Diverse structural and functional changes occur within blood vessels during hypertension. In relation to vascular structure, hypertension is generally associated with hypertrophy (increased cross-sectional area of the vessel wall) in aorta and other large arteries but inward remodeling (with or without increases in the cross-sectional area) in smaller resistance vessels. Inward vascular remodeling, which represents a rearrangement of the vessel wall around a smaller lumen (Figure), has been described in models of hypertension and, thus, blood flow. Thus, inward remodeling may have change likely has the greatest impact on vascular resistance and, thus, blood flow. Thus, inward remodeling may have greater functional consequences than vascular hypertrophy.

In this issue of Hypertension, Cipolla et al describe novel observations of changes in cerebral vascular structure brought on by hypertension during pregnancy. The findings highlight the dynamic nature of vascular remodeling under these conditions. In their study, female rats were made hypertensive using the common approach of chronic treatment with an inhibitor of NO synthase ($N^\omega$-nitro-$L$-arginine methyl ester). Administration of $N^\omega$-nitro-$L$-arginine methyl ester increased arterial pressure and produced inward remodeling of small cerebral arteries with no change in the cross-sectional area of the vessel wall (ie, eutrophic inward remodeling; Figure). When the animals then became pregnant, the reductions in vessel diameter that had occurred during hypertension were largely reversed (Figure). Because arterial pressure was not altered by pregnancy, this important determinant of vascular structure did not appear to play a role in these changes.

Previous work from this group demonstrated that pregnancy prevented changes in cerebral vascular structure in response to subsequent hypertension. However, these are the first findings showing that pregnancy also reverses preexisting inward vascular remodeling.

Previous studies have tested whether experimental interventions could prevent structural changes in the vasculature during hypertension. For example, treatment with a thiazide-like diuretic prevents vascular hypertrophy without preventing inward vascular remodeling in spontaneously hypertensive rats. These findings and others suggest that mechanisms that produce vascular hypertrophy differ from those that produce inward vascular remodeling. Previously, very few studies have evaluated the regression (reversibility) of inward vascular remodeling.

Many studies continue to model changes in vascular structure using aorta in vivo or aortic smooth muscle in cell culture. Although these approaches are valuable and may help to define mechanisms that contribute to vascular hypertrophy, they may not be optimal if the goal is to model the 3D rearrangement that occurs with inward remodeling in resistance vessels during hypertension. Despite the fact that inward vascular remodeling may have a greater impact on hemodynamics, few studies have examined mechanisms that produce inward remodeling during hypertension.

What mechanism(s) accounts for inward remodeling in the cerebral circulation during hypertension? Is the same mechanism involved in the regression of vascular remodeling during pregnancy? Although oxidative stress plays an important role in producing hypertrophy in cerebral arterioles, oxidative stress may not produce inward vascular remodeling. One mechanism that may play a key role in promoting this process involves the renin-angiotensin system. For example, hypertrophy of cerebral arterioles occurs in models of angiotensin II–dependent and angiotensin II–independent hypertension, but inward vascular remodeling occurs only with angiotensin II–dependent hypertension. Thus, angiotensin II may be a key determinant of inward vascular remodeling. Because vascular responses to angiotensin II are generally reduced during pregnancy, it seems possible that regression of cerebral vascular structure during pregnancy may reflect a loss or withdrawal of angiotensin II–mediated effects that promote inward vascular remodeling.

Activity of the transcription factor peroxisome proliferator-activated receptor-$\gamma$ (PPAR-$\gamma$) may be another important determinant of vascular structure. Previous work suggested that pharmacological activators of PPAR-$\gamma$ prevent inward remodeling of small mesenteric arteries during angiotensin II–dependent hypertension. Mice that express a human dominant-negative mutation in PPAR-$\gamma$ exhibit hypertrophy...
Hypertension is a common complication of pregnancy, and pregnancy predisposes the brain to greater edema formation during acute hypertension. Cerebral vascular features of eclampsia are often similar to those seen in hypertensive encephalopathy and include breakthrough of autoregulation, marked cerebral vasodilation, and disruption of the blood-brain barrier. Seizures are a hallmark of eclampsia, and seizures produce these same physiological responses (acute hypertension and maximal cerebral vasodilation with disruption of the blood-brain barrier). Some forms of hypertension produce inward remodeling of small cerebral arteries and arterioles. By causing regression of this remodeling, pregnancy may predispose the blood-brain barrier to disruption and formation of cerebral edema during acute hypertension or seizures (Figure).

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