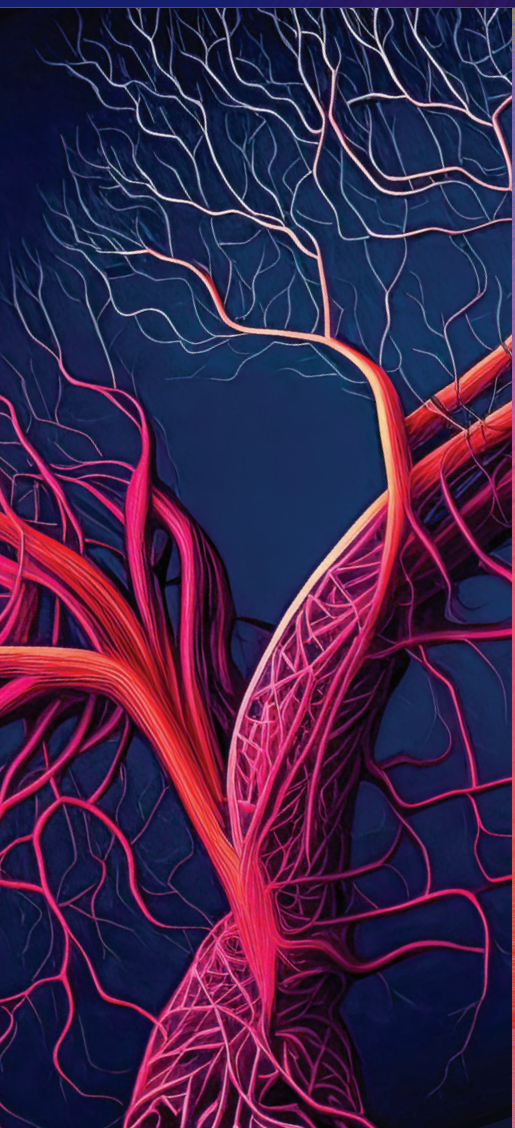
National Institute of Neurological Disorders and Stroke

Arteriovenous Malformations



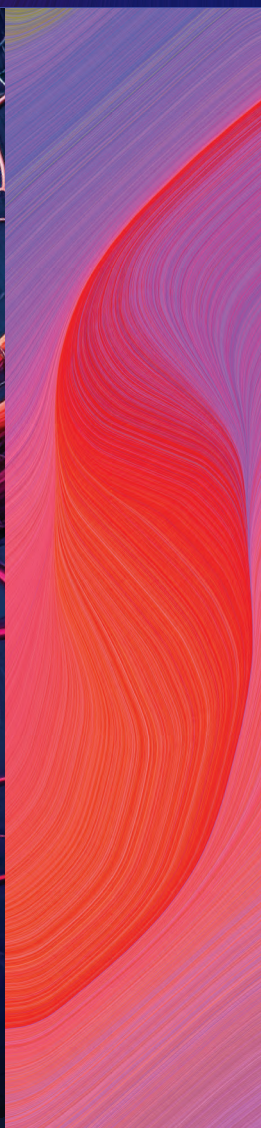
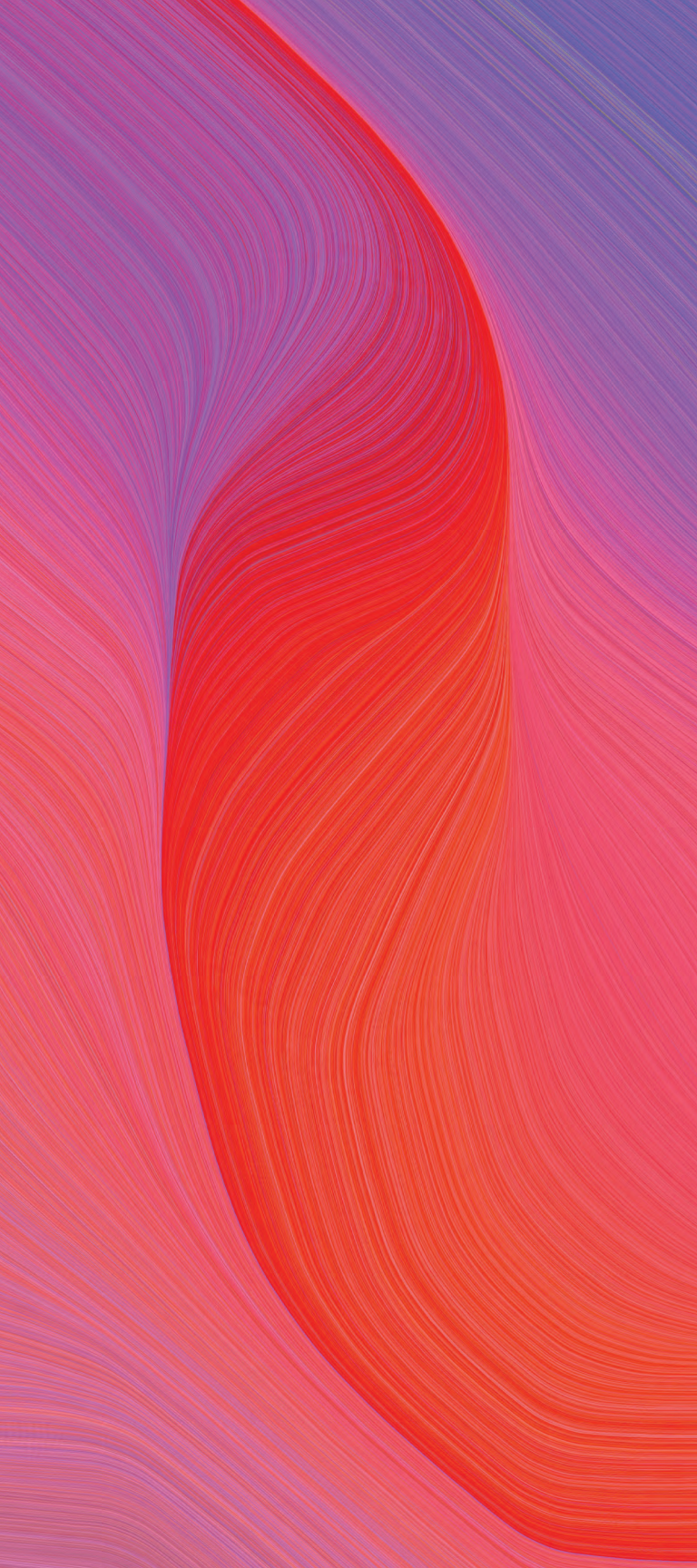


Table of Contents



What are arteriovenous malformations?

An arteriovenous malformation (AVM) is an abnormal tangle of blood vessels that causes problems with the connections between your arteries and veins. AVMs most often occur in the spinal cord and in the brain but can develop elsewhere in the body.

Normally, arteries carry oxygen-rich blood away from the heart to the body's cells, organs, and tissues and veins return blood with less oxygen to the lungs and heart. But in an AVM, the absence of capillaries—small blood vessels that connect arteries to veins and deliver oxygen to cells—allows blood to pass directly from arteries to veins, missing tissue that needs oxygenated blood. This can lead to tissue damage and the death of nerve cells and other cells. Over time, some AVMs get progressively larger as the amount of blood flow increases.

In most cases, people with AVMs in the brain or spinal cord experience few, if any, significant symptoms. In some cases, a weakened blood vessel may burst, spilling blood into the brain (hemorrhage) that can cause stroke and brain damage.

Most malformations tend to be discovered only incidentally, usually during treatment for an unrelated disorder or at autopsy.

Treatment depends on the type of AVM, its location, symptoms, and the individual's general health.

Symptoms of AVM

Symptoms can be mild or severe. They may include:

- **Seizures.** Seizures can be focal (meaning they involve a small part of the brain) or generalized (widespread), involving convulsions, a loss of control over movement, or a change in the level of consciousness.
- **Headache.** Headaches can vary greatly in frequency, duration, and intensity, sometimes becoming as severe as migraines. Headache pain can occur on either one side of the head or on both sides. Sometimes, headaches that are consistently felt in the same place indicate the location of an AVM.
- **Pain.** Most often, the location of the pain is not specific to the malformation and may affect most of the head. Attacks of sudden, severe back pain and pain in the lower limbs may be caused by a spinal AVM.

- **Visual problems.** AVMs located on the frontal lobe close to the optic nerve or on the occipital lobe (the rear portion of the cerebrum where images are processed) may cause a variety of vision problems, including a loss of part of the visual field, inability to control eye movement, or swelling in a part of the optic nerve.
- **Muscle weakness.** Muscle weakness or paralysis may occur in one part of the body. A spinal cord AVM can lead to degeneration of the nerve fibers within the spinal cord below the level of the AVM, causing widespread paralysis in parts of the body controlled by those nerve fibers.
- **Problems with speech.** An AVM in the brain or spinal cord can cause difficulty speaking or understanding language (aphasia).
- **Problems with movement.** AVMs in the brain stem and cerebellum can cause a loss of the ability to coordinate complex movements such as walking.
- **Abnormal sensations.** Some people with an AVM feel sensations such as numbness, tingling, or spontaneous pain.
- **Cognitive difficulties.** This may include trouble carrying out tasks that require planning, memory problems, confusion, hallucinations, or dementia.

- **Dizziness.** AVM damage to the cerebellum and the brain stem can result in dizziness.
- **Loss of consciousness.**
- **Developmental differences.** A person with AVMs may have subtle learning or behavioral differences during childhood or adolescence.

Symptoms caused by AVMs can appear at any age. Because the malformations tend to result from a slow buildup of neurological damage over time, they are most often noticed when people are in their 20s or older. If a person does not have symptoms by the time they reach their late 40s or early 50s, the AVMs tend to remain stable and are less likely to produce symptoms. Some pregnant women may experience a sudden onset or worsening of symptoms due to accompanying cardiovascular changes, especially increases in blood volume and blood pressure.

Risk of severe hemorrhage in AVM

The greatest potential danger posed by AVMs is hemorrhage. Most episodes of bleeding remain undetected at the time they occur because they are not severe enough to cause significant damage. But massive, even fatal, bleeding episodes do occur.

AVMs that cause serious hemorrhage share some features. For example, smaller AVMs have a greater likelihood of bleeding, and AVMs that have bled once are much more likely to bleed again, especially within the first year, than AVMs that have never bled. Impaired drainage by unusually narrow or deeply located veins can lead to a greater likelihood of serious hemorrhage. Bleeding in deeply located AVMs also usually causes more serious damage than bleeding on the surface of the brain or spinal cord. Pregnancy appears to increase the likelihood of clinically significant hemorrhage, mainly because of increases in blood pressure and blood volume.

Vein of Galen Malformation

Although most AVMs in the brain and spinal cord have very few, if any, significant symptoms, one particularly severe type of AVM causes symptoms to appear at, or very soon after, birth. Called a vein of Galen malformation (named after the major blood vessel involved), this lesion is located deep inside the brain. It is frequently associated with hydrocephalus (an accumulation of fluid within certain spaces in the brain, often with visible enlargement of the head), swollen veins visible on the scalp, seizures, failure to thrive, and congestive heart failure. Children born with this condition who survive past infancy often continue to have developmental challenges.

How do AVMs damage the brain and spinal cord?

AVMs can form anywhere in the brain or spinal cord—wherever arteries and veins exist. AVMs damage the brain or spinal cord by:

- Reducing the amount of oxygen reaching the tissues
- Causing bleeding (hemorrhage) into surrounding tissues
- Compressing or displacing parts of the brain or spinal cord.

AVMs affect oxygen delivery to the brain or spinal cord by altering normal patterns of blood flow through the arteries, veins, and capillaries. In AVMs, arteries pump blood directly into veins through a passageway called a fistula, rather than into the normal network of tiny vessels called capillaries that helps slow down the blood flow.
The uncontrolled blood flow into the veins is too rapid to allow oxygen and nutrients to be distributed to surrounding tissues, causing the cells that make up these tissues to become oxygen-depleted and begin to deteriorate, sometimes dying off completely.

This abnormally rapid rate of blood flow frequently causes blood pressure inside the vessels to rise to dangerously high levels. The arteries feeding blood into the AVM often become swollen and distorted; the veins that drain blood away from it often become too narrow (a condition called stenosis). Also, the walls of the involved arteries and veins are often very thin and weak. This can cause aneurysms (balloon-like bulges in blood vessel walls that are susceptible to bursting) to develop.

Bleeding into the brain, called intracranial hemorrhage, can result from the combination of high blood vessel internal pressure and vessel wall weakness. Such hemorrhages are often microscopic in size (called microbleeds) and cause limited damage and few significant symptoms. Generally, microbleeds do not have short-term consequences on brain function, but over time they can lead to an increased risk of dementia and cognitive impairment.

Massive hemorrhages, however, can occur if the physical stresses caused by extremely high blood pressure, rapid blood flow rates, and vessel wall weakness are great enough. A burst aneurysm can release a large volume of blood into the surrounding brain and cause a catastrophic stroke.

Large AVMs can press on surrounding brain or spinal cord structures and cause damage. They can range in size, depending on the number and size of the blood vessels making up the AVM. The largest may compress several inches of the spinal cord or distort the shape of an entire hemisphere of the brain. Massive AVMs also can constrict the flow of cerebrospinal fluid (a clear liquid that normally nourishes and protects the brain and spinal cord) by distorting or closing the passageways and open chambers (ventricles) inside the brain that allow this fluid to circulate freely. The buildup of cerebrospinal fluid can cause hydrocephalus and further increase the amount of pressure on fragile neurological structures, adding to the damage caused by the AVM itself.

Other vascular lesions that affect the central nervous system

Besides AVMs, four other main types of vascular lesion can arise anywhere in the brain or spinal cord. Unlike AVMs, they are not caused by high-velocity blood flow from arteries to veins. Instead, these low-flowing lesions involve only one type of blood vessel and do not pose the same risk of significant hemorrhage.

In general, low-flowing blood lesions tend to cause fewer troubling neurological symptoms and require less aggressive treatment than do AVMs.

- **Cavernous malformations** are formed from groups of tightly packed, abnormally thin-walled, small blood vessels that displace normal neurological tissue in the brain or spinal cord. The vessels are filled with slow-moving or stagnant blood that is usually clotted or in the process of decomposing. Like AVMs, cavernous malformations can range in size, depending on the number of blood vessels involved. Some people develop multiple lesions. Cavernous malformations sometimes leak blood into surrounding tissues because the walls of the blood vessels are very fragile. They can cause seizures in some people.

- **Capillary telangiectasias** are groups of abnormally swollen capillaries. They are usually not harmful and rarely cause extensive damage to surrounding brain or spinal cord tissues. Any isolated hemorrhages that occur are very small. However, in some inherited disorders in which people develop large numbers of these lesions, telangiectasias can lead to headaches or seizures.

- **Developmental venous anomalies**, previously known as venous malformations, consist of abnormally enlarged veins. They usually do not interfere with the function of the blood vessels and rarely hemorrhage. Most do not produce symptoms and remain undetected.

- **Dural arteriovenous fistulas** can occur in the membrane surrounding the brain and spinal cord. They are thought to arise from an injury to the membrane that creates a fistula between an artery and vein in the membrane. The veins of these arteriovenous fistulas drain blood under high pressure into nearby veins in the brain or spinal cord. The overloaded veins cause the brain or spinal cord to swell. Arteriovenous fistulas enlarge over time and can cause brain and spinal cord symptoms like AVMs.

Who is more likely to get AVMs?

It is unclear why AVMs form. Most often AVMs are congenital (the person is born with them), but they can appear shortly after birth or later in life. In some cases, they may be inherited, but it is more likely that other inherited conditions increase the risk of having an AVM.

Causes of vascular lesions

The cause of vascular problems like AVMs is not yet well understood. Scientists believe they most often result from issues that occur during development in the womb. During this development, new blood vessels continuously form and disappear as the body changes and grows. Problems with the chemicals in the body that stimulate blood vessel formation and growth may contribute to the formation of AVMs and other vascular lesions. Other issues in development may be linked to genetic mutations in some cases. A few types of vascular malformations are hereditary and thus have a genetic basis.

Evidence also suggests that at least some of these lesions are acquired later in life as a result of injury to the central nervous system.

Other vascular lesions are part of larger medical syndromes known to be hereditary. They include hereditary hemorrhagic telangiectasia, Sturge-Weber syndrome, and Klippel-Trenaunay syndrome.

How are AVMs diagnosed and treated?

Diagnosing AVMs

One of the more distinctive signs physicians use to diagnose an AVM is a sound called a bruit—a rhythmic, whooshing sound caused by unusually rapid blood flow through the arteries and veins of an AVM. A bruit can sometimes become a symptom of an AVM. When it is especially severe, it can compromise hearing, disturb sleep, or cause significant mental distress.

Imaging technologies used to discover AVMs include:

- **Cerebral angiography,** also called cerebral arteriography, provides the most accurate pictures of blood vessel structure in brain AVMs. A special water-soluble dye, called a contrast agent, is injected into an artery and highlights the structure of blood vessels so that they can be seen on X-rays.
- **Computed tomography (CT)** uses X-rays to create an image of the head, brain, or spinal cord. It is especially useful in revealing the presence of hemorrhage.
- **Magnetic resonance imaging (MRI)** uses magnetic fields and radio waves to create detailed images that can show subtle changes in neurological tissues.
- **Magnetic resonance angiography (MRA)** can record the pattern and speed of blood flow through vascular lesions and the flow of fluid throughout the brain and spinal cord.

- **Transcranial Doppler (TCD)** ultrasound can diagnose medium to large AVMs and detect the presence and extent of hemorrhage. It directs high-frequency sound waves through the skull at particular arteries. The resulting sound wave signals are interpreted by a computer to make an image of the speed of blood flow.

Treating AVMs

Whenever an AVM is detected, the individual should be carefully and consistently monitored for any signs that may indicate an increased risk of hemorrhage.

There are several options for treating AVMs. Although medication can often lessen general symptoms such as headache, back pain, and seizures caused by AVMs and other vascular lesions, the definitive treatment for AVMs is either surgery or focused radiation therapy. Developmental venous anomalies and capillary telangiectasias rarely require surgery. Cavernous malformations are usually well defined enough for surgical removal, but surgery on these lesions is less common than for AVMs because they do not pose the same risk of hemorrhage.

Because so many variables are involved in treating AVMs, doctors must assess the danger posed on a case-by-case basis. A hemorrhage from an untreated AVM can cause serious neurological problems or death. For that reason, many doctors recommend surgical intervention whenever an AVM appears to pose a higher-than-usual risk of significant bleeding. However, surgery on any part of the brain or spinal cord carries some risk of serious complications or death.

Surgical options for treating AVMs

Three surgical options are used to treat AVMs: conventional surgery, endovascular embolization, and radiosurgery. The choice of treatment depends largely on the size and location of an AVM. Endovascular embolization and radiosurgery are less invasive than conventional surgery and offer safer treatment options for some AVMs located deep inside the brain.

- **Conventional surgery** involves entering the brain or spinal cord and removing the central portion of the AVM, including the fistula, while causing as little damage as possible to surrounding neurological structures. This surgery is most appropriate when an AVM is located in a superficial portion of the brain or spinal cord and is relatively small in size. Conventional surgery is generally not used for AVMs located deep inside the brain because of the risk of damaging or destroying important brain tissue.

- **Endovascular embolization** involves guiding a catheter though an artery until the tip reaches the site of the AVM. The surgeon then injects a substance (such as fast-drying glue-like substances, fibered titanium coils, or tiny balloons) that will travel through blood vessels and create an artificial blood clot in the center of the AVM. Since embolization usually does not remove or obliterate the AVM, it is generally used as a complement to surgery or radiosurgery to reduce blood flow through the AVM and make surgery safer. Endovascular embolization may be effective alone in treating dural arteriovenous fistulas.

- **Radiosurgery** is an even less invasive therapeutic approach often used to treat small AVMs that haven't ruptured. A beam of highly focused radiation is aimed directly on the AVM and damages the walls of the blood vessels that make up the lesion. Over the course of the next several months, the vessels gradually degenerate and eventually close, leading to the resolution of the AVM.

Embolization frequently proves incomplete or temporary, although new embolization materials have led to improved results. Radiosurgery often has incomplete results as well, particularly when an AVM is large, and it poses the additional risk of radiation damage to surrounding normal tissues. Even when successful, complete closure of an AVM takes place over the course of many months following radiosurgery, during which the risk of hemorrhage is still present. However, both techniques can treat deeply situated AVMs that had previously been inaccessible. And in many people, staged embolization followed by conventional surgical removal or by radiosurgery is successful.
Some people with unruptured AVMs may consult with an AVM expert and decide that the risks of treatment outweigh the benefits and that it is better to postpone treatment.

What are the latest updates on AVMs?

The National Institute of Neurological Disorders and Stroke (NINDS), a part of NIH, conducts and supports research on disorders of the brain and spinal cord, including AVM.

NINDS-funded investigators working with the Brain Vascular Malformation Consortium (BVMC)—part of NIH's Rare Disease Clinical Research Network—recently completed a clinical trial readiness project on a specific type of cerebral cavernous malformation called cavernous angioma with symptomatic hemorrhage (CASH). The project addressed issues necessary for the design of future trials such as the ability to screen and enroll individuals with CASH at multiple study sites and to assess rates of re-bleeding and relevant features and measure outcomes.

In another BVMC effort, NINDS-supported researchers are developing biomarkers (signs that may indicate risk of a disease) for rare vascular diseases that involve the brain such as hereditary hemorrhagic telangiectasia, which results in the development of vascular lesions and AVMs. These biomarkers for disease progression may provide important data for future drug trials.

Other scientists funded by NINDS are using a novel approach to identify biomarkers for CASH that can help diagnose and predict hemorrhaging risk and be used in clinical trials.

Vessels in brain AVMs have abnormal wall structure and are prone to rupture, which can cause life-threatening bleeding in the brain and long-term disability. At the present time, it is not well understood how these vessels are formed. Vascular endothelial growth factor (VEGF) is a protein involved in the formation of new blood vessels during embryonic development and following injury. Excessive expression of VEGF may play a role in the cause and development of brain AVMs. NINDS-funded researchers are learning more about the formation of brain AVM vessels and studying an adeno-associated virus (which causes a slight immune response and is not known to cause disease) as a way to block the effects of VEGF and thus prevent progression of or reverse the production of abnormal blood vessels.

The NINDS-funded A Randomized trial of Unruptured Brain Arteriovenous Malformations (ARUBA) trial compared the outcomes of 226 patients with unruptured brain AVMs.

The patient group was divided into those receiving interventional treatment (surgery, endovascular embolization, and radiosurgery) and those receiving medical observation. The observation group had a lower risk of neurological injury over the study's 33-month follow-up period, although they still had a 1-3% risk of AVM rupture each year. While the study size was limited and the trial did not enroll as many participants as originally planned, results underscored a need to continue to improve the safety and effectiveness of AVM treatment.

In addition to NINDS, other NIH institutes and centers support research relevant to understanding, treating, and preventing AVM and vascular lesions. More information is available through NIH **RePORTER**, a searchable database of current and previously funded research, as well as research results and publications.

For research articles and summaries on AMVs, search **PubMed**, which contains citations from medical journals and other sites.

How can I or a loved one help improve care for people with AVMs?

Consider participating in a clinical trial so clinicians and scientists can learn more about AVMs and vascular lesions. Clinical research uses human study participants to help researchers learn more about a disorder and perhaps find better ways to safely detect, treat, or prevent disease.

All types of study participants are needed—those who are healthy or may have an illness or disease—of all different ages, sexes, races, and ethnicities to ensure that study results apply to as many people as possible, and that treatments will be safe and effective for everyone who will use them.

For information about participating in clinical research visit **NIH Clinical Research Trials and You**. Learn about clinical trials currently looking for people with AVMs at **Clinicaltrials.gov**, a database of past and current clinical studies.

Where can I find more information about AVMs?

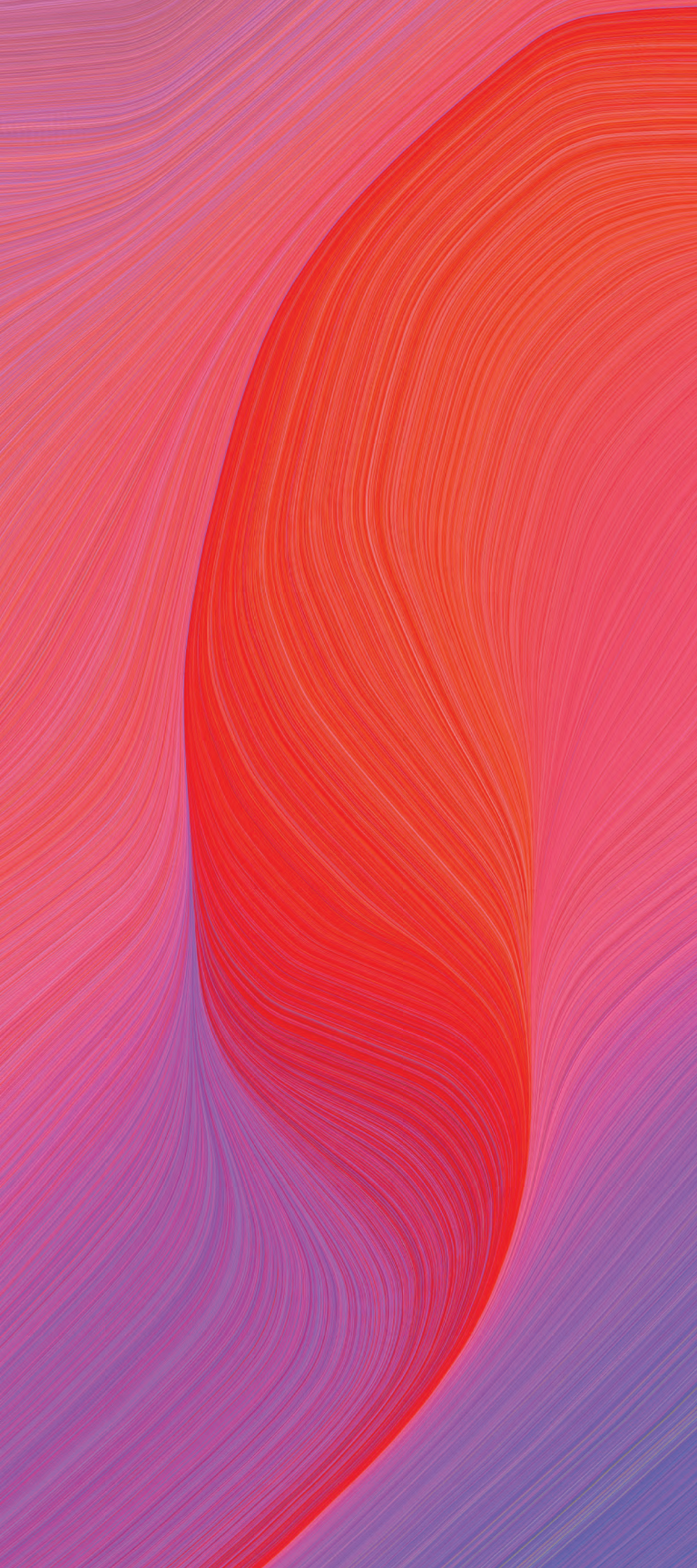
Information may be available from the following organizations and resources:

National Institute of Neurological Disorders and Stroke
800-352-9424

Brain Aneurysm Foundation
888-272-4602

National Library of Medicine
888-346-3656

National Organization for Rare Disorders (NORD)
800-999-667



Prepared by:

Office of Neuroscience Communications and Engagement

National Institute of Neurological Disorders and Stroke

National Institutes of Health

Department of Health and Human Services

Bethesda, Maryland 20892-2540

NIH Publication No. 23-NS-4854
November 2023

National Institute of Neurological Disorders and Stroke