



Small Vessel Diseases of the Brain: Pathological Definition & Classification

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Introduction

Apart from involvement of **large cerebral arteries** (Extracranial vessels supplying the brain and intracranial vessels in the subarachnoid space) which account for the majority of CVD cases, there remain a number of diseases in which the vascular lesions affect relatively **small blood vessels**, often **at many sites throughout the neuraxis**.

Definition

- Small vessel diseases are diseases of the **vessel wall**
- They must be separated from **hematological diseases compromising the vascular content** (coagulopathies and occlusive diseases, hemorrhagic diatheses and myeloproliferative disorders) which may have comparable clinical presentation.

Definition

In its broadest sense, the “**cerebral microcirculation**” includes parenchymal and leptomeningeal arteries (arterioles), veins (venules), and capillaries.

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Definition

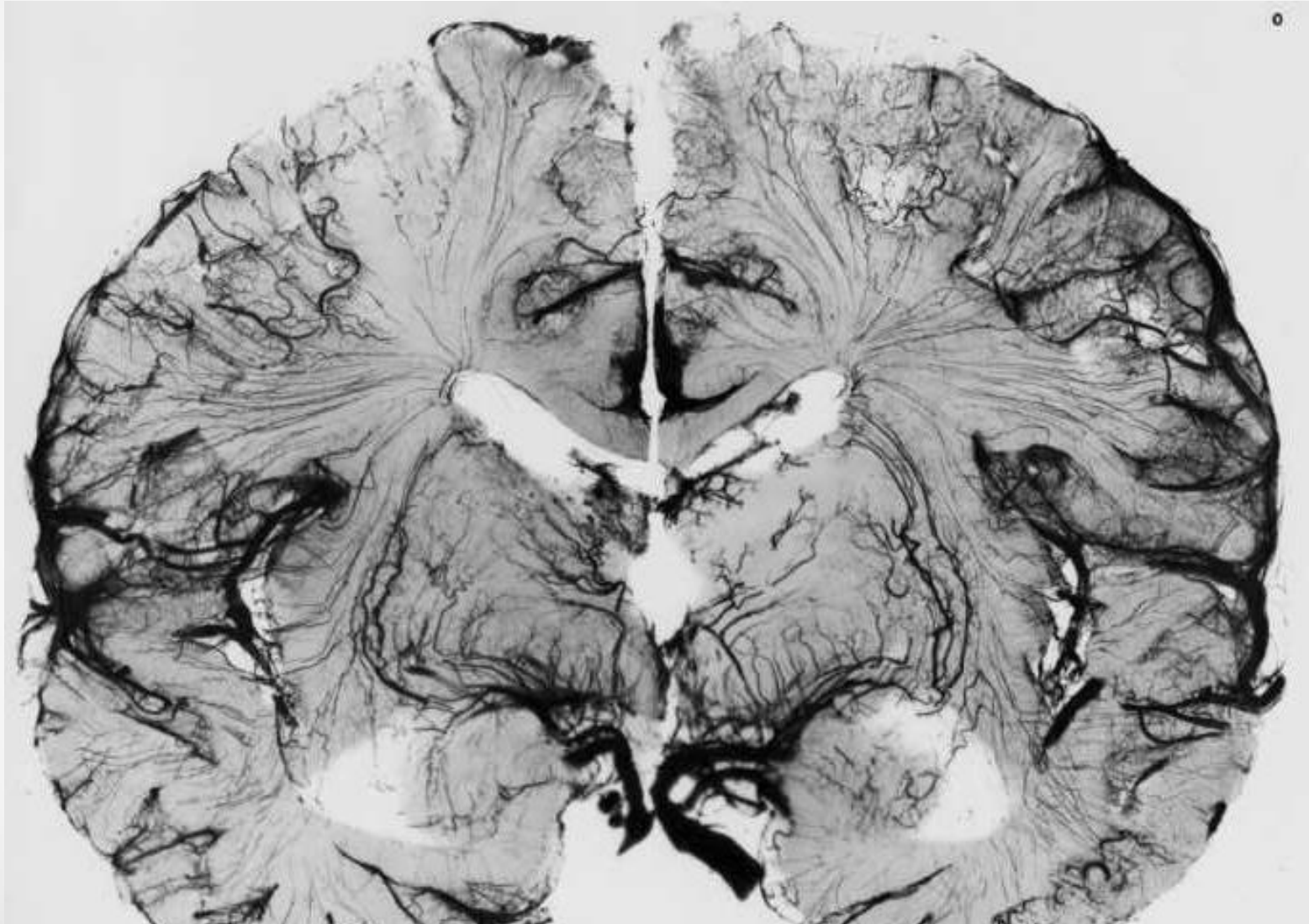
Arbitrarily, **CNS « small vessels »** are defined as:

- *Brain intraparenchymal* vessels -- including perforating arteries derived from the circle of Willis and small veins
- *Leptomeningeal* small arteries and veins

In fact “small cerebral vessels diseases” involve predominantly **arterioles and small arteries**

Distribution of small cerebral arteries

(India ink injection showing penetrating intraparenchymal vessels)



Small arteries or arterioles include perforators with diameters from 40 to 400 μ m

Distribution of small cerebral arteries

(India ink injection showing penetrating intraparenchymal vessels)



Mostly end arteries with limited collateral anastomoses until the capillary network

Diseases of small cerebral vessels

- Diseases of cerebral small vessels are associated with a variety of ischemic and/or hemorrhagic manifestations .
- These result in variable clinical neurologic syndromes:
 - Stroke-like sudden onset of focal signs
 - Progressive, multifocal disease
 - Diffuse, non-focal, gradually progressive disease, with cognitive and/or psychiatric manifestations

Diseases of small cerebral vessels

Some of these conditions **affect predominantly or exclusively the CNS**, whereas others are **systemic vascular disorder** which involve the brain and spinal cord along with other organ

Diseases of small cerebral vessels

The development of new radiologic imaging methods has enhanced awareness of these important causes of neurologic morbidity.

Correlation between the findings of neuroimaging data and neuropathology is important and may identify characteristic pattern of abnormality.

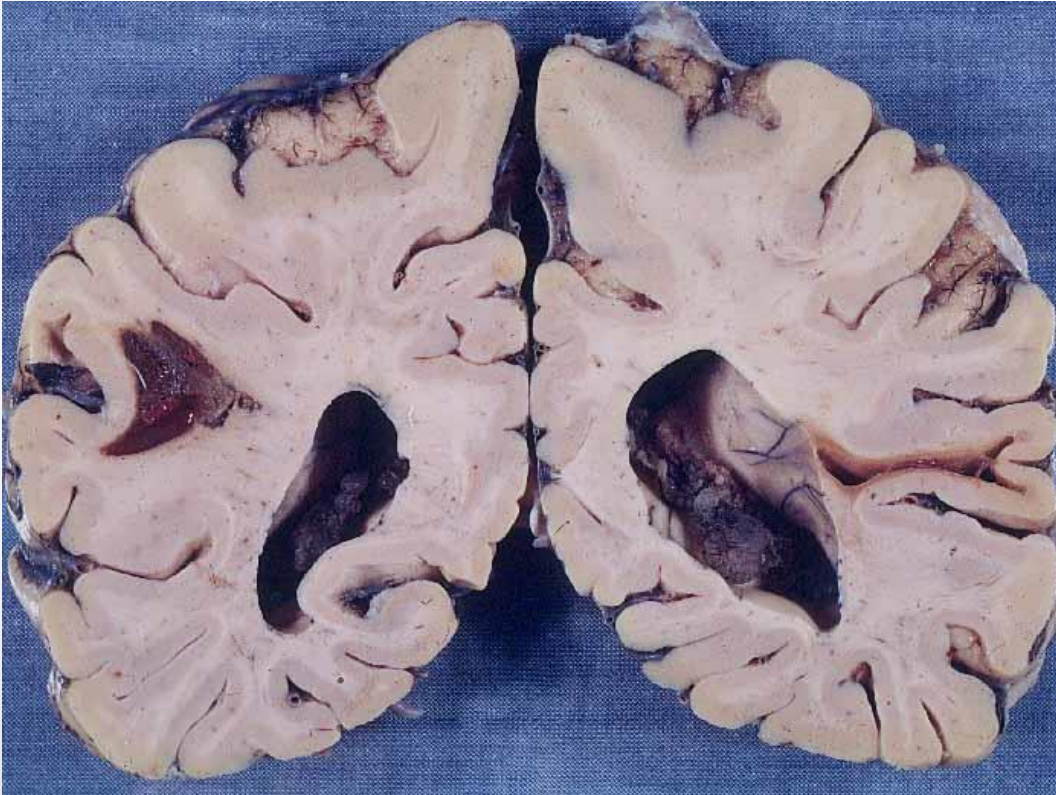
[Wardlaw JM, Smith C, Dichgans M. Mechanisms of sporadic cerebral small vessel disease: insights from neuroimaging *Lancet Neurol* 2013; 12: 483-97]

Diseases of small cerebral vessels

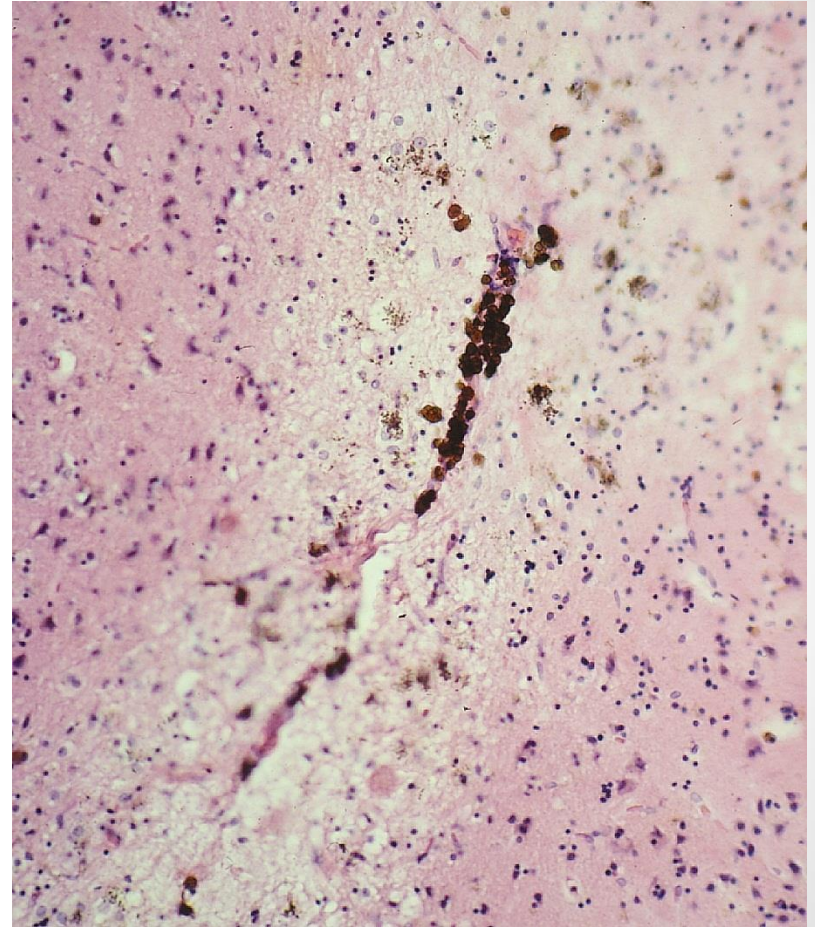
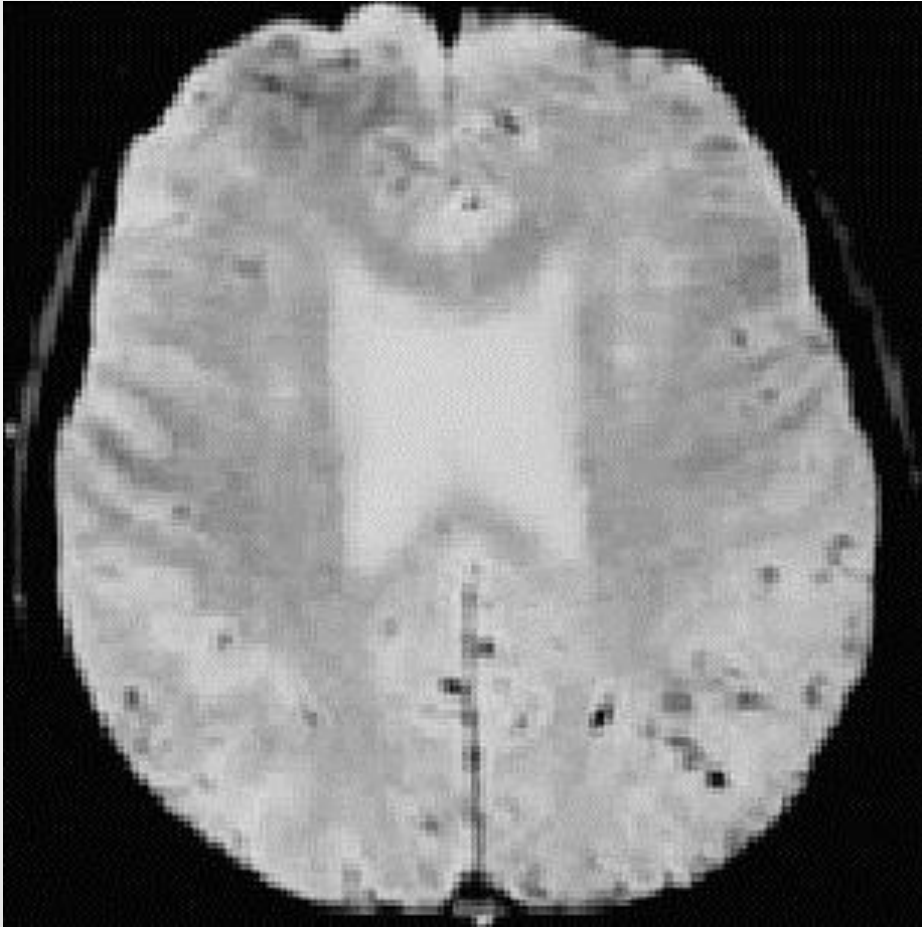
- Characteristic parenchymal changes in cerebral small vessels diseases include :
 - Small hemorrhages, and microbleeds,
 - Lacunes,
 - Status cribrosus (état criblé)
 - Arteriopathic leukoencephalopathies.

[Hauw JJ, DeGirolami U, Vinters HV: Neuropathology of Vascular Disease
In: F. Gray, C. Duyckaerts, U. DeGirolami Escourolle and Poirier *"Manual of Basic Neuropathology 5th edition"* 2014 , Oxford University Press, pp 76-113]

Small Hemorrhages

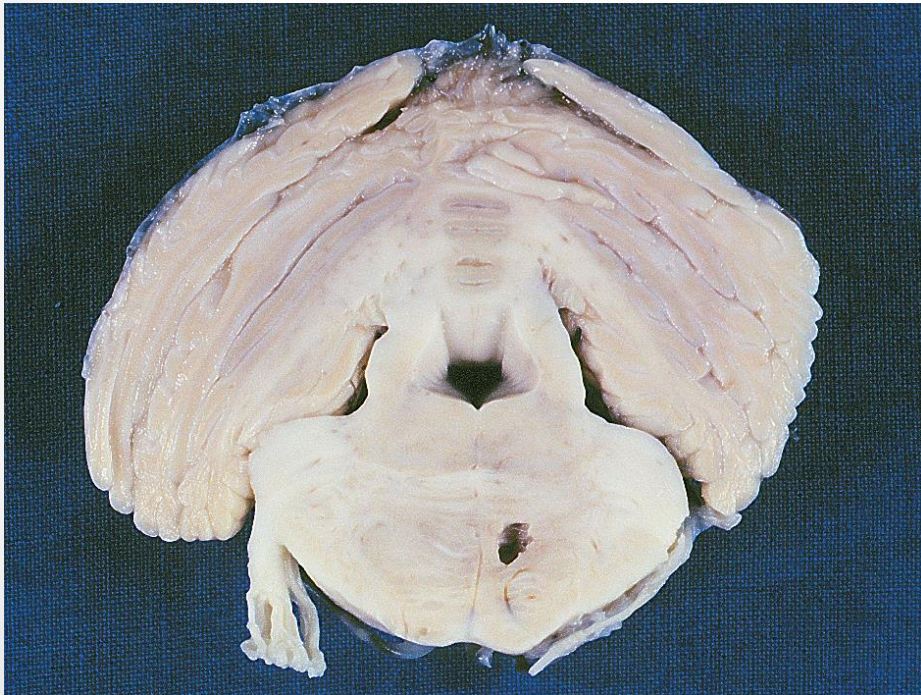


Microbleeds

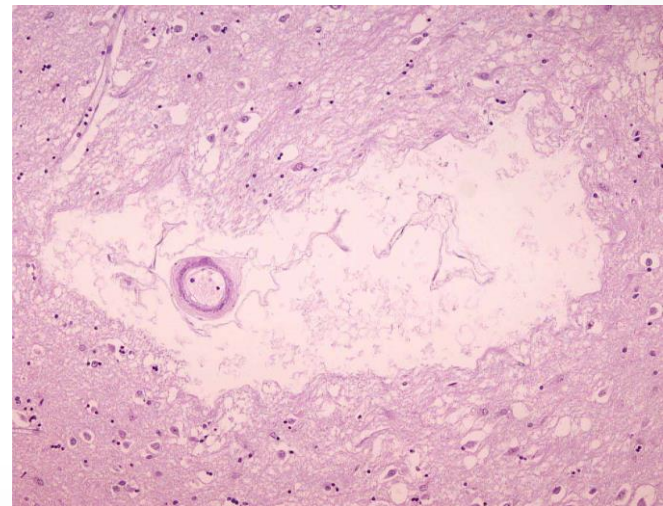
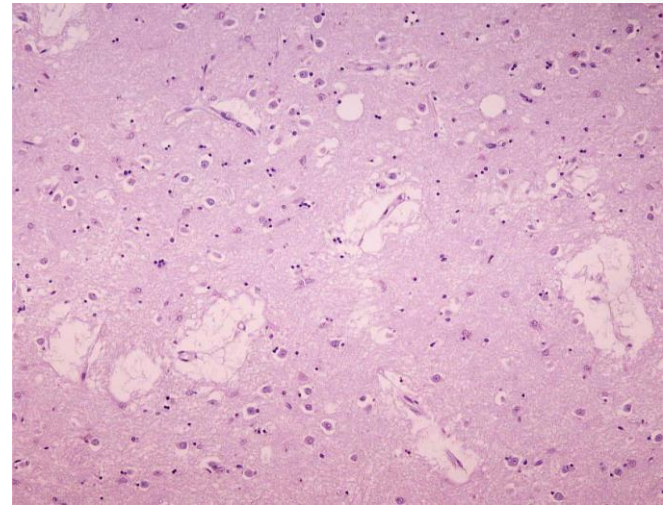
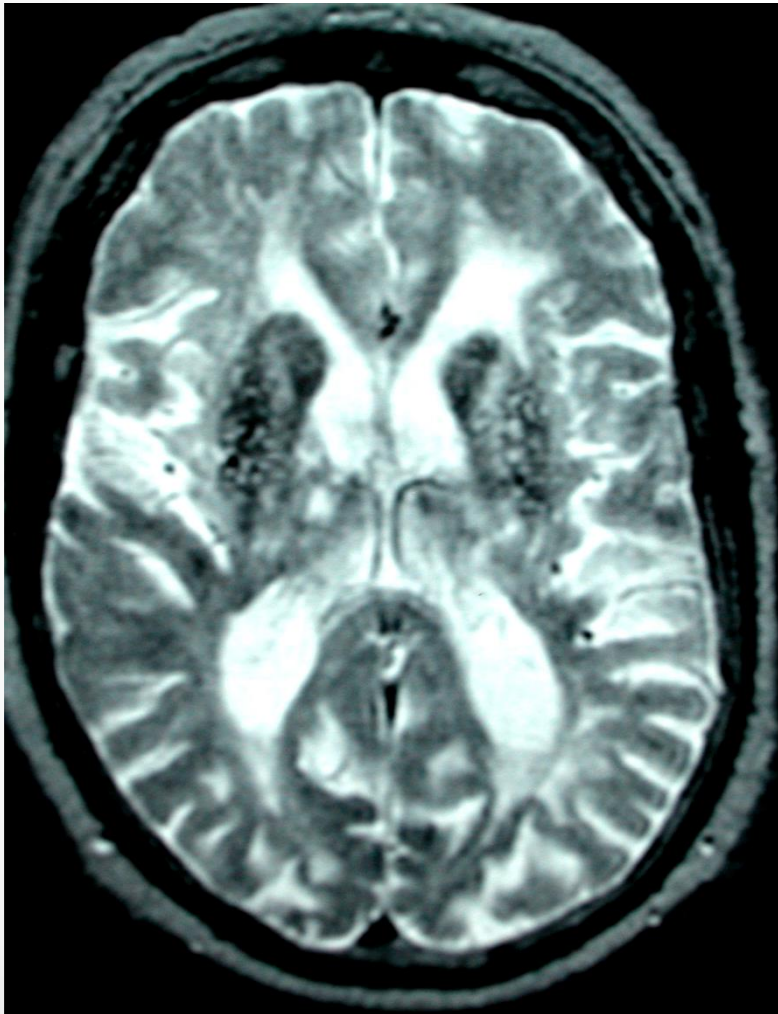


T2 Star

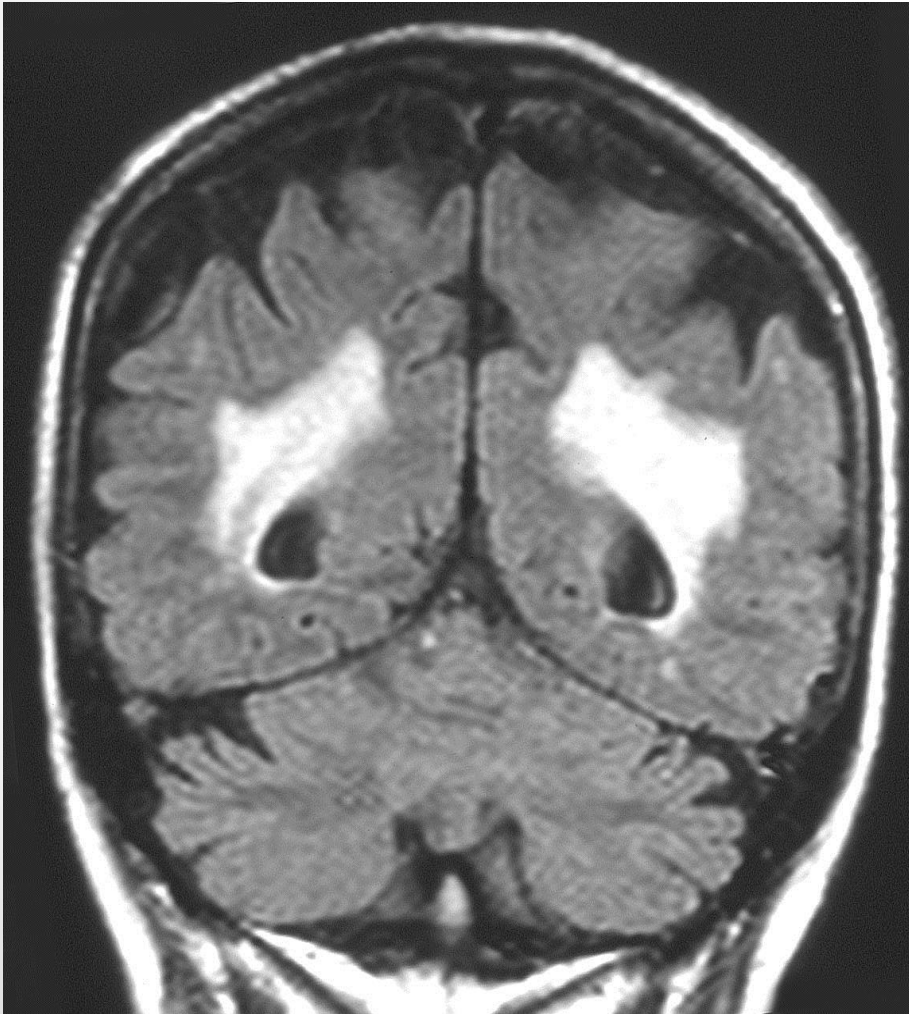
Lacunes



Status cribrosus (état criblé)



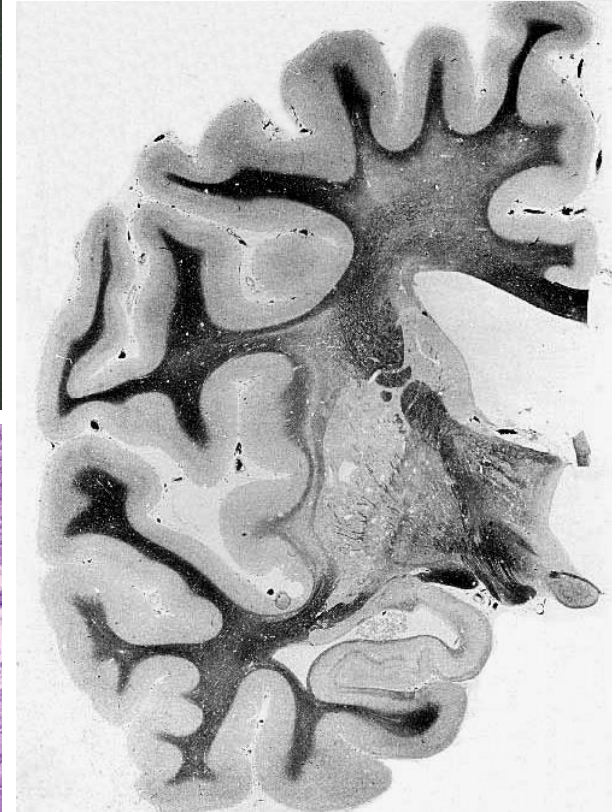
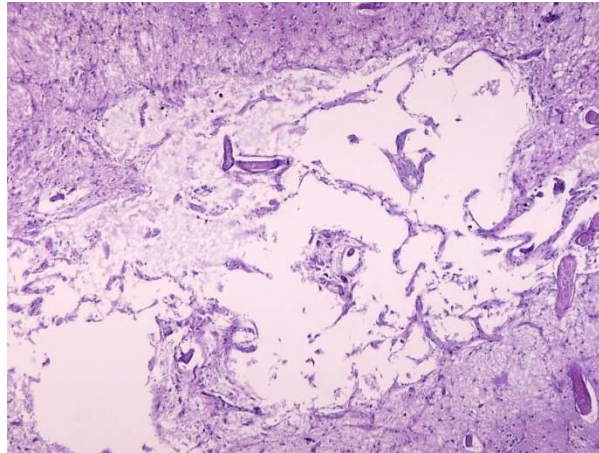
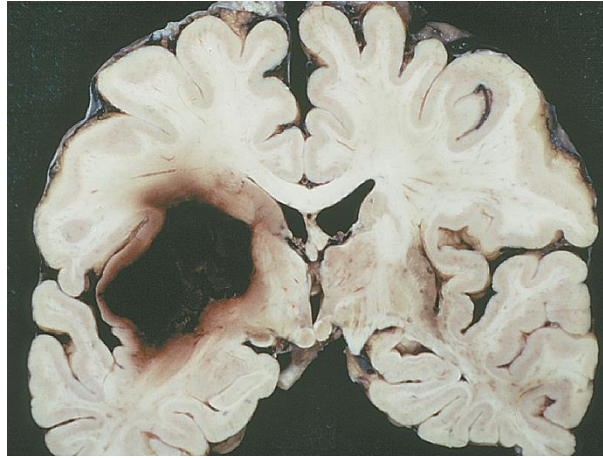
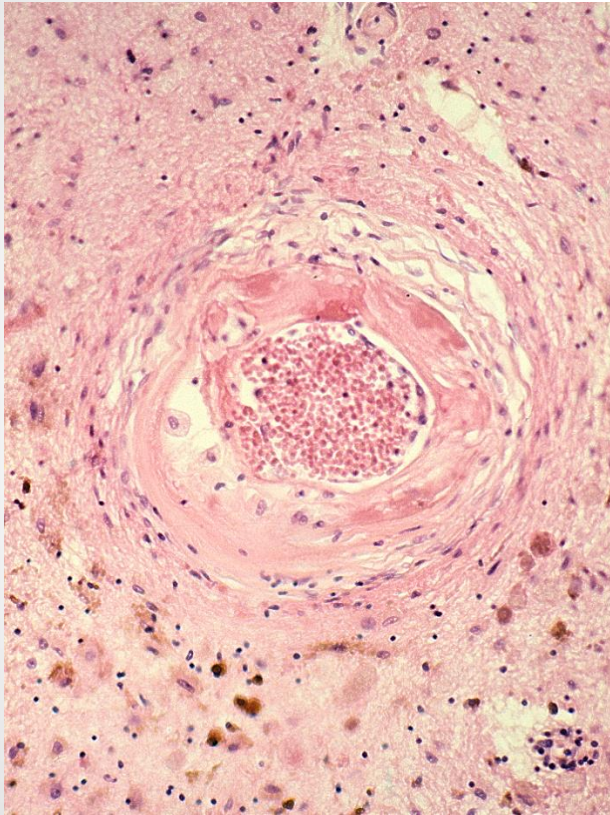
Arteriopathic Leukoencephalopathy



Classification

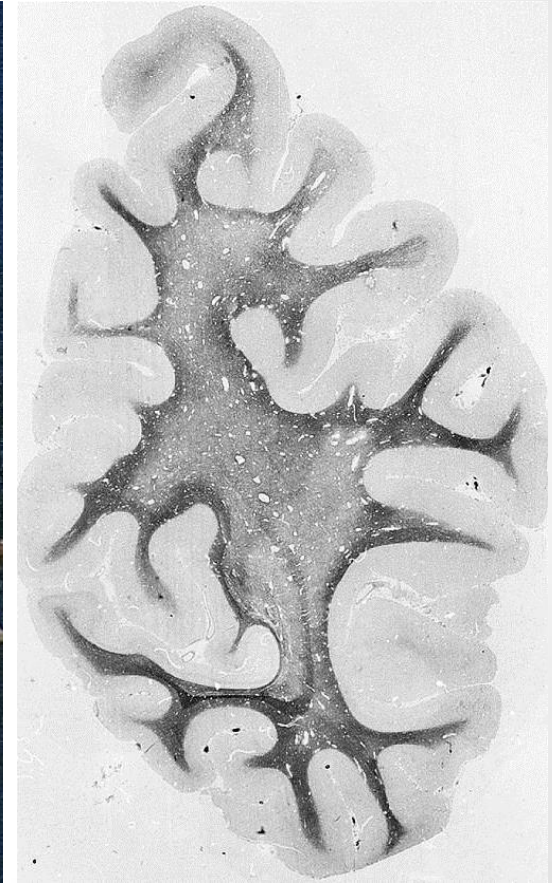
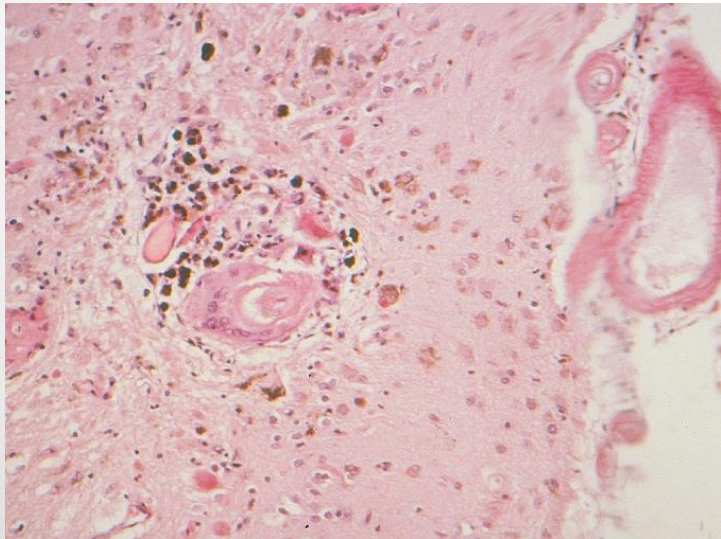
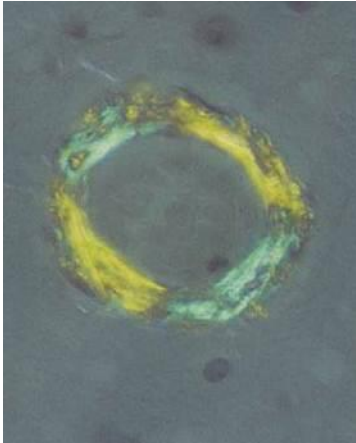
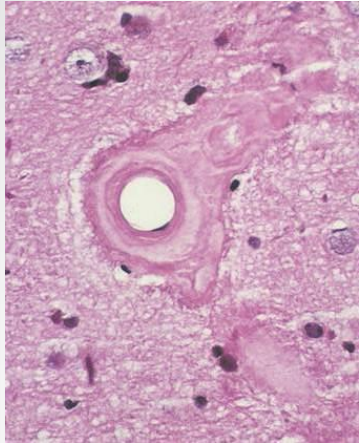
- Arteriosclerotic cerebrovascular disease (SVD)
- Cerebral Amyloid angiopathy (CAA)
 - Sporadic
 - Hereditary
- CNS vasculitis
- Non amyloid hereditary diseases of cerebral small vessels

Arteriosclerotic cerebrovascular disease



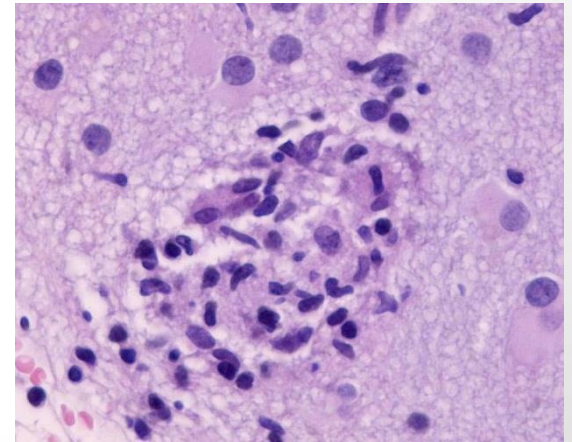
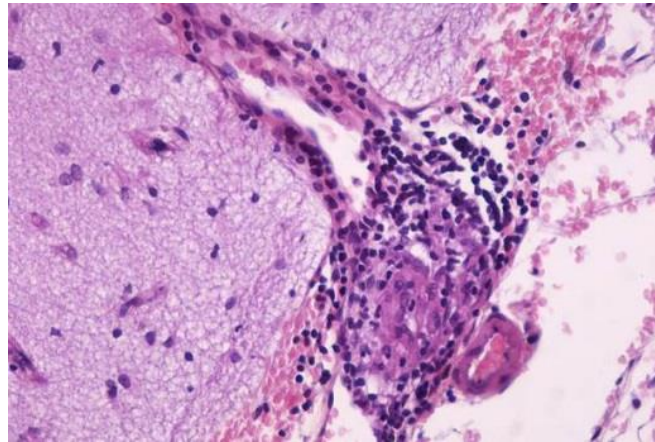
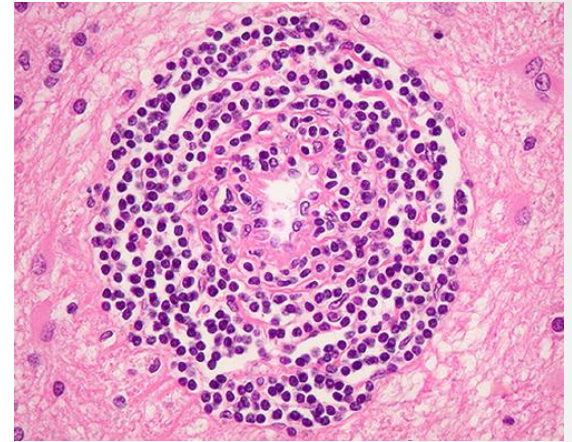
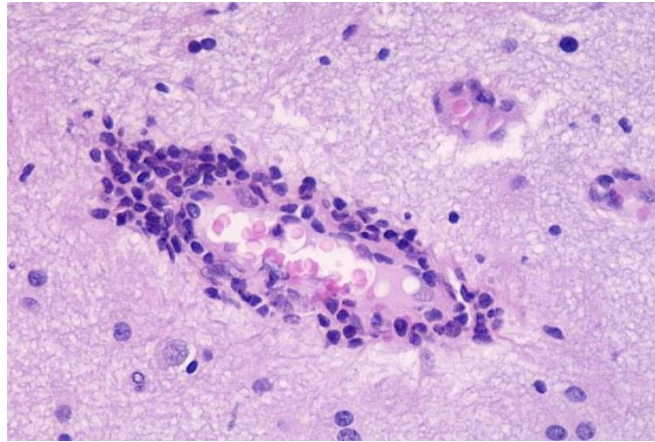
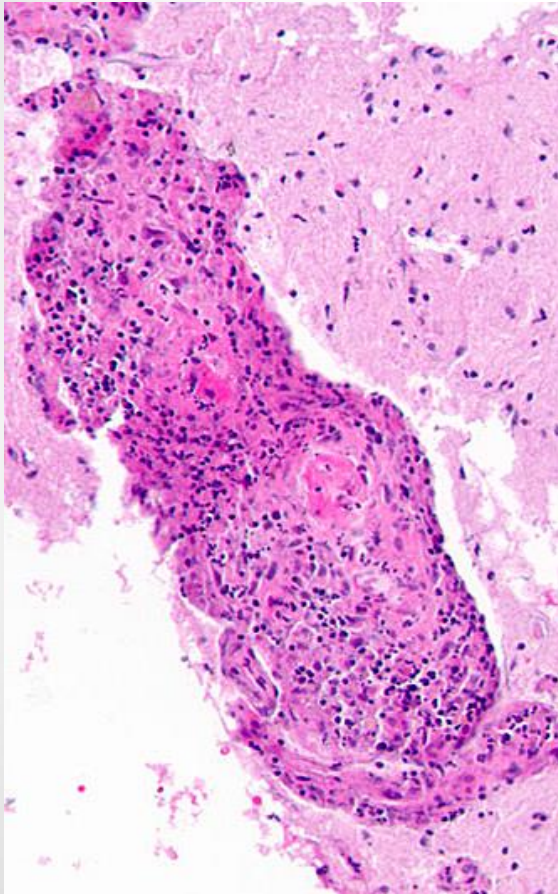
Lammie GA. Hypertensive cerebral small vessel disease and stroke. *Brain Pathology* 2002 12: 358-70

Cerebral Amyloid Angiopathies CAA



Yamada M. Cerebral amyloid angiopathy :emerging concepts. *J Stroke* 2015; 17:17-30.

Cerebral Vasculitis



Hajj-Ali RA, Calabrese LH: Diagnosis and classification of central nervous system vasculitis. *J Autoimmun* 2014;48-49:149-152; **Adams HP Jr:** Cerebral vasculitis. *Handb Clin Neurol* 2014;119:474-94

Non Amyloid Hereditary DCSV

Autosomal Dominant

- CADASIL, (NOTCH3)
- Retinal vasculopathy with cerebral leukodystrophy
- COL4A1 et COL4A2 mutations -
- SVD mapping to chromosome 20q13
- Swedish hMID & PADMAL

Autosomal Recessive

- CARASIL,
- Leukoencephalopathy Calcifications and Cysts

X-linked recessive : Fabry disease

Mitochondrial : MELAS