

# A PRESSing Problem: Posterior Reversible Syndrome

By Sarah Bhanushali  
Art by Esther Moola

Imagine waking up one morning to discover that everything around you has turned into a blurry haze. Your world is now a chaotic mix of jumbled, indistinct objects and faces. Your brain experiences significant swelling, unleashing excruciating headaches one day and triggering intense seizures the following day. These symptoms render even the simplest tasks - driving, going to school, cooking your favorite meal - impossible. These are just a few elements that illustrate what it is like living with Posterior Reversible Encephalopathy Syndrome, also known as PRES. This neurological condition appears in both children and adults, but it tends to be more prevalent among middle-aged females usually ranging from 39 to 47 years [1]. PRES is characterized by white matter abnormalities and swelling in the back and top regions of the brain, namely the occipital and parietal lobes, and is diagnosed by medical imaging techniques [2].

## SYMPTOMS & DIAGNOSIS OF PRES

The brain is composed of 40% gray matter and 60% white matter, two essential tissues crucial for various cognitive and neurological functions [3]. Gray matter is made up of neuronal cell bodies, and white matter consists of nerve fibers called axons that project from the gray matter neuronal cell bodies to other parts of the brain [4]. The occipital and parietal regions are primarily responsible for visual perception, sensory processing, spatial navigation, and language skills [5]. When these regions are impacted as a result of PRES, vital neurological and cognitive functions are disrupted.

Individuals with PRES present with a variety of disorienting symptoms and challenges. Early indications of PRES include persistent headaches and altered consciousness, such as confusion and disorientation [6]. These early signs are often accompanied by visual disturbances and irregularities, such as temporary loss of vision, blurred eyesight, and hallucinations, causing difficulties for patients in clearly distinguishing their surroundings [7]. Additionally, individuals with PRES may endure neurological deficits, including muscle weakness and speech complications. Seizures, occurring in approximately 60-75% of cases, are a common and potentially serious symptom of PRES [8]. Seizures are the body's response to cerebral edema [9]. Recognizing these symptoms and early signs is crucial for timely diagnosis and intervention to reduce the risk of further neurological complications such as brain hemorrhaging or motor deficits [10].

Patients are diagnosed with PRES after exhibiting these symptoms that can be observed through medical imaging techniques such as magnetic resonance imaging (MRI). Since symptoms of PRES often overlap with other medical conditions, such as strokes, it can be challenging for physicians to identify the syndrome [11]. An MRI provides detailed images of the brain, revealing the presence of vasogenic edema located in the posterior regions of the brain, which is a high indication of PRES [12]. Moreover, a brain MRI distinguishes between gray and white matter, aiding physicians in identifying the impacted regions, particularly the white matter, to ensure an accurate diagnosis.

# The Mystery Behind Encephalopathy

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## UNDERLYING CAUSES & RISK FACTORS:

Although the precise mechanisms that cause PRES are unclear, its symptoms arise from a variety of underlying factors. PRES typically occurs in patients with high blood pressure (known as hypertension) and renal failure [13]. Intense fluctuations in blood pressure play a crucial role in triggering PRES. The brain is typically protected from extreme blood pressure fluctuations by an autoregulation system that regulates and maintains consistent blood flow in the central nervous system [14]. During systemic hypotension, or low blood pressure, cerebral arterioles dilate to sustain sufficient perfusion. Conversely, during systemic hypertension or elevated blood pressure, cerebral arterioles constrict. This means that the small blood vessels in the brain get narrower, restricting blood flow to the brain [14]. These variations challenge cerebral autoregulation, and exceeding the limits of stable blood flow ultimately leads to brain edema, or swelling, often resulting as PRES [6,13]. Acute hypertension is a primary contributor associated with PRES, observed in approximately 75% of patients [13]. However, PRES is not exclusively linked with acute hypertension. Additional risk factors of PRES involve several conditions including chronic kidney disease, autoimmune diseases, preeclampsia, sepsis, and connective tissue disorders [10].

PRES is also associated with medications used for cancer and organ transplant procedures. People who undergo transplantation are often prescribed multiple immunosuppressant drugs to prevent organ rejection. Common immunosuppressive agents prescribed to patients following an organ transplant are classified as calcineurin inhibitors, which block the activity of the calcineurin enzyme and prevent activation of T-cells, important cells in the body that help the immune system fight harmful bacteria and germs [15]. Although these factors decrease the possibility of developing organ rejection and minimize tumors, they increase the chances of developing PRES [16].

Moreover, immunosuppressants are drugs that prohibit the immune system from attacking healthy cells and tissues [17]. Angiogenesis is a physiological process of new blood vessel formation out of existing vessels, and anti-angiogenic drugs restrict the growth of tumors within their own blood vessels [18,19]. However, immunosuppressant and anti-angiogenic drugs used for cancer treatments and organ transplants can lead to neurotoxicity and disrupt the brain's protective shield, the blood-brain barrier. The blood-brain barrier's primary function is to remove harmful compounds from the brain and protect the brain from toxic substances [20]. It is composed of important structures and specialized cells

including endothelial cells, which line interior surfaces of all blood vessels and regulate blood clot formation and exchanges between the bloodstream and surrounding tissues [21,22]. This specialized system has a complex network of defenses, especially tight junctions that seal pathways between adjacent endothelial cells and act as barriers that restrict excess substances from freely passing between cells in the brain [23]. However, specific medications and drugs create openings between cells in the blood-brain barrier and cause protein disruption and neuroinflammation, making it easier for toxins to breach the blood-brain barrier [24,25]. This breach is called increased permeability, which enables more substances and toxins to pass through the barrier, infiltrating brain tissue. Increased permeability results in a type of brain swelling known as vasogenic cerebral edema, which leads to the development of symptoms associated with PRES and further neurological complications [26,27]. Additionally, hypertension (a common cause of PRES) weakens the blood-brain barrier and disrupts the surrounding blood vessels [28]. Elevated blood pressure can lead to the formation of blood clots in arteries that lead to the brain, causing endothelial dysfunction and a disruption of the blood-brain barrier, the accumulation of fluid in the brain, and deprives the brain of oxygen [29,30]. Ultimately, transplant and cancer patients face heightened risks of developing PRES due to the side effects associated with specific drugs targeting angiogenesis or suppressing the immune system.

## REVERSIBILITY & TREATMENTS

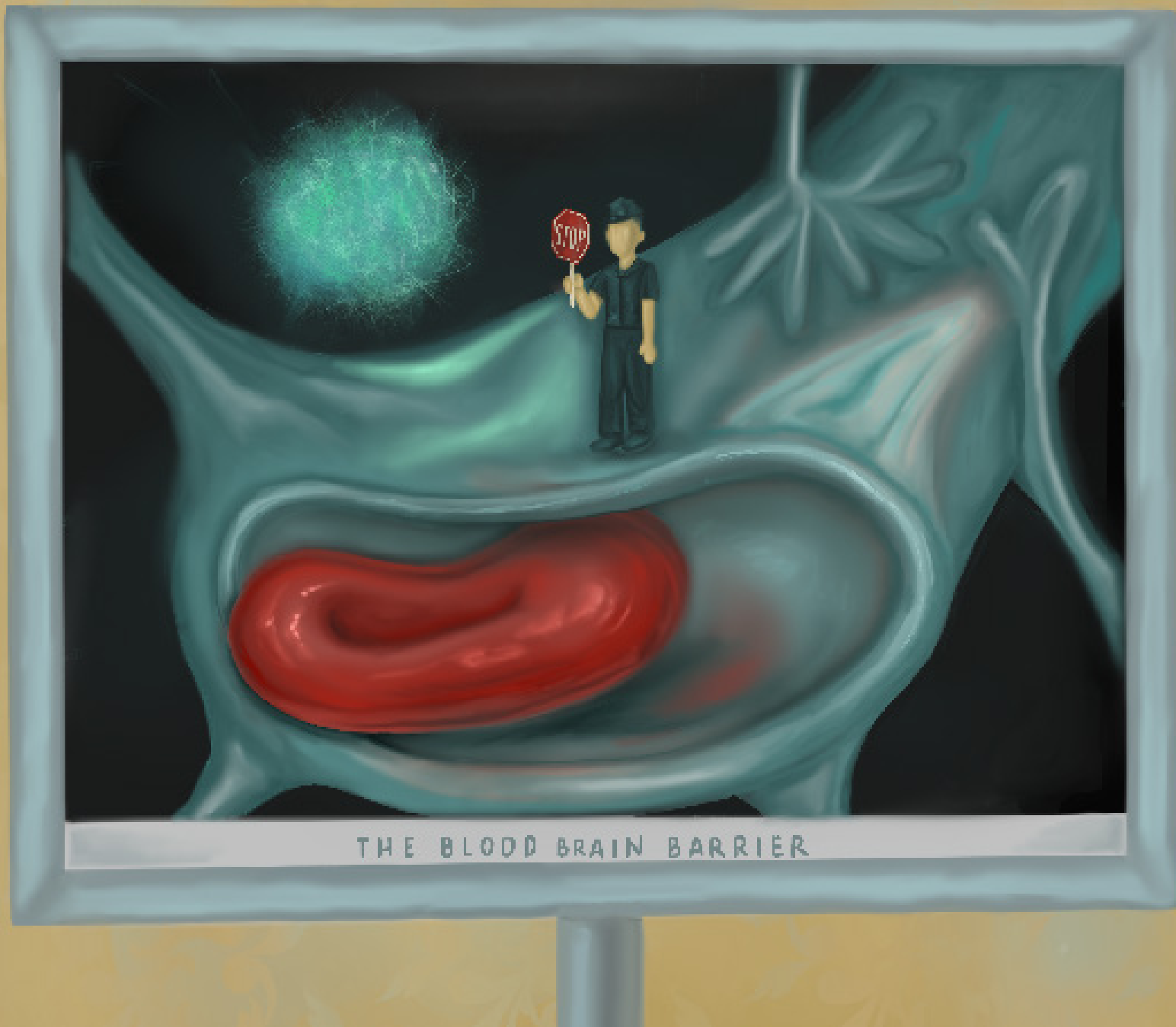
In contrast to other numerous neurological conditions, PRES has a unique and distinct capacity for reversal. Roughly 70-90% of PRES patients make a full recovery within a few days to weeks through recognition of the condition and adequate treatment [31]. However, severe cases of PRES can result in permanent neurological damage, injuries, or death due to increased levels of intracranial pressure [12]. The syndrome's reversible nature underscores the significance of early symptom recognition in order to regain a full recovery of neurological functions.

Although there is no specific treatment to cure PRES, the neurological condition can be treated by tackling the underlying cause, such as hypertension or neurotoxicity-inducing drugs in particular. By pinpointing the source of PRES, physicians are able to provide specific treatment tailored to the patient's symptoms. For example, a treatment plan for a patient diagnosed with PRES as a result of hypertension will focus on controlling and regulating their blood pressure levels. Due to the significant association between PRES and blood pressure, antihypertensive medications may be prescribed to regulate the patient's blood pressure. These

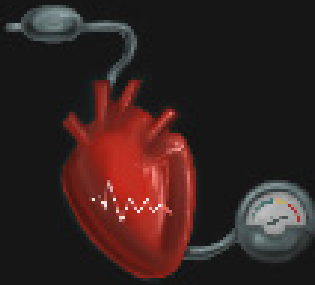
medications cause the body to eliminate excess water and salt, restrict nerve activity that can block blood vessels, and improve cognitive function, especially in older patients with PRES [32,33]. As treatments are provided, intracranial pressure monitoring may be used in severe cases of PRES to observe brain edema.

In addition to blood pressure stabilization, anti-convulsive therapy may also be prescribed to PRES patients who experience seizures [2]. Anticonvulsants, also known as anti-seizure medications, are specifically designed to prevent and control abnormal electrical activity that occurs in the brain [34]. Depending on the severity of a patient's seizures, they are typically prescribed a low dosage that is increased until the seizures are under control. Neurologists

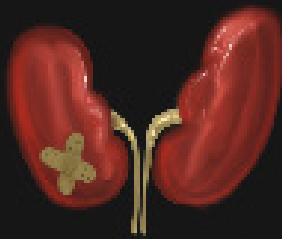
most commonly prescribe anticonvulsants such as topiramate, gabapentin, and levetiracetam. The main physiologic attribute of seizures involves neuronal hyperexcitability, which refers to a state when neurons become overly active and start firing signals rapidly [35]. The human brain consists of over 100 neurotransmitters, chemical substances that facilitate communication between neurons throughout the body [36,37]. During a seizure, hyperexcitability releases excess amounts of neurotransmitters, which is toxic for the brain, and leads to significant spikes in neuronal activity [38]. Anti-seizure medications alter electrical activity in neurons through ion channels in the cell membrane and affect the synapse by regulating the concentration of neurotransmitters within the synapse to reduce membrane excitability [39]. Most



## RISK FACTORS



HYPERTENSION

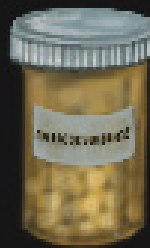


RENAL FAILURE

## POSSIBLE TREATMENTS



ANTIHYPERTENSIVES



ANTICONVULSANTS



topiramate gabapentin levetiracetam

anticonvulsants also inhibit abnormal electrical signals and excitatory synaptic transmission, a process that helps regulate neuronal activity and prevent excess firing [40]. The interventions involving anticonvulsants alongside blood pressure management not only alleviate immediate symptoms but also contribute to the overall recovery of PRES.

## CONCLUSION

Living with PRES can be an overwhelming experience, as the condition presents a myriad of challenges. Symptoms such as headaches, abnormal vision, and seizures disrupt daily life tasks and increase the risk of developing further neurological complications if left untreated. While its exact mechanisms remain somewhat unclear, contributing risk factors such as hypertension, renal

failure, specific medications, and additional diseases can lead to its development. Various elements involved in PRES, including compromised cerebral autoregulation and disruption of the blood-brain barrier, result in brain edema and the associated neurological symptoms. These complications demonstrate the importance of maintaining brain health and preventing neurological conditions like PRES. Diagnosis requires a neurological evaluation and the use of magnetic resonance imaging (MRI) to locate regions of the brain where brain edema is occurring. Although there is currently no definitive cure, PRES is reversible and treatment plans are formed on a case-by-case basis depending on each patient's medical history. By focusing on stabilizing blood pressure, managing seizures, and mitigating neurotoxicity, physicians aim to restore neurological function and pave the way for recovery. 🧠

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## HAVE A GOOD TRIP: THE EVOLUTION AND BENEFITS OF PSYCHEDELIC THERAPY

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