

Chapter 2

Types of Strokes

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Key Points

- There are two main types of strokes: ischemic and hemorrhagic.
- Ischemic strokes are far more common than hemorrhagic strokes.
- The brain has a blood supply which is fairly consistent between individuals.
- Ischemic strokes can be due to large-vessel atherosclerosis, aortocardioembolism, small-vessel occlusion, other determined causes, and undetermined causes.
- Hemorrhagic strokes are most often due to hypertension but may be caused by specific blood vessel abnormalities and other medical problems.
- The clinical impact of a stroke depends largely on the stroke's location in the brain, whether it is ischemic or hemorrhagic, and the size/severity of the stroke itself.

Keywords Stroke • Transient ischemic attack • Ischemic • Hemorrhagic • Infarct • Cerebrovascular • Aneurysm • Arteriovenous malformation • Subarachnoid hemorrhage

Abbreviations

CAA Cerebral Amyloid Angiopathy
ICH Intracerebral Hemorrhages
SAH Subarachnoid Hemorrhage

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Introduction

The word “stroke” is taken in this brief summary and by most healthcare practitioners to describe damage to the neuraxis (i.e., the brain and spinal cord) resulting from any and all abnormalities in its blood supply. “Stroke” means many things to different people, but universally inspires a certain visceral response. Comprised of about 100 billion neurons and a trillion glia [1] packed into about 3 pounds of tissue, the brain houses our consciousness, our accumulated experiences parsed and encoded by the paired temporal lobes, and stored in a network encompassing the entire brain. The brain enables our every movement and every breath. Stroke remains the leading cause of disability in the United States [2] and is the country’s fourth leading cause of death [3].

Stroke has contributed to our present understanding of the brain more than any other disease. The numerous ways in which neurologic deficits appear when one area of the brain or another is damaged were noted by physicians as early as ancient Egypt, but it was not until fairly recently that advancements in histopathology, neurophysiology, and neuroimaging informed centuries of clinical observation and forever transformed the field of neuroscience. The great revelation in the second half of the nineteenth century has been that the brain is organized into different regions with different cell types, and the pattern is relatively uniform among human beings. In other words, two right-handed people with lesions in a given region of the left hemisphere will reliably manifest the same kind of speech difficulty. Similarly, the anatomy of the arteries and veins serving the brain is much the same between individuals, so blockage of a particular artery will cause a fairly predictable constellation of physical findings. Hence, generations of neurologists have been taught “we learn the brain, stroke by stroke.”

With this in mind, it may be surprising how little is known about the various types of stroke by most non-stroke physicians and allied health professionals. One can speculate on potential reasons for this—such as perceived complexity of the subject, sociocultural stigma, or simple fear of the disease under discussion—but it seems clear that anyone engaged in the care or rehabilitation of stroke patients should be familiar with the classification of stroke subtypes and their respective etiologies, especially in this age of life-saving and brain-saving stroke treatment and specialized inpatient units devoted to the unique needs of this population.

Ischemic Strokes

By far, the most common type of stroke is the so-called ischemic stroke or cerebral infarction. According to recent data released by the American Heart Association, 87 % of strokes are classified as ischemic [4] (see Fig. 2.1). Infarcts occur as a result of insufficient or interrupted flow of blood to an area of the brain, typically caused by blockage of an artery (though “venous infarcts,” discussed below, may cause similar phenomena).

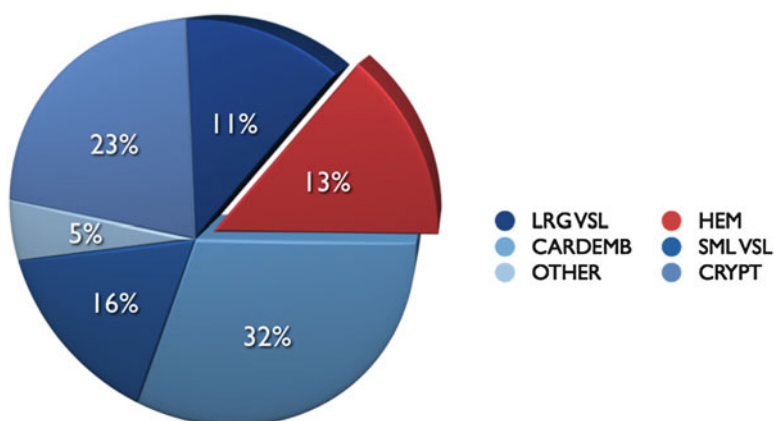


Fig. 2.1 Stroke subtype and annual incidence. Ischemic stroke in *blue* and hemorrhagic stroke in *red*. *LRG VSL* large vessel, *HEM* hemorrhagic, *CARDEMB* cardioembolic, *SML VSL* small vessel, *CRYPT* cryptogenic

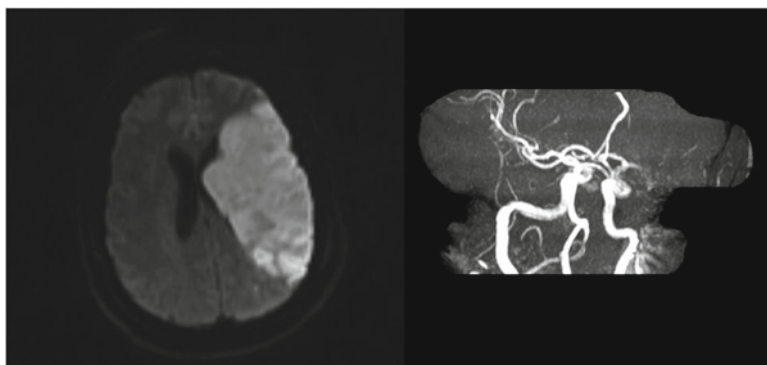


Fig. 2.2 MRI of the brain showing acute ischemic stroke in the distribution of the left middle cerebral artery territory (*left*). MR angiography shows cutoff of the left MCA in a patient with atrial fibrillation

In brief, brain tissue must be supplied with oxygen, glucose, and other vital materials by the constant influx of blood at a rate of about 50–54 ml of blood per 100 g of brain tissue per minute [5]. Brain cells deprived of adequate blood flow (cerebral blood flow [CBF] below 15–20 ml blood flow/100 g tissue/min) [6] will become ischemic; their membrane pumps will begin to fail, intracellular processes will break down, and the brain tissue becomes swollen. Importantly, the ischemic brain tissue may still be salvageable if perfusion can be restored at this point [7]. If the hypoperfusion worsens (i.e., CBF <8–10 ml/100 g/min) [7], this tissue at risk will become irreversibly damaged with cell death proceeding within 4–8 min. This event is referred to as an ischemic stroke (see Fig. 2.2).

Damage to brain tissue will occur initially in the region contiguous to the blocked artery (the so-called infarct core [6]), while a penumbra of at-risk tissue surrounding this region remains viable for some time following onset of ictus and with timely intervention may respond to efforts to restore blood flow to the region.

A Review of Relevant Anatomy

Arteries supplying blood to the brain are all branches of the large brachiocephalic arteries that stem from the aorta. The common carotid arteries on either side ascend the anterior neck and bifurcate around the level of the angle of the mandible, into the internal and external carotid arteries [8]. The external carotid arteries give off branches that supply the structures of the anterior neck and most of the head and face with blood, with the notable exception of the brain. The internal carotids, by contrast, ascend the neck, enter the skull, and through their intracranial branches will then perfuse most of the anterior 2/3 of the brain, including the entire frontal and parietal lobes and most of the temporal lobes. The internal carotid arteries and their tributaries constitute the so-called anterior circulation [8].

The posterior circulation (or vertebrobasilar system) is composed of two arteries, the right and left vertebral arteries, which are branches of the subclavian arteries arising from the aorta. These ascend laterally and posteriorly within the vertebral foramen and loop over the transverse process of the C1 vertebra to enter the skull, ascending the ventral surface of the medulla oblongata as it ascends the foramen magnum [8]. The vertebral arteries then merge to form the basilar artery at the level of the pons. The basilar artery continues to ascend and bifurcates at the level of the midbrain to parent the right and left posterior cerebral arteries. Through perforating branches, the vertebrobasilar system perfuses the brainstem, cerebellum, thalamus, occipital lobe, and part of the temporal lobe [9].

At the base of the skull, shortly after the large arteries enter the cranial cavity, the major arteries join to form anastomoses in a pattern shared to some degree by all humans—the so-called Circle of Willis (CoW—see Fig. 2.3), formed by arteries which communicate between the anterior and posterior systems and between the left and right sides of the brain [9]. Distal to the CoW, the major named cerebral arteries emerge to perfuse the brain: the anterior and middle cerebral arteries from the anterior circulation and the posterior cerebral arteries from the bifurcation at the top of the basilar artery, linked by the anterior and posterior communicating arteries, respectively [9].

There are a number of ways in which ischemic strokes can occur, and the various etiologies often result in different clinical presentations and characteristic appearance of the lesion on imaging. Several subclassification schemes for ischemic strokes have been proposed over the last four decades [10], including the Harvard Stroke Registry (1978) [11], Oxfordshire Community Stroke Project (1993) [12], TOAST (or “Trial of Org 10172 in Acute Stroke Treatment”) (1992) [13], SSS-TOAST (2005) [14], A-S-C-O, or “phenotypic” (2009) [15], and the Chinese

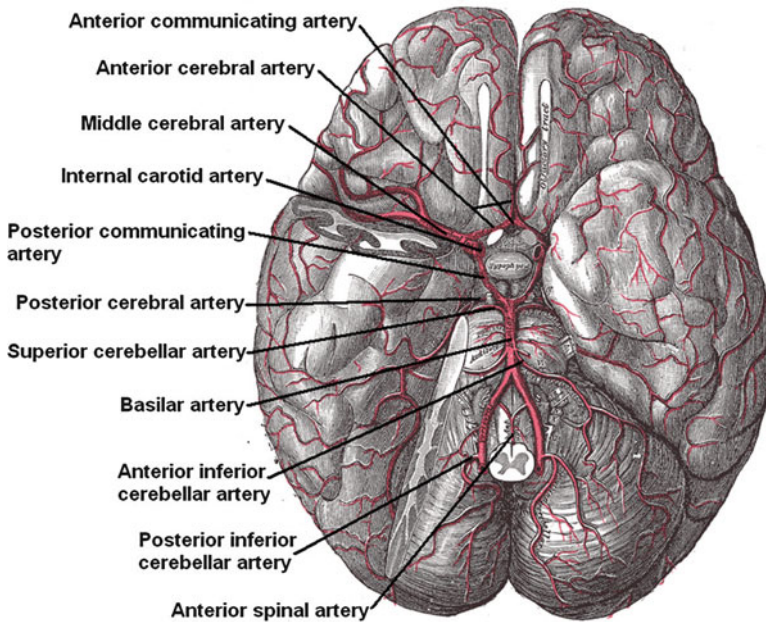


Fig. 2.3 Vascular anatomy of the brain

Ischemic Stroke Subclassification (2011) [16]. The TOAST classification is the most widely used and includes (1) *large-vessel atherothrombosis* (12.9 % of ischemic strokes), (2) *cardioembolism* (36.5 %), (3) *small-vessel disease* (18.4 %), (4) *other determined causes* (6 %), and (5) *undetermined causes*, which includes cases invoking more than one primary mechanism (26.4–42.3 %) [17].

Large-Vessel Atherothrombosis

This mechanism refers to the formation of lipid-laden atherosclerotic plaques on the inner wall of a large vessel and can affect both extracranial and intracranial arteries [18]. The most common sites for formation of atherosclerotic plaques include the bifurcations of the common carotid arteries, the origins of the vertebral arteries, and the course of the middle cerebral artery prior to its trifurcation [19]. Atherosclerotic plaques involving the cerebral vasculature are associated with the same risk factors as those which form elsewhere in the body, i.e., high blood pressure, diabetes mellitus, and dyslipidemia, among others [20]. They tend to form gradually over a prolonged time course, and the brain is able to adjust for gradual reductions in CBF without leading to infarcts until some critical level of stenosis is reached [21].

Table 2.1
Common sources of cardioembolic strokes

I.	Valvular disease
	A. Mitral stenosis
	B. Mitral annular calcification
	C. Bacterial endocarditis
	D. Nonbacterial endocarditis (i.e., thrombotic)
II.	Abnormal heart rhythms
	A. Atrial fibrillation
III.	Ischemic heart disease
	A. Mural thrombi
	B. Left ventricular aneurysms
IV.	Septal wall abnormalities
	A. Atrial septal defect
	B. Patent foramen ovale
V.	Cardiomyopathies
	A. Alcohol related
	B. Myocarditis
	C. Amyloidosis
VI.	Other
	A. Myxomas
	B. Fibroelastomas

Depending on the arteries affected and the lesion’s location within the course of the affected artery, the acuity of the process, and the presence or absence of anastomoses, this mechanism typically results in a single large territorial stroke [22]. In the case of so-called atheroembolism, a thrombus that has formed on the wall of a particular vessel may break apart and shed pieces of clot which are swept downstream and lodge in smaller arterial branches, resulting in multiple smaller strokes within the expected territory of the parent vessel [23].

Cardioembolism

In much the same way that blood clots forming in situ within atherosclerotic large arteries can lead to ischemic stroke, blood clots forming within the heart can break loose, enter the circulation, and lodge downstream in a cerebral artery. Clots can form within the heart due to intracardiac stasis of blood (often due to paroxysmal supraventricular arrhythmias, most commonly atrial fibrillation [24]) or adhering to a thrombogenic device or lesion (such as an implanted prosthetic valve [25]). Table 2.1 includes common cardiac sources of emboli.

On neuroimaging, cardioembolic strokes tend to occur in more than one arterial distribution, often favor the anterior circulation [26], and can be bilateral; acute strokes involving both the right and left anterior circulation can be thought of as embolic until proven otherwise [27]. Here, too, if the embolus is large, it will

lodge in a large artery and result in a correspondingly large stroke; this kind of stroke, distressingly common, is also associated with a higher risk of poststroke bleeding (hemorrhagic conversion) [28]. In some cases the “shower of emboli” occurs when an intracardiac thrombus fragments and a large number of small thrombi enter the cerebral circulation, resulting in a characteristic scattershot appearance on neuroimaging of many small acute infarcts in most or all of the brain’s arterial territories [29].

Some authorities include in this category strokes resulting from thromboemboli originating from aortic arch atheroma, while others characterize such strokes as resulting from large-artery atheroembolism [30]. While the distinction may be academic to healthcare providers who are not stroke epidemiologists, choosing the appropriate treatment for a particular patient—i.e., antiplatelet agents vs. anticoagulation or surgery—may depend on this distinction.

Small-Vessel Disease

This mechanism refers to occlusive disease involving the microcirculation of the brain—the unnamed small arteries and arterioles which take off from the named intracerebral parent vessels. The classical etiology of this stroke subtype is lipohyalinotic changes in the walls of these vessels [31], but increasingly microatheromatous disease has been recognized as an important contributing pathology [32]. Common locations for small-vessel disease include deep areas of the hemispheric white matter (such as the corona radiata); the region of white matter known as the internal capsule, adjacent to the proximal middle cerebral artery and supplied with blood by its penetrating branches; the pons in the mid-brainstem, supplied by penetrators arising from the basilar artery; and the thalamus, reliant primarily on branches of the posterior cerebral arteries [33].

Infarctions of these typical regions are classically small (<1.5 cm) [34] and depending on the location within the brain usually produce one of the classic *lacunar syndromes*: (1) *pure motor* symptoms, usually face + arm or arm + leg, comprising 33–50 % of all small-vessel strokes [35]; (2) *pure sensory*; (3) *mixed sensorimotor*; (4) *ataxic hemiparesis*, which features weakness of one side with disproportionate clumsiness (ataxia) of the same side; and (5) *clumsy hand-dysarthria*, clumsiness of either hand, out of proportion to any weakness of the limb, combined with slurred speech [36]. Other lacunar syndromes referable to the posterior circulation have been recognized, such as hemiballism, hemichorea, and isolated dysarthria [37], but they are less commonly seen as results of acute stroke [38].

Other Causes

These include, but are not limited to, strokes caused by extracranial arterial dissections [39], strokes caused by vasospasm associated with subarachnoid hemorrhage (see below) [40], a broad array of hereditary arteriopathies with diverse pathophysiologies

(such as moyamoya disease and fibromuscular dysplasia) [41], primary or parainfectious cerebral vasculitis [42], and coagulopathies (including that associated with malignancy, genetic disorders, and medical therapy) [43].

Undetermined Cause

This includes patients in whom a complete workup screening for cardiac conduction or structural abnormalities, intracranial or extracranial large-artery stenosis, coagulopathy, and other conditions has been unrevealing. Clinical situations in which a complete workup cannot be done, or has not yet been done, have also often placed in this category [44].

Also, in the regrettably common eventuality (approaching 40 % of all ischemic strokes [45]) that two likely causes for a given stroke are identified, such as in the case of a patient with comorbid atrial fibrillation and intracranial arterial stenosis, one primary cause cannot be assigned. Especially as this is such a large tranche of stroke patients, the desire for information about their outcomes and risk factors has led to the proposal of arguably more nuanced subclassification schemes such as ASCO [14] and the computer-aided SSS-TOAST [46]. These account for the presence of multiple potential etiologies or attempt to assign a level of likelihood (evident, likely, or possible) to a given etiology from those listed above.

A word should also be said about *watershed* and *borderzone* (*terminoterminal*) strokes, which tend to occur at the junction between two arterial territories. If a stroke develops in a region between adjacent arterial territories which share collateral circulation, such as the ipsilateral ACA and MCA, the stroke is termed watershed [47]. Borderzone infarcts occur when the infarct occurs between two arterial territories whose parent vessels do not share collateral flow [48], whether via the CoW or other regions of anastomosis (beyond the scope of this review). These are most commonly precipitated by a global or regional hemodynamic insufficiency, although they can at times be embolic [49]. For example, transient ICA occlusion and recanalization will result in a band of infarcted tissue in the borderzone between the ACA and MCA territories, furthest from the two respective parent vessels. These strokes may often be preceded by hypotension and/or hypovolemia and in post-cardiac arrest and shock patients [50].

Hemorrhagic Strokes

In this type of stroke the primary pathology is an area of bleeding causing direct damage to brain tissue. These constitute up to 10–15 % of all strokes and have a significantly higher morbidity and mortality than do ischemic strokes [51]. There are primarily two different types of hemorrhagic strokes: subarachnoid hemorrhage and intracerebral hemorrhage. In the former, blood accumulates in the potential spaces around and within the brain where cerebrospinal fluid is normally found,

Fig. 2.4 Head CT showing left basal ganglia intraparenchymal hemorrhage with surrounding edema and extension into the ventricular system

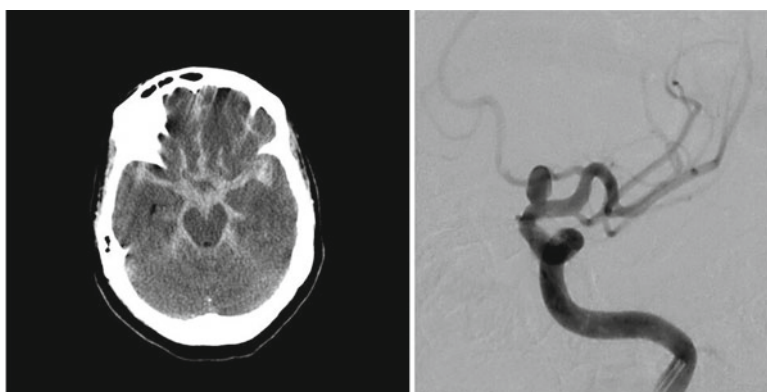


Fig. 2.5 Head CT showing diffuse subarachnoid hemorrhage in the basal cisterns (*left*). Digital subtraction angiography demonstrating left internal carotid artery aneurysm (*right*)

whereas in the latter the extravasation of blood occurs directly into the parenchyma (see Figs. 2.4 and 2.5) [52].

Intracranial hemorrhages are associated with the following etiologies.

Hypertension

Most intracerebral hemorrhages (ICH) are associated with rupture of an artery in the setting of acute or chronic arterial hypertension, which increases risk of spontaneous ICH two- to sixfold [53]. This has been attributed to the presence of

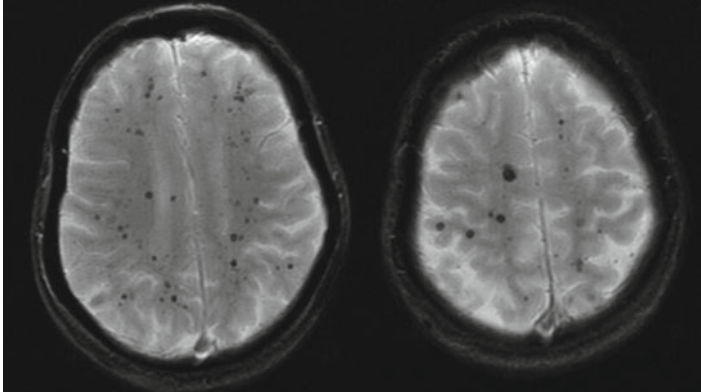


Fig. 2.6 Brain MRI showing multiple lobar microbleeds as a result of cerebral amyloid angiopathy

lipohyalinotic changes within the small arteries or the formation of microaneurysmal outpouchings (Charcot-Bouchard aneurysms) [54], which weaken the arterial wall. It should be noted that systemic hypertension is often caused by ICH as the body attempts to overcome raised intracranial pressure to perfuse the brain, and may not necessarily be the causative etiology in some ICH patients presenting to the Emergency Department [55].

The most common sites of hypertensive hemorrhages are the paired deep gray-matter structures referred to as the basal ganglia (putamen and lentiform nuclei as well as caudate nuclei); the thalamus; the pons; the cerebellum; and larger lobar hemorrhages affecting the cerebral hemispheres [56]. These will cause different presentations with varying degrees of neurologic compromise depending on size and location.

A significant proportion of hypertensive hemorrhages occur in the setting of sub-optimal adherence to a medical antihypertensive regimen, such as the abrupt discontinuation of a blood pressure medication due to an inability to afford the medication, or as a result of illicit catecholaminergic drug use, such as cocaine or methamphetamine [57]. Such cases illustrate on a daily basis the myriad social and cultural issues that accompany the ICH patient in the neuro-ICU and beyond.

Cerebral Amyloid Angiopathy

This is a disease characterized by deposition of fibrillary proteins in the walls of arterioles, making them stiff and brittle and predisposing them to rupture. These characteristically occur at the junction of the gray and white matter in the cerebral hemisphere and therefore typically present as lobar bleeds [58]. This etiology of intracranial hemorrhage is commonly seen in the elderly and is often diagnosed when an MRI of the brain discloses the existence of multiple microbleeds, which were previously undetected (see Fig. 2.6). Cerebral amyloid angiopathy (CAA)

typically occurs sporadically, though hereditary forms have been described. Because of the superficial location of the amyloid depositions, patients with CAA may also present with subarachnoid hemorrhage [59].

Bleeding Diathesis-Associated Hemorrhage

Patients may suffer intraparenchymal hemorrhages in the setting of bleeding disorders either due to a primary factor deficiency such as hemophilia A, an acquired factor deficiency such as that seen in hepatic failure, thrombocytopenia with its diverse causes, or disseminated intravascular coagulation [60].

Therapeutic Anticoagulation

A rather large subset of patients with ICH present with clotting dysfunction from use of anticoagulants, usually for primary or secondary prevention of cardioembolic stroke in the setting of valvular heart disease or atrial fibrillation. Patients also may be on anticoagulation therapy for deep vein thrombosis and/or pulmonary embolism, thrombophilia secondary to neoplastic disease, coagulopathy associated with rheumatologic conditions such as systemic lupus erythematosus, or due to intrinsic sporadic or hereditary coagulopathies [61]. The use of antiplatelet agents such as aspirin and/or clopidogrel, common in the outpatient treatment and secondary prevention of ischemic stroke, also confers a small but statistically significant risk of intracranial hemorrhage [62].

Hemorrhage in the Setting of a Vascular Malformation

The presence of certain abnormalities of the blood vessels within the brain or on its surface carries an increased risk of intracranial hemorrhage. These abnormalities include ruptured aneurysms (typically leading to subarachnoid hemorrhages), arteriovenous malformations (especially in the presence of venous aneurysms), dural arteriovenous fistulas, or cavernous angiomas. Rarely, intraparenchymal hemorrhages may occur due to dissection of intracranial arteries, in the form of a pseudoaneurysm [63].

Hemorrhagic Conversion of Ischemic Stroke

Hemorrhages in this category may occur after administration of thrombolytic drugs for acute stroke treatment, or in the setting of a large territorial stroke. The latter occurs

more commonly in the setting of cardioembolic strokes, which tend to be larger [28]. Furthermore, when a thrombus embolizes to the brain, it will usually be broken up after some time by the body's intrinsic process of thrombolysis, and blood flow will be restored to that region [64]. This is often after the point at which the blood vessels themselves have become ischemic and friable, leading to rupture of the vessel wall and extravasation of blood when hydrostatic pressure is restored. A small amount of petechial hemorrhage within a territorial stroke is not unexpected and may not significantly affect outcomes [65], but large, devastating lobar hemorrhages can occur as well.

Hemorrhage Due to Cerebral Venous Thrombosis

If a patient develops a blood clot in a superficial or deep cerebral vein or venous sinus, hydrostatic pressure will increase upstream of the venous side of the capillary bed until ultimately water is forced through the capillary walls and into the interstitium of the adjacent brain tissue reliant on the affected vein for normal fluid balance [66]. This process can cause edema and tissue dysfunction leading to variable neurologic deficits, altered sensorium, and seizures. If this continues unabated, hemorrhagic necrosis and vasogenic edema can develop in the affected area. This is sometimes referred to as venous infarction, though unlike true ischemic stroke, arterial supply may not be compromised [67].

Other Causes

Intraparenchymal hemorrhages may also occur in the setting of neoplastic disease, both in primary brain tumors and metastatic disease [68]. Indeed, acute neurologic deficits found to be due to a hemorrhagic metastasis may often be the initial presenting sign of the disease's existence. Additional causes within this category include hemorrhage due to sympathomimetic drugs such as cocaine (often ascribed to hypertension, as above); those due to head trauma with blunt or penetrating brain injury; and those due to systemic or primary cerebral arteriopathy (i.e., moyamoya), primary CNS or systemic vasculitis, infectious vasculitis, and infective endocarditis (i.e., due to rupture of a mycotic aneurysm) [69].

Subarachnoid Hemorrhage

Subarachnoid hemorrhage (SAH) is defined as bleeding into the subarachnoid space, between the pia mater—the delicate lining directly adherent to the surface of the brain—and the arachnoid membrane which overlies it. This space is usually occupied only by a small quantity of clear, colorless cerebrospinal fluid (CSF), which among other functions cushions the brain from injury and plays a key role in

autoregulation of cerebral blood flow at the arteriolar level [70]. When blood is introduced to this space, it causes marked painful irritation of the meninges and may obstruct the normal flow of CSF. (see Fig. 2.5) [70, 71]. Craniocerebral trauma is overall the most common cause of SAH, while aneurysm rupture (saccular or berry) accounts for over 80 % of nontraumatic SAH [72]. Other less common etiologies include perimesencephalic (presumably venous) hemorrhages, arterial dissections, vascular malformations, drug abuse, coagulopathies, and sickle-cell disease [73].

The estimated annual incidence of SAH varies greatly with the population studied and with other demographic and geographical factors. In a recent meta-analysis the pooled incidence of SAH was 10.5 per 100,000 person-years, and in the United States alone 30,000 new cases are reported every year [74]. The relative risk of developing SAH is increased with alcohol intake, hypertension, smoking, and history of a first degree relative with SAH [74]. The prevalence of intracranial aneurysm in the general United States population is 0.5–1.0 % [74]. After an episode of aneurysmal SAH, only 80 % of patients reach the hospital alive, 30 % die during their hospital admission, and only about 16 % ultimately regain independence without cognitive deficits. Overall, less than 50 % of independent patients return to their prior level of work after SAH [75].

Hydrocephalus, vasospasm, cerebral salt wasting, stress cardiomyopathy, neurogenic pulmonary edema, and delayed cerebral ischemia are among the common complications encountered following aneurysmal SAH. Due to the need for frequent patient monitoring after the ictus and the high risk of poor neurologic outcomes and death if these conditions are not treated expectantly, patients presenting with aneurysmal SAH are best cared for in the setting of a Neurosciences Intensive Care Unit [76]. SAH patients are often young and had high functional status at baseline prior to their hemorrhage [77]; as such, of all the patients in the hospital, these patients may have the most to lose.

Conclusion

Stroke—whether ischemic or hemorrhagic—is a disease with many faces. A small-vessel lacunar infarct which involves the deep subcortical white matter may produce nothing but a subtle arm weakness, but an identical lesion located in the upper pons might result in a persistent vegetative state. One patient with paroxysmal atrial fibrillation might present with a dozen infarcts in numerous vascular territories, while another with the same arrhythmia presents instead with isolated transient vision loss. The variety in clinical manifestation can be dizzying; however, with the application of clinical data and some pathophysiology, this protean disease can be thought of as caused by just a few basic etiologies, briefly outlined above.

Due to the unique needs of this population, the stroke patient requires a high level of specialized care, which must be provided by an interdisciplinary team. A good working knowledge of the fundamentals of neuroanatomy and cerebrovascular anatomy is crucial to caring for this patient population and to preventing future events.

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