fugax:

## Etiology

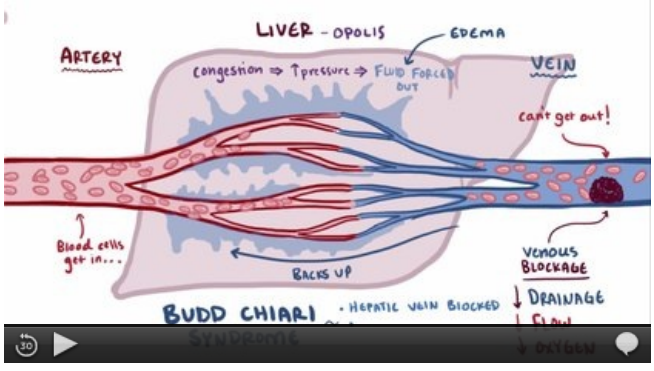
Cerebral ischaemia results from inadequate blood supply. Normal cerebral perfusion is **50-60 ml/100 g** of tissue/min. When it drops below **20 ml/100 g/min** - **hypoperfusion** - hypoxic tissue, the so-called ischemic penumbra ('*zona penumbra*), is reversible. Decrease below **10 ml/100 g/min.** - **ischemia** - leads to failure of regulatory mechanisms and encephalomalacia occurs. Obliteration of cerebral vessels is caused by thrombosis or embolism.

- **Thrombosis** is caused by atherosclerosis of the cerebral arteries and can occur at:
  - large arteries - **macroangiopathic etiology** - the feeder cerebral arteries (arteries of the neck) and the main cerebral arteries (arteries of the Willis circuit and the first few branches.
  - small arteries - **microangiopathic etiology** in **small-vessel disease** - terminal arteries branch the cerebral supply, leading to **lacunar icts**, often with significant wall damage in metabolic syndrome, diabetes mellitus or hypertension.
- **Embolism** is caused by the rupture of a thrombus and its entrapment in the cerebral arteries. The source of embolization may be:
  - at the atherosclerotic plaque of a large artery - **macroangiopathic etiology** - thrombus is carried into a more distal vessel,
  - in the heart - **cardioembolization etiology** - most often in atrial fibrillation from the left atrial appendage, also in myocardial infarction from the akinetic wall.
  - in veins in deep vein thrombosis - **paradoxical embolization** - most commonly via the foramen ovale patens, less commonly in pulmonary arteriovenous malformation.
  - from an unknown source - **embolic stroke of undetermined source** (ESUS), sometimes referred to as **cryptogenic**.
- Other causes may be **dissection** of the aorta, dissection of the carotid artery or dissection of the a. vertebralis.
- There are other, **other**, less rare causes:
  - inflammation of blood vessels - vasculitis,
  - hypercoagulation - thrombophilic conditions,
  - sickle cell anemia
  - genetic causes (CADASIL, Fabry disease, MELAS, etc.)

Classification systems are used to clinically classify the etiology of ischemic stroke in a particular patient. The **ASCOD** classification system is phenotypic and describes 5 etiologies simultaneously: A - **a** therosclerosis, S - **s** mall-vessel disease, C - **c** ardiac pathology, O - **o** ther, D - **d** issection[2]. For each aetiology, it gives a numerical indication of the probability with which it contributes to the stroke, e.g. A1-S3-C1-O3-D3. In contrast, the **SSS-TOAST** classification system is causative and attempts to select one specific most likely etiology from similar categories (large artery atherosclerosis, small artery disease, cardioembolization, cryptogenic, other) and omits other etiologies[3]. The new version of the SSS-TOAST classification, in which the most likely cause of cerebral ischemia is selected by a computer program based on the questions answered on each examination, is called the Causative Classification System (CCS)[4].

## Transient ischaemic attack

If a brief transient ischaemia of brain tissue develops that does not lead to a permanent infarction of brain tissue, the condition is referred to as **transient ischaemic attack** (**TIA**)[5].



Video - generally about ischemia

> Sometimes different time points are used to classify TIA (e.g. symptoms less than 24 hours), but detailed imaging studies show that even with a short duration of symptoms, a cerebral infarction can develop[5]. It is therefore appropriate to use this tissue definition rather than an arbitrary time point by which symptoms must resolve. In the past, the term RIND - reversible ischaemic neurological deficit - was still distinguished for TIAs lasting more than 24 hours, but this has been completely abandoned

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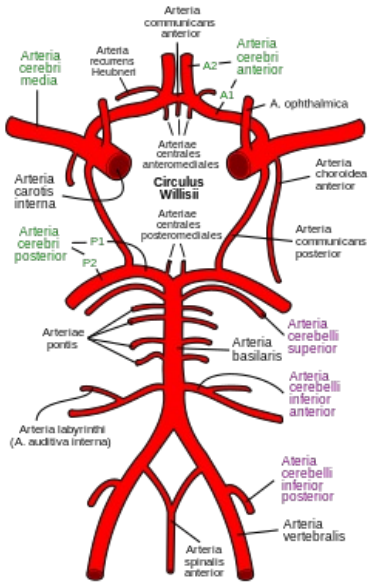
If it is a TIA with symptoms from the retina (basin of the arteria ophtalmica), the condition is referred to as **amaurosis fugax**. **Transient ischaemic attack is one of the ischaemic strokes**, the term only refers to the resolution of clinical symptoms, but the condition has the same risk of recurrent ischaemic stroke as completed cerebral ischaemia itself, so the same retrospective investigation of the aetiology and initiation of secondary prevention is in order. The **early risk** of recurrent cerebral ischemia is estimated by the ABCD2 score or ABCD3-I score[6].

## Clinical picture

Sudden development of focal neurological symptoms of central origin, manifested according to the territory of the affected cerebral artery (weakness to paralysis and/or impaired sensation of half of the body, impaired symbolic functions, deviation of the head and eyeballs, visual paresis, visual field disturbances, diplopia, sudden onset of dizziness or sudden fall in association with previous central neurological symptoms, amaurosis, incoordination, event. other symptoms depending on the location of the lesion.)

Lacunar infarcts are manifested mainly by isolated motor and/or sensory deficits, atactic hemiparesis, dysarthria, "clumsy hand". More rarely, ischaemic ictus manifests with headache, initial vomiting, impaired consciousness, and even more rarely, the initial symptom is epileptic paroxysm.

- a. cerebri media - contralateral motor disturbances (mainly acral and mimic muscles);
  - lesions of the dominant hemisphere - impairment of symbolic functions;
  - FEF (frontal eye field) lesion - looking at the lesion;
- a. cerebri anterior - also contralateral paresis, but mainly DK (homunculus has legs between hemispheres);
  - is rare, think more of a tumor;
- a. ophthalmica - sudden blurring to loss of vision (*amaurosis*) of the visual field of the affected eye;
- a. cerebri posterior - visual disturbances (mainly contralateral homonymous hemianopsia), agnosia, alexia;
- a. cerebelli post. inf. (PICA) - *Wallenberg syndrome'* - homolaterally - neocerebellar syndrome, Horner syndrome, trigeminal nerve involvement.




The National Institute of Health Stroke Scale (NIHSS) assesses the severity of symptoms. It was originally developed for use in clinical trials [7], however, it is currently the guiding principle for therapy [8][9].

# Diagnosis

The **sudden onset of a focal neurological deficit** is essential in the diagnosis. In further diagnosis (differentiation of different types of stroke), imaging - CT or MRI scanning - is subsequently used.

- **Native CT** distinguishes ischemia from hemorrhage. *Hyperacute ischemia is not visible on native CT*. After a few hours, a focus of mild hypodense develops. After about a week, it may be overlaid by oedema, so that the lesion is again not visible (*fogging effect*), and a markedly hypodense lesion (density corresponding to the liquor) develops.
- **Perfusion CT** shows blood flow through the brain using a contrast agent. The flow (perfusion) differentiates between the **ischemic core** area (irreversible malacia) and the **penumbra** area, a hypoperfused area where tissue death has not yet occurred and which can potentially be saved by recanalization therapy.
- **CT angiography** - a contrast agent is injected intravascularly into the patient, which allows us to visualize the arterial occlusion and assess the vasculature.
- **Magnetic resonance imaging** can very well image hyperacute ischemia (effusion on diffusion-weighted imaging without foci on FLAIR images) and thus evaluate tissue that can be salvaged by recanalization therapy. The disadvantages are less availability, high cost and longer time for examination.

> For **MRI** examinations in the acute setting, it is necessary to select sequences in a targeted manner so that the examination provides sufficient information to decide on the therapeutic approach, but in the shortest time to avoid delays. The so-called *stroke protocol* takes 6 minutes and only a few sequences are used - diffusion weighting (DWI), FLAIR, gradient recalled echo (GRE), MR contrast angiography, dynamic susceptibility contrast perfusion (DSC) MRI [10].

## Diagnosis of etiology

Investigation of the aetiology can be divided into [11]:

- a basic panel of tests that are appropriate for each patient to evaluate the various possibilities of etiology,
- a further advanced panel of tests that indicate a targeted approach when the basic tests are negative and
- a detailed panel of investigations that is indicated in younger patients when the advanced panel is negative.

Examination sequence by [11]

| Examination target | Basic panel | Advanced panel | Detailed panel |
|---|---|---|---|
| **Cardiogenic embolization** | TTE, TEE, ECG, ECG monitoring (ICU bed, telemetry), troponin I, NT-proBNP | TCD of right-sided shunt, Holter ECG monitoring (24 hours, 7 days, 3 weeks, event-loop), CT-angiography of the chest | contrast-enhanced cardiac MR, implantable monitor |
| **Macroangiopathy** | duplex ultrasonography of carotid arteries, TCCS, CT-angiography | MR-angiography of cerebral arteries | DSA of cerebral arteries |
| **Microangiopathy** and brain parenchyma | brain CT, brain MRI | brain contrast MRI, immunological screening, liquidology | brain biopsy |
| **Prothrombotic conditions** | APTT, PT, D-dimer | protein S, protein C, factor VIII, APC resistance, homocysteine, factor II, factor V Leiden, lupus anticoagulans | lupus anticoagulans recurrence |
| **Oncoscreening** | chest scan | abdominal sonography, chest and abdominal CT | whole-body PET |
| **General vascular risk** | total cholesterol, triglycerides, HDL, LDL, blood pressure monitoring, glycaemic profile, glycated haemoglobin, renal tests, liver tests | apolipoprotein B, lipoprotein A, genetics of familial hypercholesterolaemia | targeted genetic and metabolic testing (CADASIL, Fabry, MELAS) |

# Therapy

## Acute therapy - recanalization therapy

**Recanalization procedures** include **intravenous thrombolysis** and **mechanical thrombectomy**, as well as possibly less commonly **carotid stenting** or **carotid endarterectomy**. Rarely used methods (outside the guidelines) include, for example, sonothrombolysis. Treatment of cerebral ischaemia depending on the time elapsed since its onset:

- **Standard therapeutic interval** for administration of **intravenous thrombolysis** is **4.5** hours from onset of symptoms.[12]. Jedná se o podání alteplázy.
- **Standard therapeutic interval** for **mechanical thrombectomy** is **6** hours from the onset of first symptoms[13].

Standard therapeutic intervals **can** be extended to longer periods of time in some cases (selected patient groups, favourable findings on multimodal imaging according to the DAWN and DEFUSE-3 studies), in some cases **up to 24 hours**[14]. It is therefore advisable to consult an ictal centre immediately in patients with stroke within 24 hours of the onset of symptoms.

## Supportive therapy

- ensuring cerebral perfusion (blood pressure rises spontaneously - do not lower it in the acute phase);
- anti-edema therapy (mannitol, hypertonic sodium chloride, furosemide).

## Secondary prevention

Secondary prevention consists of preventing recurrence of the event in question and thus depends on the etiology. In the case of embolization etiology of ischemic stroke, consideration of anticoagulation therapy is appropriate. In atrial fibrillation, direct oral anticoagulants are the first choice. If anticoagulation is contraindicated, then left atrial appendage occlusion may be considered. If paradoxical embolization through the *foramen ovale patens* is involved, occlusion with an occluder is the method of choice. In the case of atherosclerotic aetiology, antiplatelet therapy is deployed. In small ischaemia (*minor stroke*), dual antiplatelet therapy is appropriate for 3 weeks to 3 months before continuing with monotherapy. Other procedures include carotid endarterectomy or stenting for carotid stenosis. It is always essential to simultaneously **influence cardiovascular risk factors** - smoking, hypertension, dyslipidemia, diabetes mellitus.

In the case of bleeding, it depends on whether the cause of bleeding persists and if there is a risk of recurrence. If the source of the bleeding can be surgically removed, either neurosurgery, stereotactic irradiation or monitoring the evolution of the pathology on surveillance imaging (*watchful-waiting*) is chosen. In most cases, the patient's experience of intracerebral haemorrhage contraindicates future anticoagulation, although the potential risk and potential benefit must always be weighed. Evaluation of microbleeds using hemosiderin-sensitive brain MRI sequences can sometimes help in this regard.

- **Surgical treatment** - carotid endarterectomy and extra-intracranial anastomosis (most commonly between a. temporalis superficialis and a. cerebri media);
  - indication endarterectomy - haemodynamically significant stenosis of the ACI in the neck, thereby making the artery patent;
    - in cases where carotid stenosis is the cause of ischemia;

    - indication of E-I anastomosis - in case of complete closure of the arteria carotis interna, the principle is to rapidly drive blood to where a complete infarction has not yet occurred;
        - in the current era of modern pharmacotherapy, E-I anastomoses are scarce.
- **Interventional radiology** - angioplasty.

## Summary video of cerebral ictus

## Links

### Related articles

- Cerebral ictus

### External links

- Template:Akutně

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