Cerebral Vasospasm Following Aneurysmal Subarachnoid Hemorrhage


SUMMARY Cerebral vasospasm following aneurysmal subarachnoid hemorrhage is one of the most important causes of cerebral ischemia, and is the leading cause of death and disability after aneurysm rupture. There are two definitions of cerebral vasospasm: angiographic and clinical. Care must be exercised to be certain that it is clear which entity is being addressed. The diagnosis of the clinical syndrome is one of exclusion and can rarely be made with absolute certainty. The pathogenesis of cerebral vasospasm is poorly understood. Most current theories focus on the release of factors from the subarachnoid clot. More attention must be given to the role of endothelial damage and alterations in the blood-arterial wall barrier. The application of modern techniques for studying vascular smooth muscle which have been developed as a result of research in the areas of hypertension and atherosclerosis must be applied to the problem of cerebral vasospasm. A stress test to select patients with angiographic arterial narrowing who have adequate cerebral vascular reserve to undergo surgery should be developed. The optimal treatment of vasospasm awaits development of agents for blocking or inactivating spasmogenic substances or blocking arterial smooth muscle contraction. Rheological or hemodynamic manipulations to prevent or reverse ischemic consequences of vasospasm are relatively effective, but complicated and hazardous, and should be viewed principally as interim measures awaiting development of more specific therapies for the arterial narrowing.

RUPTURED INTRACRANIAL ANEURYSM is a major public health problem affecting more than 28,000 individuals in North America each year. In excess of 19,000 will ultimately die or be disabled. For perspective, the annual incidence of primary intracranial neoplasm is only 10,000 per year. Paradoxically, brain tumors are generally perceived as being the more common neurological disorder and have received disproportionate (although entirely appropriate) attention and research funding.

In the past, rebleeding — the most dramatic and dreaded complication following aneurysm rupture — was considered the major cause of morbidity and mortality. However, recently it has been demonstrated that the leading cause of death and disability in patients with aneurysmal subarachnoid hemorrhage is cerebral vasospasm. Of those patients who reach neurosurgical referral centers, vasospasm will kill 7% and maim another 7%, and 6% will perish and 1% will be ruined as a result of rebleeding. (Kassell NF, Torner JC, and Jane JA: International Cooperative Study on the Timing of Aneurysm Surgery: Preliminary results. Presented at the Annual Meeting of the American Association of Neurological Surgeons, Atlanta, Georgia, April, 1985.)

While vasospasm is of fundamental interest in the management of patients with intracranial aneurysms, there are certain aspects of this disorder which are of more general interest and which have for the most part been neglected in the field of ischemic stroke. Most victims of aneurysmal subarachnoid hemorrhage are young (average age 51), otherwise healthy individuals who gradually develop ischemic neurological deficits while hospitalized for treatment of their ruptured aneurysm (Kassell NF, Torner JC, and Jane JA: International Cooperative Study on the Timing of Aneurysm Surgery: Preliminary results. Presented at the Annual Meeting of the American Association of Neurological Surgeons, Atlanta, Georgia, April, 1985). If they recover, they can return to their premorbid state with many years of productive life ahead of them. In contrast, most patients who suffer thromboembolic stroke do so suddenly and then present with fixed neurological deficits to hospital usually after an interval sufficient for infarction to have occurred. These patients are mostly older and in whom the thromboembolic stroke is but an indicator of generalized atherosclerosis — a progressive, fatal, systemic disease from which approximately 45% will die within five years. Furthermore, since the ischemic deficits from vasospasm occur with a significant delay prior to infarction in a hospital setting under the observation of neurologists and neurosurgeons, this disorder may be used as an important model for evaluating diagnostic tests for decreased cerebral perfusion as well as for studying therapeutic interventions for ischemic protection and rescue. To date, full advantage has not been taken of these opportunities.
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Diagnosis

There are two definitions of cerebral vasospasm — angiographic and clinical — which may not be used interchangeably. Angiographic vasospasm is a narrowing of the dye column in the major cerebral arteries which is usually focal but may be diffuse. The narrowing is time-dependent, rarely pronounced before the 4th day following the initial hemorrhage and reaches a peak around the 7th day. At that time 40 to 70% of patients will have some reduction in the caliber of one or more of the arteries of the Circle of Willis or its branches. Due to the variability in the normal anatomy of these vessels and the variability in the degree and extent in which these arteries are affected, attempts to quantify vasospasm in a reliable manner have been frustrating. At this time the most useful means are those developed by Fisher and Weir, although the most practical remains the gestalt of an experienced neuroradiologist or neurosurgeon.

Clinical vasospasm is the syndrome of the ischemic consequences of cerebral arterial narrowing and is characterized by the insidious onset of confusion and decreased level of consciousness followed by focal motor and speech impairments and is often heralded by worsening headache and increasing blood pressure. Appearance of the clinical syndrome may be accelerated or precipitated by a reduction of blood pressure (usually from antihypertensive therapy), a decrease in intravascular volume, or by surgical manipulations. The time course for clinical vasospasm parallels that of angiographic vasospasm but while 70% of patients may develop arterial narrowing only 20 to 30% will manifest neurological deficits. The discrepancy between the incidence of angiographic and clinical vasospasm is probably best explained by differences in the location and degree of arterial narrowing and the adequacy of collateral circulation.

While the risk of clinical vasospasm is omnipresent in patients who have sustained rupture of an intracranial aneurysm, it is often exceedingly difficult to prove that the neurological deficits which occur are related to the arterial narrowing. The etiology of neurological deterioration in patients with aneurysmal subarachnoid hemorrhage is protean with more than one factor being operant in the majority of instances (Kassell NF, Peerless SJ, Drake CG: Progressive neurological deterioration following subarachnoid hemorrhage. Presented at the Annual Meeting of the Congress of Neurological Surgeons, New Orleans, Louisiana, October, 1976). Currently the diagnosis of vasospasm is primarily based on the time of onset of the deficits (usually 4–9 days following subarachnoid hemorrhage), the rate of development of the deficits (hours), the nature of the deficits (impaired orientation and decreased level of consciousness preceding focal deficits) and the exclusion of other causes including: rebleeding, intracerebral hematoma, or hydrocephalus (by CT scan), metabolic disturbances (hypoxia, hyponatremia), angiographic or surgical complications, etc. In the past, angiographic confirmation of arterial narrowing was usually considered mandatory for making the diagnosis of clinical vasospasm. Currently, however, the above criteria are considered to be adequate in most instances for the following reasons: 1) even when the arterial narrowing is present other causes are not excluded since, as noted previously, the deficits are frequently multifactorial; 2) the inherent risk of angiography plus the hazard of moving patients from carefully controlled environments; and 3) the expense of the procedure. However, in certain instances angiography is still warranted, particularly prior to embarking on complicated and potentially risky therapy, if the diagnosis is suspect. A promising alternative to angiography for demonstrating narrowing of the major cerebral arteries is transcranial pulsed Doppler.

From the aforementioned comments it is apparent that it is almost impossible to make the diagnosis of clinical vasospasm with absolute certainty in many instances. This point must be considered carefully in designing and evaluating clinical trials.

Pathogenesis

The pathogenesis of cerebral vasospasm is poorly understood. Since the original description of angiographic vasospasm more than 30 years ago considerable effort has been expended — mostly by neurosurgeons — in investigating the etiology of vasospasm. Studies thus far have failed to yield conclusive evidence as to the causative agent(s) or the nature of the arterial narrowing. It remains unclear as to whether vasospasm is a normal or abnormal contraction or failure of relaxation of arterial smooth muscle cells or whether it represents a cytoarchitectural thickening in the vessel wall.

The uncertainty regarding the pathogenesis of vasospasm is exemplified by the controversy regarding the histopathological changes in the involved arteries. While it has been reported that the narrowed arteries are morphologically normal following experimental subarachnoid hemorrhage, there is little doubt that microscopic alterations do occur in vasospasm. Changes which have been described include: intraluminal platelet adhesion and aggregation with white cell adhesion and thrombus formation, increased endothelial pinocytotic activity or channel formation, intimal swelling, proliferation, degeneration, and desquamation, opening of interendothelial junctions, subendothelial fibroses, and migration and proliferation of smooth muscle cells, medial infiltration of lymphocytes, plasma cells and macrophages, and deposition of IgG and complement, necroses of smooth muscle cells, corrugation of the internal elastic lamina, degranulation of perivascular nerve terminals and degeneration of perivascular nerves. No conclusive evidence has yet been forthcoming to indicate whether or not any of these changes are causally related to the arterial narrowing and development of neurological deficits or whether they represent epiphenomenon or a nonspecific reaction to vascular injury. Furthermore, it is unclear as to the role of intravascular phenomena such as thromboembolism in the genesis of cerebral ischemia.
At this time there is little doubt that blood in the subarachnoid space is related to the development of vasospasm and that there is a close association between vasospasm and the amount of blood in the subarachnoid space.44-50 Antifibrinolytic therapy which prevents dissolution of the clot in the subarachnoid space increases the incidence and perhaps the severity of clinical vasospasm51-53 and removal of the clot may decrease the incidence or severity of the ischemic deficits.54-56 While bleeding into the subarachnoid space appears to be the fundamental initiating event, identification of specific spasmogenic substances released from the clot has not been accomplished with certainty.57 Putative spasmogens include epinephrine,58-60 norepinephrine,58-63 seroton in,58-61,64-68 angiotensin,59, 65 hemoglobin,59-74 thrombin or plasmin,75 fibrin degradation products,76, 77 prostaglandins,78-83 thromboxane,84-87 hydroperoxides,88-92 potassium,93-95 and others.

In addition, it must be noted that subarachnoid hemorrhage is associated with an abrupt increase in intracranial pressure and blood pressure as well as some degree of cerebral ischemia and hypoxemia.96-99 These factors may also contribute to the development of vasospasm.

The major contemporary hypotheses regarding the pathogenesis of the arterial narrowing are as follows:

1) Contraction of cerebral arterial smooth muscle cells secondary to vasoactive substances in the CSF.77, 100-103 Denervation supersensitivity,104-106 or a prostacyclin/thromboxane A2 imbalance.104-106

2) Impairment of vasodilatory activity due to:
   a. prostacyclin/thromboxane A2 imbalance. Arterial wall prostaglandin decreases progressively following subarachnoid hemorrhage, probably in association with the progressive endothelial degeneration.104-106
   b. oxyhemoglobin, which is present in bloody CSF, has been shown to inhibit acetylcholine-mediated vasodilatation.107 This acetylcholine-mediated vasodilatation is also inhibited by hypoxia,108 and the arterial muscle cell may be hypoxic as a result of clogging of the adventitial pores with fibrin and red blood cells.109 Furthermore, the hemoglobin in the CSF may inhibit neurogenic vasodilatation,110 as well as endothelial derived relaxing factor-induced vasodilatation (Fujiwara S, Kassell NF, unpublished data).

3) Proliferative vasculopathy. The mitogenic substances in the platelets — either those in the subarachnoid clot or those that adhere to the arterial lumen as well as a similar substance released from injured endothelium may cause proliferation of smooth muscle cells and fibroblasts in the media.111, 112

4) Vasospasm may be an immunoreactive process. Both an increase in circulating immune complexes58 and IgG and C3 deposition in the media of the arterial wall of patients with chronic spasm have been shown.113 It is unclear whether this immunoreactivity is responsible for the initiation of an anaphylactoid reaction (and by release of chemical mediators causing spasm) or a by-product of an inflammatory process taking place in and around the vessel wall and/or a response to the formation of antigens (such as smooth muscle or endothelial injury or destruction)114, 115 that may be occurring during the vasospastic process.

5) Vasospasm may be an inflammatory process. Considerable indirect evidence has been gathering that suggest vasospasm may be the result of an inflammatory process taking place in the arterial wall and initiated by the surrounding clot.36, 116-119 Morphological changes compatible with an inflammatory process,120, 121 leukocytes within the blood vessel wall122 and adherent to the endothelial surface (Nazar G, Kassell NF, unpublished data), the multiple complex origins of vasospasm,123 experimental responses to non-steroidal anti-inflammatory drugs124 and steroids,125 and studies on the inflammatory process126-128 support the concept.

6) The arterial narrowing may be a mechanical phenomenon either because the arteries are compressed by the periarachnoid clot or due to distortion of the arachnoid bands which tether the major cerebral arteries in the subarachnoid cisterns.129

From the above it is apparent that most of the hypotheses regarding the development of the arterial narrowing assume that the etiology is related to substances liberated from the subarachnoid clot resulting in contraction or morphological changes in the vessel wall. However, it has recently been hypothesized that the endothelial damage resulting from the subarachnoid hemorrhage may be related to the subsequent arterial narrowing.130 The cause of the endothelial injury has not been established but arterial hypertension, increased intracranial pressure and, in particular, subarachnoid blood all increase transendothelial permeability acutely, by increasing vesicular transport or channel formation (Sasaki T, Kassell NF, unpublished data). Instillation of synthetic TXA2 into the CSF produces similar effects (Zuccarello M, Kassell NF, unpublished data).

Clinically, it has been observed that contrast enhancement in the basal cisterns in the region of the major cerebral arteries indicating increased arterial permeability occurs in certain patients following aneu- rysm rupture and that these patients are most prone to develop vasospasm.131-134 In the subacute and chronic stages of subarachnoid hemorrhage, arterial endothelial cells degenerate and there is opening of the interendothelial tight junctions, resulting in marked disturbance in the blood arterial wall barrier.130 This breakdown of the blood arterial wall barrier may allow access of constrictor substances in plasma (such as catecholamines or prostaglandins) to the smooth muscle cells. Furthermore, platelets may adhere to either damaged endothelium or denuded subendothelium and
release additional constrictor substances such as serotonin. The effect of the vasoactive substances in plasma may be particularly pronounced since the smooth muscle cells closest to the lumen are the most sensitive to constrictor agonists. In addition, subarachnoid hemorrhage has been shown to result in de-polarization of arterial smooth muscle cells, making them more prone to contraction. Damage of endothelium may result in loss of the potent vasodilator, prostacyclin, while allowing the unopposed action of thromboxane A\(_2\) released from platelets. Additional vasoactive substances may be released from these adhering platelets as well as white blood cells.

Medial thickening and luminal narrowing may be produced by proliferation of smooth muscle cells and fibroblasts, either caused by platelet derived growth factor released from platelets in the subarachnoid clot or from platelets adhering to the arterial luminal surface of the arterial wall or to a similar substance released from damaged endothelium, or the spasmodenic effects of thrombin, plasmin, and fibrinogen.

From the previous discussion it may be surmised that the pathogenesis of cerebral vasospasm is most likely a complicated, multifactorial process. Investigations in the past have been hampered by lack of a satisfactory animal model of vasospasm. Many studies have been conducted in the acute stage following applications of blood or other substances to arteries in vivo or in vitro. These studies may be appropriate for understanding short-lived arterial contraction but are not optimal for unraveling the complexities of the delayed, prolonged arterial narrowing resulting from subarachnoid hemorrhage.

The problems with most models of subarachnoid hemorrhage were that: 1) it was difficult to create reproducible arterial narrowing, probably because most animals have a more simple, less trabeculated subarachnoid space and perhaps a more active fibrinolytic system in the CSF than humans and 2) almost all animals failed to develop delayed progressive neurological deficits.

Recently, reasonably good models of angiographic vasospasm have been developed using application of blood around major cerebral arteries under direct vision or double injections of blood into the basal cisterns. The difficulty in producing neurological deficits is probably related to the relative resistance of lower species to cerebral ischemia perhaps because of more effective collateral pathways as well as less eloquent brains. This is not a major limitation in studies of the pathogenesis of arterial narrowing since morphological and angiographic endpoints are adequate for most investigations, but may be of greater concern in studies of treatment of clinical vasospasm where the most relevant endpoint is reversal of ischemic neurological deficits. Another problem with animal models is the rather marked species differences in regulation of the cerebral circulation.

In the past decade, there have been profound advances in vascular smooth muscle morphology, physiology, and pathology stimulated as a result of the intense interest in atherosclerosis and hypertension. Most developments have related to the systemic circulation, rather than the cerebral circulation. In the not-too-distant future, substantial advances in the understanding of the pathogenesis of cerebral vasospasm may be anticipated as state-of-the-art techniques are applied to the problem. These include sophisticated morphological techniques, tissue culture of smooth muscle and endothelium, and in vivo and in vitro methods for studying biochemistry and pharmacology of cerebral arteries.

Parenthetically, the appropriateness of the term vasospasm may be questioned since the pathogenesis of vasospasm is unclear, and the arterial narrowing may not at all be related to a spastic phenomenon of smooth muscle cells. For example, the delayed, prolonged, irreversible arterial narrowing which occurs after subarachnoid hemorrhage appears to be much different from the vasospasm observed in the coronal circulation of patients with Prinzmetal's angina. Nonetheless, the term cerebral vasospasm is well defined and ingrained in the literature. Accordingly, its use should be continued with the only qualification that it must always be clear as to whether reference is being made to the clinical or angiographic variety.

**Pathophysiology**

Compared to the pathogenesis of cerebral vasospasm the pathophysiology of this disorder appears more straightforward and is better understood. The arterial narrowing which occurs following subarachnoid hemorrhage results in increased cerebral vascular resistance. How far down the arterial tree this narrowing extends remains problematical, since the only vessels visualized by angiography are the Circle of Willis and its primary and secondary branches. Whether pial and penetrating arteries and arterioles are narrowed has not been established. It is likely, however, that the process does extend to arteriolar level, since red blood cells and presumably plasma containing spasmodogenic substances extend well into the Virchow-Robin spaces following subarachnoid hemorrhage. This notwithstanding, the angiographically demonstrated vasospasm is probably sufficient to reduce cerebral blood flow to ischemic levels, since approximately half of the cerebral vascular resistance is located in these conducting vessels. Initially, in the presence of arterial narrowing autoregulation maintains cerebral blood flow constant, but if the narrowing progresses, the limits of autoregulation may be exceeded and cerebral blood flow falls. Since the brain is supplied with roughly twice the amount of blood flow required for normal function, no neurological impairments may initially result. However, as blood flow decreases below the ischemic threshold, neurological signs and symptoms may become overt and, if narrowing progresses and the flow decreases further, infarction may occur.

In ischemic situations caused by vasospasm, the
major cerebral arteries are narrowed and blood flow is reduced but cerebral blood volume is paradoxically increased. This may be due to dilatation of more distal resistance vessels and collateral channels as well as collection of blood in the capacitance vessels of the ischemic zones.  

As noted previously, patients may evidence a significant degree of angiographic arterial narrowing yet have adequate cerebral blood flow to be essentially normal clinically or because of the excess cerebral blood flow because perfusion is preserved through autoregulation. Whether or not these patients are candidates for surgery is controversial. While these patients may be normal preoperatively, their cerebral circulatory reserve may be exhausted so that the surgical or anesthetic manipulations such as brain retraction, systemic arterial hypotension, temporary arterial occlusion, etc. may decrease flow and cause infarction which becomes evident upon awakening from the operative procedure. The timing of surgery for such patients is still controversial, but most surgeons will wait until vasospasm resolves before proceeding with operation. In these circumstances, dynamic tests of the reserve capacity of the cerebral circulation may be useful in determining which patients can tolerate surgery. Such tests could involve stressing the cerebral circulation by lowering arterial pressure or increasing arterial pCO2 while measuring the cerebral blood flow, the brain's electrical activity, and the neurological examination.

A possible factor contributing to the development of ischemic deficits may be intra-arterial thromboembolism, particularly involving the smaller arteries. If intravascular thromboembolism proves to be a component of the syndrome of vasospasm, new avenues of therapy, namely, anticoagulation or antiplatelet agents, may prove beneficial.  

Treatment

The treatment of cerebral vasospasm may be considered in the following categories: 1) prevention or reversal of the arterial narrowing; 2) prevention or reversal of the ischemic neurological deficits; and 3) protection from infarction.  

Efforts to prevent vasospasm from developing and to reverse it once it has occurred have been hampered by lack of understanding of the etiology of the arterial narrowing and, to date, no measures have proven successful. A theoretically attractive approach for preventing or ameliorating the arterial narrowing is removal of clot from the basal cisterns in the days immediately following the hemorrhage, prior to the onset of vasospasm. The clot can be removed mechanically with suction and irrigation at the time of craniotomy or perhaps more attractively, by instillation of fibrinolytic substances such as streptokinase, urokinase or plasmin into the cerebrospinal fluid. A surprisingly large amount of subarachnoid clot can indeed be removed through a unilateral craniotomy and some surgeons have even resorted to bilateral craniotomies in an attempt to remove as much of the clot as possible. Mechanical removal of the clot can only be accomplished with some bruising of pial banks or damage to small vessels. While there are a number of optimistic reports that this measure is effective, other reports indicate that the incidence or severity of vasospasm is not significantly decreased. Lysis of the subarachnoid hematoma pharmacologically is much more attractive in theory, since it should be accomplished more completely and with less damage, but, although clinical studies have been started, there is currently little information regarding the effectiveness of this approach. However, subarachnoid fibrinolytic therapy is definitely an area which warrants further investigation.  

A large number of agents have been used to prevent or reverse the arterial narrowing; an exhaustive review of this topic was published by Wilkins in 1980. Presently, no means have been definitely identified for treating cerebral vasospasm. The drugs which have received the most contemporary interest are the calcium channel blocking agents, based on the assumption that contraction of cerebral arterial smooth muscle cells is a calcium-dependent phenomenon which can be inhibited by preventing influx of extracellular calcium. However, the contraction of cerebral arterial smooth muscle cells to a variety of agonists, particularly those found in the CSF following subarachnoid hemorrhage, has been shown to rely in large part upon intracellular calcium. This may account for the observation that these calcium channel blocking agents do not appear to prevent or reverse narrowing of the major arteries, although there is a reasonable suggestion that calcium channel blocking agents may prevent or reverse ischemic neurological deficits. Perhaps the most attractive approach to preventing or reversing arterial narrowing is to prevent or reverse activation of the actin-myosin complex by calmodulin, the final step in all processes leading to arterial smooth muscle contraction. Initial studies with calmodulin blocking agents have been encouraging. Other drugs which have recently been evaluated for the treatment of vasospasm include the angiotensin converting enzyme inhibitor teprotide, thromboxane A2 synthetase inhibitors, prostacyclin, steroids, and free radical scavenging agents such as Vitamin E. The efficacy of all of the above must be considered controversial at best; there is currently little to suggest that any is effective in the treatment of the arterial narrowing that is such an enormous clinical problem.  

Effective efforts for preventing and reversing angiographic vasospasm await definition of the pathogenesis of the process. The nature of the arterial narrowing must be worked out and agents found for blocking or inactivating the spasmogenic substance or preventing the contraction of arterial smooth muscle cells. Specific agents for blocking or inactivating the spasmogenic substances should be more effective than nonspecific agents for preventing arterial smooth muscle cell contraction since the latter would affect not only the
volved cerebral vessels, but the normal vessels in the brain and perhaps other organs.

The prevention or reversal of ischemic deficits from vasospasm can be considered in three categories: measures to improve blood flow by altering the rheological characteristics of the blood; measures to improve oxygen delivered to the tissues; and hemodynamic measures to increase cerebral blood flow. These approaches are generally complicated, hazardous, and non-physiological and should be considered primarily interim solutions until measures for specifically preventing or reversing the arterial narrowing can be developed.

Drugs for improving the rheological characteristics of the blood include the use of calcium channel blocking agents, prostacyclin, heparin, hemodilution, dextran, mannitol, and albumin.

Calcium channel blocking agents exert their effect primarily by dilating the leptomeningeal collateral arteries but may also work by improving red blood cell deformability and by exerting an antiplatelet aggregating effect. Heparin and prostacyclin may prevent intravascular thromboembolism and the latter may also be effective in dilating leptomeningeal collaterals. Mannitol has the effect of improving red blood cell deformability and it also is a free radical scavenging agent. Hemodilution may decrease viscosity and thereby improve cerebral blood flow. However, the optimum hematocrit in ischemic situations has not been established and there may be a considerable trade-off between decreased viscosity, increased blood flow and oxygen delivery.

There are two approaches for improving oxygen delivery to brain tissue made ischemic by vasospasm. The first is the use of hyperbaric oxygen and the second is the use of fluorinated hydrocarbons such as fluosol. The two approaches may be combined advantageously.

Improving the hemodynamic status of patients with neurological deficits from vasospasm in an attempt to improve cerebral blood flow has proven to be a reasonably effective, although complicated, approach. Cardiac output may be increased by increasing intravascular volume and by the use of chronotropic and inotropic agents such as isoproterenol. Increasing intravascular blood volume without increasing cardiac output or mean arterial pressure may improve cerebral blood flow by increasing pulse pressure. This is a relatively new concept developed by Kindt and associates and it appears to be of considerable importance. The final approach is to increase cerebral perfusion pressure, defined as the difference between systemic arterial and intracranial pressures, either by reducing intracranial pressure or by increasing systemic arterial pressure. The theory behind this is that the blood flow in the ischemic zones is pressure passive since the vessels are maximally dilated and autoregulation is abolished and therefore arterial hypertension is induced with vasopressor agents. In practice, at least 70% of neurological deficits from vasospasm can be reversed using a combination of increased cardiac output and increased arterial pressure if treatment is initiated prior to infarction. Hypertensive/hypervolemic therapy is complicated and hazardous and requires invasive monitoring and intensive care.

In those instances where the ischemic deficits cannot be prevented or reversed, there are several treatments which may be employed in an attempt to provide a degree of protection. Steroids may stabilize lysosomal and cell membranes. Calcium channel blocking agents may be beneficial in these circumstances by preventing the passage of lethal amounts of extracellular calcium into the cell. High dose barbiturate therapy has been employed as a last ditch effort in a number of cases in an attempt to decrease the metabolic activity of the brain to a level which can be supported by the compromised delivery of substrate. Barbiturate coma is a heroic measure and the results have been discouraging to date.

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