

## Cerebral small vessel disease

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Small and large arteries of the brain are affected by different diseases. Large arteries are arbitrarily considered those with a diameter of more than 0.1 mm and comprise the carotids, vertebral and basilar arteries, as well as the components of the circle of Willis. Diseases of the large cerebral arteries and their consequences are well known: atherosclerosis, thromboembolic events, and subarachnoid hemorrhages. Together, large vessel disease accounts for about two-third of symptomatic strokes. Recently, substantial gains in stroke prevention have been accomplished, and these gains mainly apply to large vessel disease. These gains are mostly based on the fact that, due to the caliber of the vessels, a) segments at risk for occlusion or rupture can be detected with imaging modalities and b) affected segments can be reached for interventions using surgical or endovascular techniques.

Small vessel diseases affect arteries with a diameter smaller than 0.1 mm, and together they account for one-third of symptomatic strokes. The inability to directly visualize these blood vessels *in vivo* has contributed to the relative lack of awareness of small vessel disease among clinicians, and to the lagging behind compared to large vessel disease in terms of recent therapeutic gains. The two most prevalent small vessel diseases are arteriolosclerosis and cerebral amyloid angiopathy (CAA).

Arteriolosclerosis is characterized by thickening of and damage to the wall of arterioles. This disease is associated with chronic hypertension and affects the flow territories of the perforating arteries of the thalamus and basal ganglia in particular. These vessels are more prone to the consequences of high blood pressure because the blood pressure of the circle of Willis is directly transmitted to these thin-walled arteries that directly branch from the circle of Willis, whereas the arterioles in other parts of the brain the blood pressure is much lower, since these vessels are the result of a gradual branching of the arterial tree. The first response of the arterioles to the elevated blood pressure is proliferation of smooth muscle cells, and later degeneration and necrosis occurs in the vessel wall. The consequences of these changes are hypoperfusion (due to narrowing of affected blood vessels and loss of autoregulation) and hemorrhages (due to increased brittleness of affected vessels) that characteristically occur in the thalamus and basal ganglia. Large parenchymal hemorrhages, smaller hemorrhages (also known as “microbleeds”), and lacunar infarcts in these areas are the radiological hallmarks of arteriolosclerosis.

CAA also is an arteriolar disease, but unlike arteriolosclerosis, it does not affect arterioles in the thalamus and basal ganglia, but rather those on the surface of the brain in the leptomeninges and cortical gray matter. In CAA amyloid accumulates in the vascular wall, probably as a result of disturbances of the metabolism and clearance of amyloid from the brain. Accumulation of amyloid induces changes in the vascular wall. These changes comprise fragmentation and microaneurysm formation, luminal narrowing, loss of smooth muscle cells, and perivascular inflammation, and they can give rise to hemorrhages, hypoperfusion, and vasculitis. The prevalence of CAA increases with age, and up to 40% of the elderly have CAA at autopsy. Furthermore, CAA is found in about 80% of patients with Alzheimer’s disease. Up to one-third of spontaneous intracranial hemorrhage in the elderly is based on CAA, and there is an increasing awareness of the contribution of CAA to dementia in the elderly. The radiological hallmarks of CAA are large hemorrhages and

microbleeds with a lobar distribution, and leukoencephalopathy with or without inflammatory changes.

In conclusion, although relatively unknown, cerebral small vessel disease constitutes a major threat to public health, in particular in the ageing Western societies. Once familiar with the radiological manifestations of these diseases, they can be identified in many patients.