

# A Review on Recurrent Ischemic Stroke

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**Abstract-** Stroke is a state of focal neurological deficit of an abrupt onset, presumably of vascular origin and it can be Ischemic (85%) or Haemorrhagic (15%). In haemorrhagic stroke mortality rates are high (50%) while in Ischemic strokes, mortality is less (20%) [1]. The knowledge of the risk factors for stroke in stroke survivors was also very low and the knowledge varied among the subjects depending on their level of education. Our findings strongly recommend that effective control of blood pressure, blood glucose and smoking may be important avenues for stroke prevention in this population. Stroke is a clinical syndrome consisting of rapidly developing clinical signs of focal or global disturbance of cerebral function that lasts more than 24 hours; and/or leads to death with no apparent cause other than a vascular -brain-origin. Stroke globally is the second leading cause of mortality; however, it is the third most common cause of mortality in low-income countries.

**Keywords-** stroke type, treatment, symptoms.

## I. INTRODUCTION

The knowledge of the risk factors for stroke in stroke survivors was also very low and the knowledge varied among the subjects depending on their level of education. Our findings strongly recommend that effective control of blood pressure, blood glucose and smoking may be important avenues for stroke prevention in this population. Stroke

Most CVA cases (up to 80%) are ischemic, with hemorrhages being responsible for the remaining 20%. Hemorrhagic strokes cause brain damage in two main ways: ischemia due to the pressure of adjacent structures, and direct neuronal injury from the hemorrhage. [Unnithan AKA, et. al. 2022 May ].

The disease by and large can be prevented by making simple Changes in the way people live their lives or simply by changing our lifestyle.

Sudden numbness or weakness in the face, arm, or leg, especially on one Side of the body . Sudden trouble walking, dizziness, loss of balance, or lack of coordination. [DijiKuriakose and et. al. October 2020]

An ideal stroke risk assessment tool that is simple, widely applicable and accepted, and takes Into account the effects of multiple risk factors does not exist. For patients with volvuli AF at high risk for stroke, long-term oral anticoagulant Therapy with warfarin at a target INR of 2 to 3 is recommended. [Abduljalil Hussain Almarzooq, et.al 2022] Stroke is the second leading cause of death and a major contributor to disability worldwide. The prevalence of stroke is highest in developing countries, with ischemic stroke being the most Common type. Considerable progress has been made in our understanding of the pathophysiology of Stroke and the underlying mechanisms leading to ischemic insult. Stroke therapy primarily focuses On restoring blood flow to the brain and treating stroke-induced neurological damage. Lack of Success in recent clinical trials has led to significant refinement of animal models, focus-driven study Design and use of new technologies in stroke research. [Robert Brown, M.D. et.al Nov 2019]

Improvements in pre-clinical and clinical care are likely to underpin successful stroke Treatment, recovery, rehabilitation and prevention. In this review, we focus on the pathophysiology of Stroke, major advances in the identification of therapeutic targets and recent trends in stroke research. [Shilpa Haldal, et. al. January 2018]

Stroke is a neurological disorder characterized by blockage of blood vessels. Clots form in the Brain and interrupt blood flow, clogging arteries and causing blood vessels to break, leading to bleeding . The reclassification of stroke as a neurological disorder has led to more Accurate documentation of data and statistical analysis, supporting improvements in acute healthcare and acquisition of research funding for stroke. [DijiKuriakose et. al. October 2020]

Due to this misclassification within the ICD, stroke patients and researchers did not benefit from government support or grant funding directed towards neurological disease. Rupture of the arteries leading to the brain during stroke results in the sudden death of brain cell Owing to a lack of oxygen. Stroke can also lead to depression and dementia. [Chandril Chugh ,et. al. 2019]

Under the previous ICD coding rationale, clinical data generated from stroke patients were included as part of the cardiovascular diseases chapter, greatly misrepresenting

the severity and specific disease burden of stroke. If symptoms last less than one or two hours, the stroke is a transient ischemic attack (TIA), also called a mini-stroke. The symptoms of a stroke can be permanent. Long-term Complications may include pneumonia and loss of bladder control. [Abduljalil Hussain Almarzooq et. al.-Dec. 2020]

An ischemic stroke is typically caused by blockage of a blood vessel, though there are also less common causes. Treatment to attempt recovery of lost function is called stroke rehabilitation, and ideally takes place in a stroke unit; however, these are not available in much of the world. Prevention includes decreasing risk factors, surgery to open up the arteries to the brain in those with problematic carotid narrowing, and warfarin in people with atrial fibrillation. [Robert Brown, M.D. et. al. Nov 2019]

Stroke patients should be admitted to a dedicated stroke service to determine stroke mechanism, manage risk factors, and initiate Preventive therapies. The purpose of this study is to evaluate our institution's experience with patients presenting with acute stroke symptoms during the early months of the COVID-19 pandemic. [Abduljalil Hussain Almarzooq, et. al. December 2020]

Stroke is classically characterized as a neurological deficit attributed to an acute focal injury of the central nervous system (CNS) by a vascular cause, including cerebral infarction, intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH), and is a major cause of disability and death worldwide. Despite its global impact, the term "stroke" is not consistently defined in clinical practice, in clinical research, or in assessments of the public health. Advances in basic science, neuropathology, and neuroimaging have improved the understanding of ischemia, infarction, and hemorrhage in the CNS. [Diji Kuriakose and et. al. October 2020]

Term ischemic stroke is used to describe a variety of conditions in which blood flow to part or all of the brain is reduced, resulting in tissue damage. Although in some cases this may be a chronic condition, most strokes occur acutely. [Abduljalil Hussain Almarzooq, et. al. Dec. 2020]

The goal of this review is to provide an overview of the underlying factors, such as the hemodynamic changes and molecular and cellular pathways, which are involved in stroke-related brain injury. It is estimated that the lifetime risk for stroke is between 8% and 10%. Vessel occlusions (ischemic Stroke) account for 85% of all strokes, while primary

Intracerebral bleeding (hemorrhagic stroke) accounts for the remainder. [Shilpa Haldal, et. al. Jun 2018]

Ischemia is defined as a reduction in blood flow sufficient to alter normal cellular function. Brain Tissue is exquisitely sensitive to ischemia, such that even Brief ischemic periods to neurons can initiate a complex sequence of events that ultimately may culminate in cellular death. Different brain regions have varying thresholds for ischemic cell damage, with white matter being more resilient than gray matter. Early restoration of blood flow remains the treatment of choice for limiting brain injury following stroke. [Abduljalil Hussain Almarzooq, et. al. December 2020]

Hence, a rapidly evolving area of emphasis in stroke research involves defining the molecular and cellular basis for the augmented tissue injury and inflammation associated with transient cerebral ischemia. Clinical evidence suggests that the majority of stroke patients exhibit a slow evolution of brain injury that occurs over a period of hours-to-days following the attack. [Drs Sacco and Kasner, et. al. 2013 Jul]

An ischemic stroke occurs when the blood supply to part of the brain is interrupted or reduced, preventing brain tissue from getting oxygen and nutrients. Brain cells begin to die in minutes. [Unnithan AKA, et. al. 2022 May 15].

A stroke is a medical emergency, and prompt treatment is crucial. Early action can reduce brain damage and other complications. [Shilpa Haldal, et. al. Jun 2018]

Several attempts to generate a neuroprotective drug that will reduce ischemia-associated destruction of neuronal tissue improving the general outcome after AIS have had dismal results. These drugs display a formidable benefit during the animal model phase of research but have been unable to reproduce this effect in human clinical trials. These interventions are aimed at treating stroke in its acute phases and preventing sequels that will result in permanent disability. The ideal treatment of AIS begets a multistep approach: necessary due to the fact that the pathophysiology of stroke is multi-mechanistic. This work will present the current status of drug therapy in AIS and analyze the direction in which the field is moving. The aim of this review is to guide the reader through a general panorama of interventional pharmacological treatment of AIS. [Unnithan AKA, et. al. 2022 May]

Stroke is defined by the World Health Organization as a clinical syndrome consisting of rapidly developing clinical signs of focal (or global in case of coma) disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin. 1

## Pathophysiology

More than 85% of strokes are ischemic with the Remainder being hemorrhagic . The Trial of ORG 10172 in the Acute Stroke Treatment (TOAST) etiologic classification system divides Ischemic strokes based on their etiology as Follows: large-vessel atherosclerosis, Cardioembolic source, small-vessel disease, Other determined causes, and cryptogenic . A recent analysis of an acute ischemic stroke Confirmed by diffusion-weighted imaging (DWI) in a large Asian cohort utilizing TOAST classification found large-artery atherosclerosis to be the most common stroke subtype with the middle cerebral artery (MCA) territory most frequently affected .[ShilpaHaldal, et. al. January 2018] Hemorrhagic stroke occurs when a blood vessel in the brain becomes weak and ruptures. The blood then leaks into other parts of the brain, damaging the surrounding tissue. Hemorrhagic stroke may be classified in one of two ways, depending upon the location of the bleed.The causes of an ischemic stroke may be more generally categorized as embolism and thrombosis, with thrombosis occurring more frequently. Thrombotic stroke occurs when a clot forms in a vessel and reduces blood flow to the brain from the location where the clot originates. In embolic stroke, the clot forms in an area apart from the brain, loosens, and travels until it reaches a blood vessel that is too narrow to allow it to pass. This occlusion impedes the flow of blood to the brain. [Shari N. Allen, et. al. January 2012]

Narrowing is commonly the result of atherosclerosis–the occurrence of fatty plaques lining the blood vessels. As the plaques grow in size, the blood vessel becomes narrowed and the blood flow to the area beyond is reduced. Damaged areas of an atherosclerotic plaque can cause a blood clot to form, which blocks the blood vessel – a thrombotic stroke. ( World organization academy )

The blood flow to the brain is managed by two internal carotids anteriorly and two vertebral arteries posteriorly (the circle of Willis). Ischemic stroke is caused by deficient blood and oxygen supply to the brain; hemorrhagic stroke is caused by bleeding or leaky blood vessels. [DijiKuriakoseet. al. October 2020]

The main mechanism behind ischemic stroke is the reduction Of blood flow delivered to the brain, which results in an insult To its tissues. Due to the complex brain blood vessels, usually, Ischemic strokes are focal. When the insult happens, the central region has almost no blood flow, and the area rapidly Dies within minutes. However, the surrounding tissues still Have their blood flow above the “death” threshold, but with below functional levels and such zone is named

“penumbra”.This penumbra has a very limited time, and cells usually die after a certain period of time. Thus, such a time window is the Main focus for clinicians to try and restore the blood flow in order to save such regions from permanent death .[Abduljalil Hussain Almarzooqet. al, December 2020]

## Type of stroke:

1. Ischemic stroke
2. Hemorrhagic stroke
3. Transient Ischemic Attack or Mini-Stroke
4. Brain stem stroke

### 1. Ischemic stroke:

This is the most common type of stroke, making up 87% of all cases. A blood clot prevents blood and oxygen from reaching an area of the brainTreatment starts with taking drugs that break down clots and prevent others from forming. A doctor may administer blood thinners such as aspirin or an injection of tissue plasminogen activator (TPA). Another option is angioplasty. This involves a surgeon inflating a small balloon inside a narrowed artery using a catheter. Afterward, they will insert a mesh tube, or a stent, into the opening. This prevents the artery from narrowing again. [Heidi Moawad, et. al., March , 2020]

## Symptoms :

Headache. A sudden, severe headache, which may be accompanied by vomiting, dizziness or altered consciousness, may indicate that you’re having a stroke.

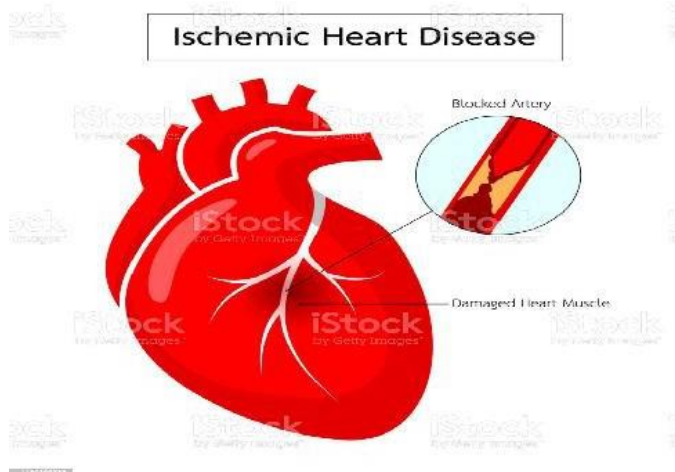
Problems seeing in one or both eyes. You may suddenly have blurred or blackened vision in one or both eyes, or you may see double. [Heidi Moawad, et. al. March 2020]

## Causes

There are two main causes of stroke: a blocked artery (ischemic stroke) or leaking or bursting of a blood vessel (hemorrhagic stroke). Some people may have only a temporary disruption of blood flow to the brain, known as a transient ischemic attack (TIA), that doesn’t cause lasting symptoms.Blocked or narrowed blood vessels are caused by fatty deposits that build up in blood vessels or by blood clots or other debris that travel through the bloodstream, most often from the heart, and lodge in the blood vessels in the brain.[Heidi Moawad, et. al. March , 2020]

## Treatment :

Rapid diagnosis is important for reducing brain damage and enabling the doctor to treat the stroke using a suitable method for the type.



- **Emergency IV medication:** Therapy with drugs that can break up a clot has to be given within 4.5 hours from when symptoms first started if given intravenously. The sooner these drugs are given, the better. Quick treatment not only improves your chances of survival but also may reduce complications.
- **Emergency endovascular procedures:** Doctors sometimes treat ischemic strokes directly inside the blocked blood vessel. Endovascular therapy has been shown to significantly improve outcomes and reduce long-term disability after ischemic stroke.

## 2. Hemorrhagic stroke:

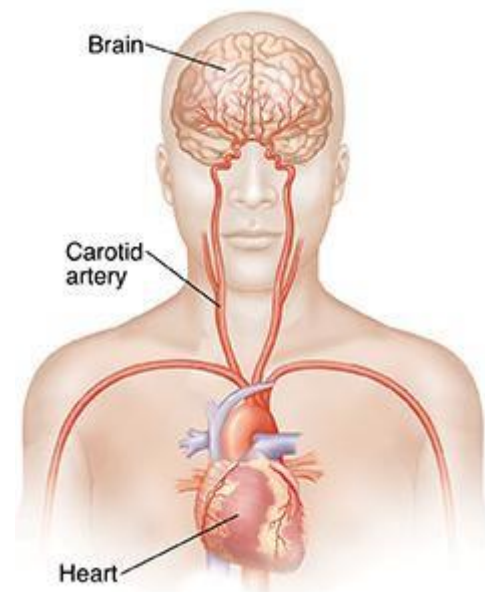
This occurs when a blood vessel ruptures. These are usually the result of aneurysms or arteriovenous malformations (AVMs). Treatment often begins with taking drugs that reduce pressure in the brain and control overall blood pressure, as well as preventing seizures and any sudden constrictions of blood vessels. [Heidi Moawad, et. al. March 2020]

### Symptoms:

Seizures, loss of consciousness, sensitivity to light, and a sudden, severe headache, also known as a thunderclap headache. A hemorrhagic stroke shares many of the same symptoms as other types of stroke. However, it may also cause other symptoms, such as vomiting, neck stiffness, and increased blood pressure. [ Heidi Moawad, et. al. March , 2020]

### Causes:

- Uncontrolled high blood pressure
- Overtreatment with blood thinners (anticoagulants)
- Bulges at weak spots in your blood vessel walls (aneurysms)
- Trauma (such as a car accident)
- Protein deposits in blood vessel walls that lead to weakness in the vessel wall (cerebral amyloid angiopathy)
- Ischemic stroke leading to hemorrhage



### Treatment

If the person usually takes blood thinners or other anti-clotting drugs, the doctor may give medication to counter their effects. A surgical procedure known as a craniotomy may be necessary if there is brain swelling. A surgeon will open a small section of the skull to help relieve pressure on the brain that is building up due to the bleeding. [ Heidi Moawad , et. al. March 2020]

## 3. Transient Ischemic Attack or Mini-Stroke:

Ischemic strokes also include something called a "mini-stroke" or a TIA (transient ischemic attack). This is a temporary blockage in blood flow to your brain. The symptoms usually last for just a few minutes or may go away in 24 hours. [BrunildaNazario, et. al. sept 2011]

The newer definition also added the limitation that there should be no evidence of acute brain tissue infarction, to recognize that acute injury to the brain can result from

ischemia of <24-h duration. However, several recent findings suggest that having a TIA correlates with deficits that can persist far beyond the resolution of clinical symptoms, even in the absence of imaging evidence of ischemic tissue injury. These deficits may be the result of subtle perturbations to brain structure and/or function that are not easily appreciated using the standard clinical and imaging tools that are currently employed in practice. [Leif Simmatis, et. al. March 2019]

### Symptoms :

All strokes are caused by reduction or loss of blood flow. The most common cause is a blood clot. This is same for a major stroke. Blood clots are caused by cholesterol buildup. As cholesterol blocks your arteries, it forms a blood clot. Eventually, the clot breaks free. The clot travels to your brain. That's where the TIA occurs. Managing your cholesterol levels through diet, exercise, and medicine lowers your risk.[Dr. PayalKohli ,et. al. November 2021]

### Treatment :

**Anticoagulants (blood thinners).** Blood thinners don't actually thin the blood. They decrease the ability of the blood to clot. This helps prevent clots from forming in the blood vessels. It also may prevent clots from becoming larger. Large clots can cause more serious problems.

**Antiplatelet medicine.** Antiplatelet medicines help prevent blood clots. They don't allow certain cells in the blood (called platelets) to clump together. This reduces the risk of blockages in the coronary arteries that can lead to heart attack and stroke. They are sometimes prescribed along with aspirin therapy.[American Academy of Family Physicians. et. al.2018]

### 4. Brain stem stroke:

This type happens in your brain stem. It can affect both sides of the body. If this happens you're left in a "locked in" state where you're unable to speak or move below the neck.[BrunildaNazario, et. al. August , 2020.]

Sitting just above the spinal cord, the brain stem controls your breathing, heartbeat, and blood pressure. It also controls your speech, swallowing, hearing, and eye movements.[Seunggu Han, et. al. 2018.]

The blockage of an artery in the brain stem can cause a serious condition to occur. The brain stem is the portion of the brain that sits at the base of the brain and leads to the spinal cord. It functions to relay messages for body

movements and some very pertinent functions of the body that keep us alive such as breathing, heartbeat, consciousness, swallowing and blood pressure. If an artery in the brain stem is blocked, then there may be a loss of oxygenated blood supply to the brain stem which causes death and damage to brain stem tissue which we call a brain stem stroke. [Adrienne Baron , et. al. Dec 2021]

### Symptoms :

The brain stem receives various signals from the brain and sends them to different parts of the body. Brain stem strokes disrupt these signals, which is why people experience physical symptomsTrusted Source, including numbness or weakness in the face, arms, or legs.[Sachin S. Kapur, et. al.August 2018.]

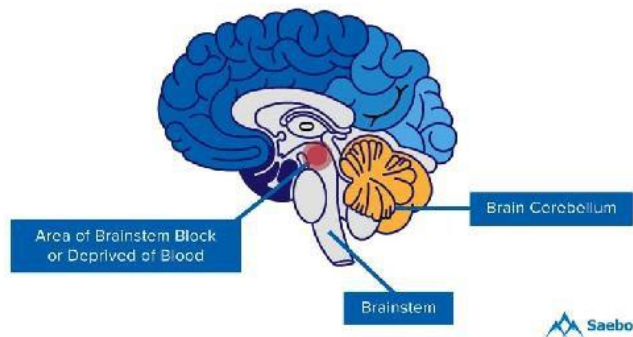
One of the characteristics that distinguishes a brainstem stroke from a stroke of the cerebral cortex is the effect on facial sensation. When a brainstem stroke produces a sensory deficit of the face, the face is numb on the same side as the stroke. This is in contrast to a stroke of the cerebral cortex, which causes a sensory deficit on the opposite side of the face. This is one of the clues that a neurologist uses to diagnose a brainstem stroke. [ Heidi Moawad, et. al. 2021, ]

Eye movement may become more difficult due to a brain stem stroke. The eyes may become stuck in one position. Or they may partially move, but not go through the full range of movement. They may also not have coordinated movement so that they move in the same direction together. There are a set of rare, but possible symptoms, too. You may experience hallucinations and lose your sense of taste and smell. There is also the possibility of experiencing locked-in syndrome which is when you can think and do everything except move your body. The eyes are the only part of the body that you can move with locked-in syndrome. [Adrienne Baron , et. al. Dec 2021]

### Treatment :

Brain stem strokes caused by a blood clot will require something to dissolve the blood clot. Medications such as antiplatelet drugs will dissolve the blood clots and keep others from forming. Anticoagulants are another option to help prevent blood clot formation and keep current blood clots from getting any bigger. An embolectomy is a surgery that can be done by inserting a catheter into the artery to remove the blood clot that is causing the blockage. The other possibility is making the opening of the artery wider by inserting a stent or balloon into the artery.[Adrienne Baron ,et. al. Dec 2021]

## Brainstem Stroke



### Epidemiology :

A large international study recently identified Hypertension, lack of exercise and elevated serum lipids as the most significant risk factors for an acute stroke . Attention to these and Other independent stroke predictors including Diabetes mellitus, obesity, smoking and Cardiovascular disease decreased stroke Incidence in the last 30 years . Adoption of the Mediterranean diet alone can reduce first stroke events by 40% . The use of statins and antihypertensive medications correlates with a 40% decrease rate of stroke in Medicare patients Older than the age of 65 . Recurrent stroke Rates dropped from 9% in the 1960s to 5% in the 2000s with a projected rate of under 3% in the Coming decade . Despite these trends, stroke remains the second leading cause of death Worldwide, the fifth leading cause of death in the US and a primary cause of long-term disability

(ShilpaHaldal, Jonathan Beary,

PremkumarNattanmai, Pravin George ,Christopher Newey ) Generally, strokes can be classified into two major categories, namely, ischaemic stroke and haemorrhagic stroke. Ischaemic stroke is caused by interruption of the blood supply to a part of the brain resulting in sudden loss of function, while haemorrhagic stroke is attributed to rupture of a blood vessel or an abnormal vascular structure [7]. Generally, ischaemic strokes account for about 80% of stroke cases while haemorrhagic stroke accounts for 20% but the actual proportions of stroke types depend on the population [7]. Data from the first INTERSTROKE study involving 22 countries showed that the proportions of ischaemic and haemorrhagic stroke in Africa were about 66% and 34%, respectively, compared to about 91% of ischaemic stroke and 9% of haemorrhagic stroke in high-income countries .[Eric S. Donkor , et. al. Nov 2018 ]

India has the highest burden of acute coronary syndrome (ACS) in the world and the three most common risk

factors for ACS are smoking (40%), high blood pressure (38%), and diabetes (30%).<sup>10</sup> Taking account of the above mentioned data and considering the fact that stroke shares common risk factors with ACS, we can safely assume that India has a very high incidence of stroke as well. [Antonio Ibarra, et. al.2018 Nov]

Lipohyalinosis, fibrinoid necrosis of the subendothelium, microaneurysms, and focal dilatations are seen in the arterioles. The microaneurysms are named as Charcot-Bouchard aneurysms. The incidence of CAA increases with age to the extent that around 50% of those aged more than 70years have CAA. Recurrent hemorrhages can occur due to CAA. [Unnithan AKA, et. al. 2021 Aug ]

Strokes that occur in small vessels(lacunar infarcts) are most commonly caused by chronic, uncontrolled hypertension resulting in the pathological entity of lipohyalinosis and arteriolosclerosis. These strokes occur in the basal ganglia, internal capsule, thalamus, and pons. Uncontrolled hypertension in these areas can also lead to hypertensive intracerebral hemorrhages (ICH). In the United States, stroke is the fifth leading cause of death, and 60% of strokes occur outside of hospitals. On average, every 40 seconds, a person suffers from a stroke, and every 4 minutes, there is one death caused by a stroke.Stroke is a leading cause of disability.[TadiP, et. al. 2022 Jan]

Stroke is the fifth most commonest cause of death if considered separately from other cardiovascular diseases. In the United States, an estimated 795,000 patients suffer from stroke annually, and the prevalence of stroke escalates with age. The lifetime risk of all types of stroke is higher in women; however, this is attributed to longer life expectancy. According to the Framingham Heart Study, stroke incidence is declining over time. However, the cohort was predominantly a white population .[ Channing Hui LaryssaPattet. al. 2019]

## II. CONCLUSION

Stroke is the second leading cause of death and contributor to disability worldwide and has significant economic costs. Thus, more effective therapeutic interventions and improved post-stroke management are global health priorities. The last 25 years of stroke research has brought considerable progress with respect to animal experimental models, therapeutic drugs, clinical trials and post-stroke rehabilitation studies, but large gaps of knowledge about stroke treatment remain. N conclusion, in the presented work, we sought to provider a brief overview of the current understanding of Inflammatory mechanisms involved during acute ischemic stroke and neuroprotective agents that can

curtail neuroinflammation and could have utility in the treatment of stroke. The strongest evidence for effective stroke to better outcomes associated with specialist, coordinated, multidisciplinary teams, both during early inpatient recovery and for resettlement at home.

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