

## Focus on Medicine

# When the Brain is on the Line

**Prof. Anna Członkowska** from the 2nd Department of Neurology at the Institute of Psychiatry and Neurology, a corresponding member of the Polish Academy of Sciences, discusses the definition of a stroke, new ways to help post-stroke patients recover, and reasons why time is of the essence.

ACADEMIA: Every year, stroke affects 80,000 Poles. Of these, 24,000 die within a year and 32,000 are permanently disabled. It is the most frequently diagnosed syndrome in the group of cerebrovascular diseases. By 2025, the number of cases is expected to rise by 37% among men and by 38% among women. So, what is a stroke?

ANNA CZŁONKOWSKA: A stroke is typically defined as a sudden brain injury with a vascular cause. It usually occurs when a blood vessel is blocked and blood flow to the brain is disrupted. In around 15% of cases, it involves an interruption of blood flow that occurs when a blood vessel bursts and the blood leaks out to the brain. Both are accompanied by a relatively rapid development of neurological symptoms.

# Stroke patients relate that they have the biggest difficulty saying precisely when the symptoms became worrisome.

Unfortunately, the symptoms often develop subtly, for example a mild weakness in the arms and legs that patients usually ignore. Symptoms sometimes occur during sleep. The term stroke is used to refer to incidents when symptoms last for more than 24 hours. If they disappear within 24 hours, the incident classifies as an transient ischemic attack, rather than a stroke. Sometimes, however, symptoms resolve within 24 hours but radiological examinations reveal lesions that indicate ischemia, and this is also defined as a stroke. Usually, however, there are none. In the past, we had no ways to verify this. Today, we have computer tomography (CT) and magnetic resonance imaging (MRI), so we can examine patients more accurately.

#### What are the warning signs of a stroke?

Typically, these include weakness on one side of the body – one arm, one leg, one side of the face – as well

speech problems, or situations when you have trouble saying what you want to say or you don't understand what others are saying. Also, there may be vision problems, dizziness, and numbness on one side of the body.

#### What are the causes of stroke?

These often include atherosclerosis of the arteries that supply blood to the brain or the blood vessels in the brain. A clot that forms on atherosclerotic plaque blocks the vessel. Pieces of the clot or cholesterol may also break off from the plaque buildup and travel to further parts of the brain, causing a blocking of smaller vessels (an arterio-arterial embolism). Also, a blood vessel blockage may also be caused by an embolus from the heart: in patients with atrial fibrillation, an irregular heart rhythm leads to the formation of clots in the chambers of the heart; at some point, they may travel to the brain. Also, a stroke may be a result of chronic hypertension and the hardening of small vessels in the brain or an injury of an artery that supplies blood to the brain that leads to the rupture of the artery and the formation of a blood clot. Finally, it may be caused by the constriction of blood vessels as a result of heavy smoking or the use of intoxicating substances. And so, the causes of stroke do vary. A hemorrhagic stroke occurs when a blood vessel bursts, usually as a result of damage caused by long-term hypertension.

## How is this treated?

Patients should be treated immediately, in special stroke units, which are usually parts of neurology departments. Great progress in the treatment of stroke patients in Poland was made in the late 1990s, when the National Stroke Prevention and Treatment Program came into existence. It was followed by POLKARD, which included initiatives aimed at creating a network of stroke units. That ushered in a change in the way stroke patients were



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works in the fields of clinical neurology (stroke, multiple sclerosis, Wilson's disease), neurorehabilitation (the introduction of new methods that support rehabilitation), and neuroimmunology (the impact of inflammatory reaction on neurodegeneration). A member of the Presidium of the PAS Committee on Neurological Sciences and the Academy's delegate to the Medical Research Council and the European Science Foundation (since 2008), she has received the Gold Cross of Merit (2001) and the Officer's Cross of the Order of Polonia Restituta (2009).

ly people with a history of other diseases who died from complications - they would lie at home, confined to bed, or they were treated as "second-rate" patients, put somewhere in the corridors; they would develop pneumonia or urinary tract infections. Today, such patients are referred to stroke units where they immediately undergo neurological and general examinations - blood pressure and cardiac monitoring, diabetes and blood clotting tests, etc. - and treatment involves improving the patients' general condition. Also, precise brain imaging techniques are used to diagnose such patients (CT, MRI, vascular imaging) and rehabilitation starts quickly. This is the basis of the treatment. In a hemorrhagic stroke, if the rupture of a blood vessel is not caused by an anomaly that can be removed surgically. Treatments specific for ischemic stroke are aimed at removing whatever obstructs the blood flow. A medicine called tissue plasminogen activator, first registered 20 years ago, can be administered intravenously to dissolve blood clots, but we must be certain that this is an ischemic stroke. These days, this can be easily verified by a CT scan. Still, despite its proven efficacy, this medicine cannot be given to all patients. Its use in clinical practice requires careful preparation of the whole health-care system and also

of the potential patients themselves. It is believed that

around 20% of ischemic stroke patients should be treated

treated. Before those initiatives, these were usually elder-

by intravenous thrombolysis. Today, this figure stands at only 10% Poland-wide.

## Why is this percentage so low?

Because this medicine can only be administered within 4.5 hours, in very few cases up to six hours, from the onset of the first symptoms of stroke. Before administration, it is necessary to determine the time of onset of the stroke, examine the patient very carefully, run tests (most importantly for clotting disorders and elevated blood sugar levels), and as I said a CT scan. One in seven patients who receive this medicine achieves a complete recovery. The results depend greatly on timing. If the medicine is administered within one hour from the onset of symptoms, the results are a lot better than after two hours. Still, two hours are always better than four hours.

## That's a very narrow time window.

Unfortunately, that's true. The brain is very sensitive, quickly susceptible to irreversible damage. When brain tissues, including the blood vessels, are damaged, the administration of a medicine that affects blood clotting may cause bleeding in the brain. Neurons are especially sensitive to the shortage of oxygen, and with time they die – they can't be saved if the blood flow is restored too late. Late treatment brings no clinical improvements, but it does increase the risk of hemorrhage.



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Photo 1: The middle cerebral artery before and after the removal of blockage (from the collection of Asst. Prof. Adam Kobayashi, Institute of Psychiatry and Neurology)

## So this brings us back to patients' failure to recognize stroke symptoms, leading to delayed treatment.

Not only patients are to blame. Of course, a person who has small weakness of the arm or feels numbness in one hand often just massages the area, thinking the symptoms will go away, and doesn't go to the hospital. A person who has problem with speech is often alone at home and needs to call for help but can't tell anyone that something bad is happening. Even if someone does call an ambulance, the patient may not get to a hospital in time, despite the fact that strokes, just like myocardial infarctions, are a priority dispatch. In hospital, there may be more delays, caused by organizational issues. In an overcrowded emergency room, for example, more time will pass before someone approaches and diagnoses the patient, before this patient gets referred to the stroke unit, before a CT scan and lab tests are done. It is impossible to make up for this time. It is the human factor that is to blame. Generally, however, the situation in Poland is good, compared to the situation in Europe, even Western Europe. There are no limits on admission to stroke units, funding of health care is decent, and thrombolytic treatment is available to eligible patients. Ten percent is a good average. For that matter, there are units that successfully treat even 20% of cases. The situation is improving with each passing year.

## Last year saw the publication of the results of clinical trials for a new treatment for stroke patients.

Yes. In intravenous thrombolysis, if a large clot forms in a large vessel, it is difficult to dissolve it by pharmacological means. This method proves successful in 20–30% of cases. For years, studies were conducted to find methods for accessing such blockages similar to those used in cardiology: to access the artery through the drainage tube, see which vessel is blocked, and remove the clot mechanically. The first trials, carried out with the aid of various devices, showed high rates of complications. In other words, the stroke was worse that it would have been without the intervention. A breakthrough came

in late 2014, when the results of trials conducted in the Netherlands were published. Patients were divided into two groups: one underwent mechanical thrombectomy with the use of a specially designed device called stentriever, the other didn't receive this treatment. After three months, the patients who had received that treatment had a lower degree of disability, measured using the five-degree Rankin Scale, and there was no increase in the number of deaths. Those trials were followed by other studies conducted all over the world that confirmed the outcome of the Dutch trials. One in four patients who received thrombolytic treatment and then had the clot removed made a good recovery. That was possible thanks to better understanding of the mechanism of ischemia, the development of radiological technologies, the development of better devices for the removal of clots, and finally better-educated doctors who decide if patients qualify for the procedure and those who actually perform it.

## Is there a chance this method will be introduced in Poland?

That is not so simple. First of all, the time window remains the same as for thrombolysis alone. In this case, however, 4.5-6 hours is the period needed to additionally determine if a large artery (a carotid artery or the initial section of a cerebral artery) is indeed blocked. According to guidelines, every patient (with very few exceptions) should receive intravenous thrombolysis before the procedure. In addition, according to the current guidelines, they should have no pre-stroke disability. So all decisions must be made quickly to allow embolectomy to be started not later than 6 hours after stroke onset. Secondly, there are 160 stroke units in Poland and there is no point setting up mechanical thrombectomy rooms at each of them. For thrombolysis, the drug alone costs around 5,000 zlotys, the cost of a device for the removal of clots exceeds 10,000 zlotys, not to mention the costs of radiological equipment and human labor. While around 20% of patients with ischemic stroke are eligible for intravenous thrombolysis, only 5% up to a maximum 10% meet the eligibility criteria for embolectomy. For that reason, it is hard to expect that such procedures will be performed in every hospital where there is a stroke unit. In my opinion, all stroke units should diagnose patients, start thrombolytic treatment, and transport eligible patients to an Interventional Stroke Treatment Center, where teams prepared to perform thrombectomy should be on standby. No more than 15 such centers are needed in Poland (one for every 10 stroke units). I recently talked to a professor from Canada who performs a dozen such procedures every week and that's how things are organized there. Patients within a 100-200 km radius are transported by air to his center, where doctors work around the clock. Such patients receive intravenous thrombolytic therapy at their stroke units and the treatment continues during

#### STROKE TREATMENT METHODS

transportation. But there is also a third problem: who should make up such teams?

According to all European and American guidelines, they should consist of doctors who know the brain: able to diagnose a stroke, to assess the size of the injured area (if half of the brain becomes damaged, the procedure will not help), to determine when exactly the symptoms started, and so on. To make a long story short, such teams must specialize in neurology. In addition, every team must have a specialist who knows how to perform such a procedure - this may be a neurologist, a neuroradiologist, or a neurosurgeon who has received the relevant training. An anesthesiologist must be available at all times. A team of well-trained nurses is also needed. Such a team must work around the clock. even on holidays. So a lot still needs to be done. I know that Poland's National Health Fund (NFZ) is working on how to finance and organize these things.

## Treatment is one thing, but rehabilitation is also crucial for stroke patients.

Rehabilitation starts already at the stroke units, as soon as patients' general condition allows, and should be continued for a longer period. We have a shortage of centers able to take in patients immediately after they are discharged from stroke units and rehabilitate them. Patients often go back home and wait for rehabilitation, which lower the chances of improvement. Also the system of rehabilitation at home is poorly developed.

#### What does post-stroke rehabilitation exactly involve?

Generally speaking, the purpose is to restore the brain functions that were lost as a result of brain injury. A patient who suffers from arm paresis is taught not now to do everything with the other hand but how to restore the movements of the limb that was affected. Before such paresis or contracture becomes permanent, which means quite early on, endogenous plasticity is stimulated through relatively intensive rehabilitation. Practically one or two days after the stroke, when the patient is still in the stroke unit, we start physical and breathing exercises – passive exercises, limb movements, mobilization, sitting positions, and active movements depending on the patient's condition.

#### Such things were not done two or three decades ago.

When I started as a neurologist in this Institute, patients after ischemic stroke would lie flat for two or three weeks, even if they wanted to or could walk. Those after hemorrhagic stroke would be confined to bed for six weeks or even longer. That led to bedsores, urinary tract infections, pneumonia, and pulmonary embolism. Early mobilization protects patients from that. Assessing swallowing problems is likewise important, because patients who have difficulty swallowing often develop aspiration pneumonia. Feeding patients in supine position is conducive to that. Currently, we have special tests



to determine that patients can't swallow food. We can't feed such patients, because they could start choking, so we use nasogastric tubes. When swallowing difficulties persist, a gastrostomy is performed and fluids are administered through an IV. Those with urinary incontinence receive adult diapers to prevent catheter-associated urinary tract infection. When patients lie flat for a long time and don't move their legs, blood clots start forming. Then, when they start walking, the clots may travel to the lungs. Such pulmonary embolism caused by prolonged bedrest is less frequent these days. That's because the legs are quickly mobilized and such patients receive anticoagulants. Pneumatic compression devices are becoming increasingly popular - they inflate and release air, thus stimulating blood flow. Patients who have recovered from an acute stroke are transferred, or at least should be transferred, to the rehabilitation unit, where exercises are a lot more intensive. For example, patients with arm paresis learn how to pour water into a saucepan, how to place it on a stove, and how to use the toilet. Around 30-40% of patients have speech problems, so they require speech and language therapy. Some patients have memory, spatial vision, and planning problems, which means higher brain function, and that requires training as well. Post-stroke rehabilitation is an independent branch of medicine that covers not only movement disorders but also cognitive problems.

# Is it true that the brain teaches the body in the development stage, whereas the body teaches the brain after a stroke?

That works both ways. In the past, people believed that brain damage is irreversible, that new brain cells cannot form. Now we know they do. Aside from that, neighboring areas of the brain take over the functions of the areas that were damaged. A limb will not move unless it is steered. For that reason, the brain is always the most important teacher.

INTERVIEW BY KATARZYNA CZARNECKA

#### Photo 2:

Post-stroke rehabilitation using a computer system that instructs the patient to carry out exercises and monitors their performance