

Development, Anatomical Variations, and Clinical Implications of The Circle of Willis: A Review Article

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ABSTRACT

The Circle of Willis (CW) (also known as Willis' circle, loop of Willis, Willis's polygon, or cerebral arterial circle) is a polygonal arterial network that forms a vital anastomotic system at the base of the brain, ensuring collateral blood flow between the anterior and posterior cerebral circulations. It is conserved across several vertebrate species, including birds, reptiles, and mammals, and is named after the English physician Thomas Willis (1621–1675). Its embryological development involves a coordinated sequence of vascular remodeling events derived from the primitive internal carotid and vertebrobasilar systems, establishing the mature cerebral arterial configuration during early gestation. However, substantial anatomical variations exist, with the classical complete configuration found in only about one-third of individuals. These variations significantly influence cerebral hemodynamics, affecting compensatory mechanisms in vascular occlusion and susceptibility to pathological changes. Consequently, they hold major clinical implications in the pathophysiology and management of aneurysm formation, ischemic stroke, subarachnoid hemorrhage, and other cerebrovascular disorders. Understanding the developmental origins, morphological diversity, and functional consequences of these variations is therefore crucial for improving diagnostic accuracy, guiding neurosurgical and endovascular interventions, and enhancing patient outcomes. This review aims to summarize the embryological development of the CW, delineate common and rare anatomical variants, and explore the clinical implications of these differences in stroke, aneurysm pathogenesis, and neurosurgical or interventional practice.

Keywords: Circle of Willis, Embryological development, Anatomical variation, Aneurysm, Ischemic stroke.

INTRODUCTION

The Circle of Willis (CW), also referred to as the cerebral arterial circle, represents one of the most prominent and clinically significant anatomical structures within neurovascular anatomy. It is a polygonal arterial network situated at the base of the brain, serving as a critical collateral circulation system that interconnects the internal carotid and vertebrobasilar arterial systems. This unique arrangement ensures the maintenance of cerebral perfusion in the event of vascular obstruction or hemodynamic compromise. Notably, anatomical variations in the CW are observed in more than 50% of the population, and these deviations can markedly affect the efficiency and stability of cerebral blood flow. A thorough understanding of the CW's embryological development is therefore essential, as it provides valuable insight into the origins of these structural variations and elucidates their potential implications in cerebrovascular pathophysiology and clinical practice^[1].

The classic symmetric arterial ring known as the Circle of Willis (CW) is anatomically constituted by the anterior cerebral arteries (ACA), the anterior communicating artery (AComA), the internal carotid arteries (ICA), the posterior communicating arteries (PCoMA), and the proximal segments of the posterior cerebral arteries (PCA). This intricate arterial network serves as a critical collateral circulation system at the base of the brain, ensuring cerebral perfusion continuity in the event of vascular obstruction or hemodynamic compromise^[2] (Figures 1, 2).

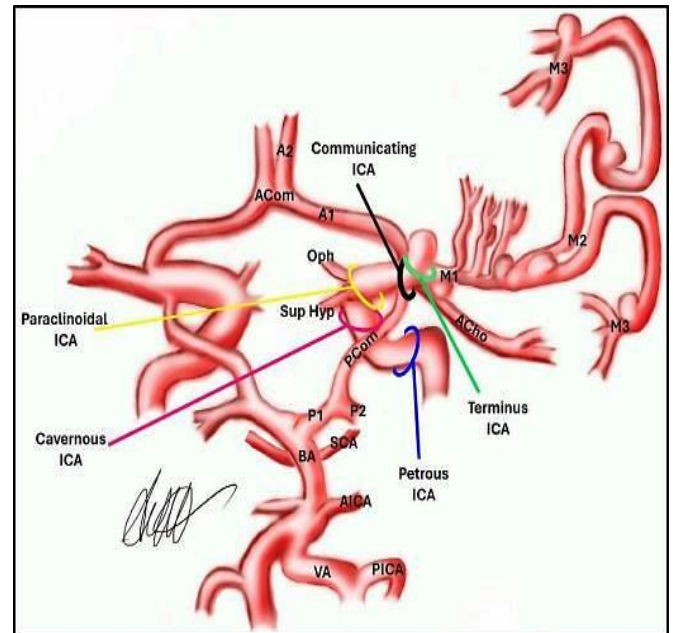


Fig. (1): Anatomy of the Circle of Willis^[3].

A1, A2: anterior cerebral artery, ACho: anterior choroidal artery, ACom: anterior communicating artery, AICA: anteroinferior cerebellar artery, BA: basilar artery, Cavernous ICA: cavernous internal carotid artery, Communicating ICA: communicating internal carotid artery, M1, M2, M3: middle cerebral artery, Oph: ophthalmic artery, P1, P2: posterior cerebral artery, Paraclinoidal ICA: paraclinoidal internal carotid artery,

PCom: posterior communicating artery, Petrous ICA: petrous internal carotid artery, PICA: posteroinferior cerebellar artery, SCA: superior cerebellar artery, Sup Hyp: superior hypophyseal artery, Terminus ICA: terminus internal carotid artery.

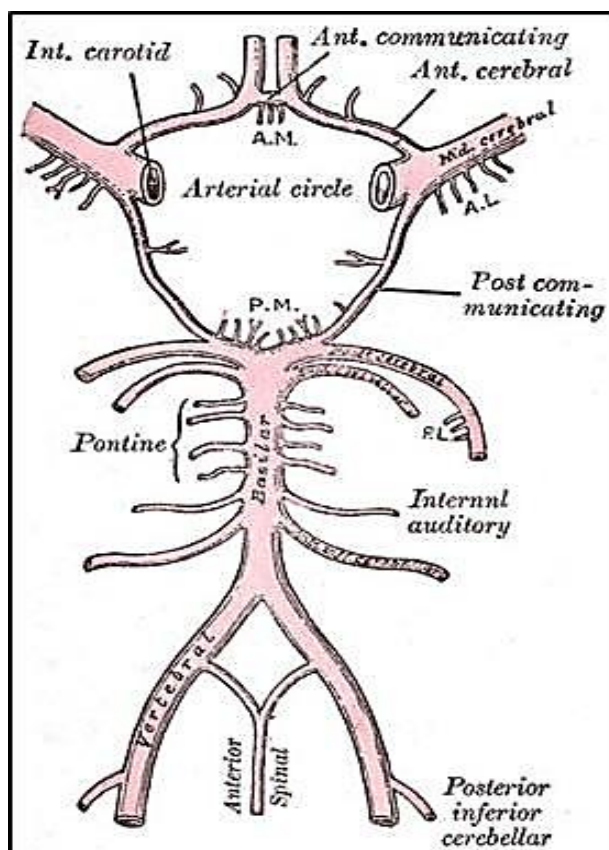


Fig. (2): CW is depicted in the upper half of the diagram of the arterial circulation at the base of the brain.

The figure demonstrates the complex interconnections among the cerebral arteries that ensure collateral blood flow. The abbreviations used in the diagram denote specific orientations and vascular branches: **A.L.** refers to the *antero-lateral* branches, **A.M.** to the *antero-medial* branches, **P.L.** to the *postero-lateral* branches, and **P.M.** to the *posteromedial ganglionic* branches. These designations correspond to the distribution of perforating arteries that supply the deep gray matter structures and adjacent white matter regions of the cerebral hemispheres [14].

However, the classical configuration of the CW is seldom observed in the majority of adults. Instead, a diverse array of anatomical variations is commonly encountered, reflecting the considerable morphological heterogeneity of the cerebral arterial system. Such deviations include hypoplasia, agenesis, and duplication of one or more arterial segments, as well as the presence of a fetal-type posterior cerebral artery (fPCA). These variants are not merely incidental findings but hold substantial clinical and hemodynamic implications, as

they may influence the efficiency of collateral circulation, alter cerebral blood flow dynamics, and affect susceptibility to cerebrovascular disorders such as aneurysms, ischemic strokes, and transient ischemic attacks [12].

These differences are significant because they affect collateral flow capacity in the case of arterial occlusion, increase the risk of aneurysm formation in certain locations, and are pertinent to endovascular and neurosurgery procedures. Understanding the development of CW aids in the explanation of these variations [12]. The posterior cerebral circulation becomes clearly delineated following contrast injection into the left vertebral artery, allowing visualization of the posterior segment of the arterial CW. This occurs through retrograde filling of the contralateral vertebral artery, basilar artery, and posterior communicating arteries, thereby outlining the complete posterior cerebral arterial network and demonstrating the collateral flow pathways that contribute to the hemodynamic integrity of the posterior circulation [15] (Figure 3).



Fig. (3): Evident posterior cerebral circulation, including the posterior part of the arterial CW following injection in the left vertebral artery [15].

Accordingly, this review is designed to achieve three principal objectives: first, to provide a comprehensive overview of the embryological development of the CW; second, to describe and categorize the most frequently observed anatomical variations within this arterial network; and third, to elucidate the clinical implications of these morphological differences, particularly in relation to cerebrovascular pathologies such as ischemic

stroke and aneurysm formation, as well as their relevance in neurosurgical and endovascular interventional practices.

DEVELOPMENT OF THE CIRCLE OF WILLIS

The establishment of the 6 pairs of branchial arch arteries marks the initial phase in the creation of the cerebral circulation. During early embryogenesis, the third pair of branchial arch arteries play a pivotal role in the development of the ICAs, which serve as the principal conduits of blood to the developing brain. The second branchial arch arteries partially contribute to the formation of the ventral pharyngeal arteries, which subsequently fuse proximally with the ICAs to form the common carotid arteries (CCAs). Around the 28th day of embryonic development, the ICA undergoes a division into anterior and posterior branches, marking a critical step in cerebral vascular differentiation. From the anterior division arise the anterior cerebral artery (ACA), middle cerebral artery (MCA), and anterior choroidal artery, which collectively supply the forebrain. Meanwhile, the posterior division gives rise to the PCA and the posterior choroidal artery, which primarily perfuse the midbrain and posterior cerebral structures. This complex and coordinated vascular differentiation establish the foundational architecture of the cerebral arterial system, culminating in the later formation of CW [6,7].

The development of the posterior cerebral circulation is initiated by the progressive growth and expansion of the brainstem and occipital lobes during embryogenesis. In the early stages of vascular formation, the hindbrain receives its arterial supply through a series of transient carotid–vertebrobasilar anastomoses, which include the trigeminal, otic, hypoglossal, and proatlantal arteries. These embryonic vessels establish critical connections between the internal carotid and vertebrobasilar systems, ensuring adequate perfusion during early neurovascular development. As maturation proceeds, the trigeminal, otic, and hypoglossal arteries undergo regression, while the proatlantal artery persists temporarily. The formation of the PComA subsequently provides a definitive link between the internal carotid and distal basilar arteries, thereby establishing the permanent configuration of the posterior circulation and contributing to the completion of CW [6]. At approximately 35 days of embryonic development, the middle cerebral artery (MCA) begins to emerge as a branch from the anterior division of the ICA. Concurrently, the ACA extends medially toward the midline, eventually giving rise to the AComA. The establishment of the ACA and AComA marks a critical stage in the maturation of the cerebral arterial network, signifying the structural completion of the CW. This developmental process typically reaches completion between the sixth and seventh weeks of gestation, by which time the major components of the cerebral

circulation are fully formed, providing the foundational arterial architecture that supports subsequent brain growth and vascular specialization [6].

ANATOMICAL VARIATIONS OF THE CIRCLE OF WILLIS (Figures 4, 5)

A completely formed and anatomically normal CW is found only in a relatively small proportion of individuals. In such cases, the CW exhibits a polygonal and bilaterally symmetrical configuration, ensuring optimal collateral circulation between the anterior and posterior cerebral systems. The ICA bifurcates at the medial end of the Sylvian fissure, giving rise to the anterior and middle cerebral arteries. The paired ACAs are interconnected at the anterior end of the longitudinal fissure through the AComA, forming the anterior segment of the circle. Posteriorly, the basilar artery divides at the ponto-mesencephalic junction into two PCAs, each of which is linked to the corresponding internal carotid artery via the PComA. This complete and symmetrical arrangement constitutes the classical configuration of the CW, providing an essential anastomotic network that maintains cerebral perfusion under varying physiological and pathological conditions [8]. CW exhibits a high degree of variation in vessel caliber, symmetry, and completeness. Common variations include:

I. Anterior circulation variations: Agenesis or hypoplasia of the AComA, fused or azygous ACA, duplicated AComA (up to 18% prevalence), and fenestration of the ACA or AComA (up to 21% prevalence) [6,9].

II. Posterior circulation variations: Fetal-type posterior cerebral artery (fPCA): PCA arises predominantly from the ICA instead of the basilar artery, hypoplastic or absent PCA, duplicated PCA or basilar artery, and persistence of primitive arteries (as persistent trigeminal artery) [10].

III. Classification of completeness: Complete CW (all components present and well developed, ~42–52% of individuals), anteriorly incomplete CW (absence of AComA or one ACA), posteriorly incomplete CW (hypoplastic or absent posterior communicating artery), and transitional forms (mixed defects in both anterior and posterior segments) [11,12].

In a study conducted by **Iqbal** [8], it was demonstrated that during routine autopsy examinations, 26 out of 50 examined Circles of Willis (52%) exhibited anatomical anomalies. These deviations from the classical configuration included attenuated vessels, characterized by hypoplasia of one or more arterial segments within the circle; the presence of accessory vessels, such as duplications or triplications of certain arterial components; anomalous embryonic origins of the PCA rising from the ICA instead of the basilar artery; and the complete absence of one or both PComAs. These findings underscore the high prevalence of morphological

variability in the Circle of Willis and highlight the significance of recognizing such variants in both anatomical and clinical contexts.

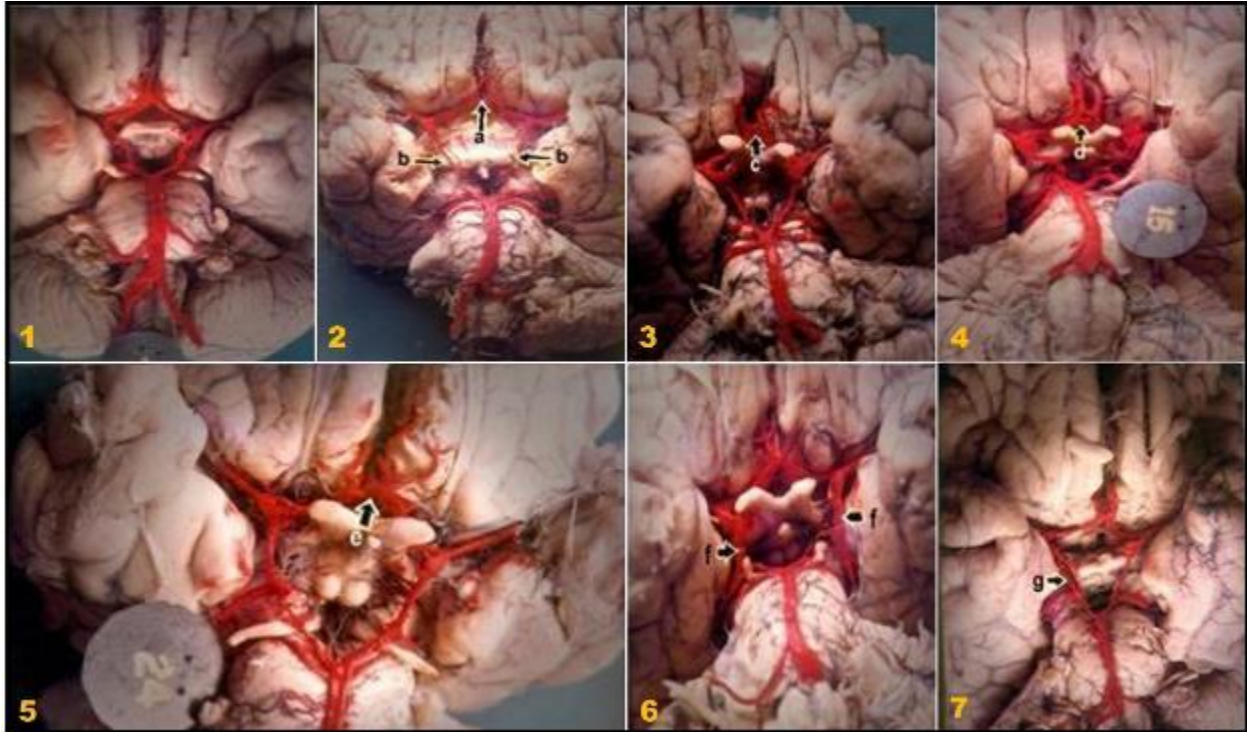


Fig. (4): Photographs exhibiting the various variations of the CW [8].

1. Normal CW, 2. Hypoplastic AComA (a) and posterior communicating artery (b), 3. Duplications of AComA (c), 4. Triplications of AComA (d), 5. Triplicate ACAs (e), 6. Bilateral embryonic origin of PCAs from ICA (f), 7. Unilateral embryonic origin of PCA from ICA (g).

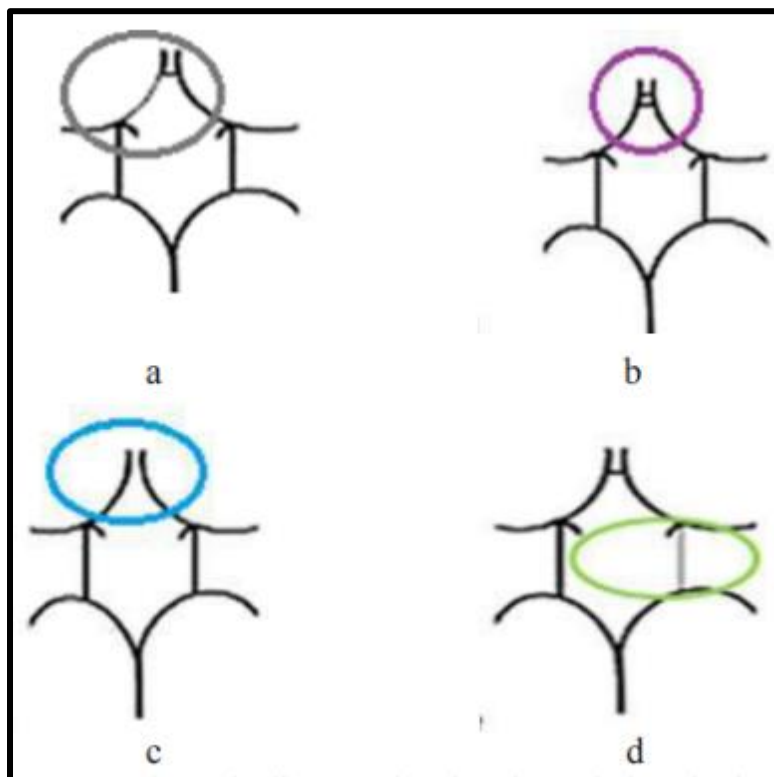


Fig. (5): Diagram illustrating variations of the CW [2].

(a) Hypoplastic ACA, (b) Double AComA, (c) Absent AComA, (d) Hypoplastic PComA.

SEX SPECIFIC ANATOMICAL VARIATIONS OF CW

Larger diameters in all semi-automatically measured CW arteries were observed to be significantly more predominant in males versus females. Furthermore, men demonstrated a higher frequency of a complete anterior CW configuration, indicating better-developed anterior circulation, whereas no significant sex-related differences were found in the completeness of the posterior CW. Aplasia or hypoplasia of the AComA was notably frequent among women, suggesting possible sex-related developmental differences in anterior cerebral circulation. Similarly, aplasia or hypoplasia of one PCA occurred more commonly in women; in contrast, aplasia or hypoplasia of both PComA was considerably more widespread among men, reflecting divergent vascular remodeling patterns between the sexes. No significant sex distinctions were detected regarding CW bifurcation angles or the presence of a fetal-type posterior cerebral artery (fPCA) in this large-scale study, which utilized Magnetic Resonance Angiography (MRA) scans from 1,052 individuals excluding intracranial vascular abnormalities. In this analysis, the diameters and bifurcation angles of major CW arteries (>1.2 mm) were quantified using a semi-automatic image processing tool, while the smaller AComA, posterior communicating arteries, and various anatomical CW variants were carefully assessed manually. Statistical comparisons of these anatomical variations between men and women were performed using Generalized Linear Models and logistic regression analyses, through appropriate additional modifications for potential confounding covariates to ensure robustness and validity of the findings ^[13].

CLINICAL IMPLICATIONS

More than just scholarly curiosity, anatomical variations of the CW have clinical applications in neurology, neurosurgery, and interventional radiology including:

1. Cerebral Collateral Circulation: A complete and symmetrical CW allows compensation during arterial occlusions. Variations, especially hypoplasia or absence of communicating arteries, reduce collateral potential, increasing susceptibility to ischemic events ^[14].
2. Intracranial Aneurysms: Approximately 85% of intracranial aneurysms happen in the CW region, particularly at arterial bifurcations such as the AComA, PComA, and MCA bifurcation. Embryological vascular

wall defects and hemodynamic stresses contribute to aneurysm formation ^[15].

3. Ischemic Stroke and Hemodynamics: Individuals with incomplete CW have limited collateral flow, predisposing them to larger infarct volumes. Fetal-type PCA is linked to posterior circulation infarcts and altered perfusion patterns in internal carotid artery occlusion ^[9].

4. Migraines: Several studies have identified significant correlations between specific anatomical variations of the (CW) and the occurrence of migraines. These associations are particularly pronounced in cases involving posterior CW variants and migraines with aura, a subtype characterized by transient neurological disturbances preceding headache onset. Variations such as hypoplasia or absence of one or more PComA or an incomplete posterior circulation have been implicated in altered cerebral perfusion and reduced collateral flow, potentially predisposing individuals to cortical spreading depression—an established mechanism underlying migraine aura. Moreover, emerging evidence suggests a hereditary component, with familial patterns of migraine linked to inherited structural variants of the CW, reinforcing the role of cerebrovascular anatomy in migraine pathophysiology ^[16].

4. Neuroimaging and Surgical Relevance: Advanced imaging (Magnetic Resonance Angiography, Computed Tomography Angiography, and Digital Subtraction Angiography) aids in identifying CW variants preoperatively. Recognition of these variants is critical during aneurysm clipping, carotid endarterectomy, or bypass surgeries ^[17].

From a clinical perspective, these anatomical variations have significant implications. Incomplete or variant configurations may reduce the CW's ability to provide adequate collateral flow during cerebral ischemia, increasing the risk of stroke, aneurysm rupture, or poor outcomes following vascular surgeries. Therefore, preoperative evaluation using MR angiography or CT angiography is strongly recommended for patients undergoing neurovascular interventions ^[18,19].

CONCLUSION

At the base of the brain, the CW is a striking illustration of collateral redundancy and vascular architecture. However, there is a great deal of variation in its structure, and many of these variations can be linked to the creation, fusion, and regression of vessels throughout embryonic development. Understanding the typical developmental sequence aids doctors and

anatomists in deciphering the wide range of adult configurations they see. Practically speaking, differences in the CW are important for aneurysm formation, stroke risk, and neurosurgical/interventional planning. In the era of high-resolution vascular imaging, it is the responsibility of practitioners to recognize the range of anatomical variance in order to incorporate that into patient therapy.

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