Cerebrovascular disease: Historical background, with an eye to the future

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If clinicians are to understand where they are now and where they are headed, they must know where they and their predecessors have been. History adds a broadening dimension to knowledge, including knowledge of cerebrovascular disease. Here is a quick survey of progress in cerebrovascular disease, from the earliest days.

THE PAST

400 BC–1700 AD: Emphasis on prognosis, early exploration of brain and vascular structures

Hippocrates wrote aphorisms (circa 400 BC) related mostly to prognosis. **Galen** (131–201 AD) dissected animals, and he related diseases and prognoses to various body humors. **Andreas Vesalius** (1514–1564) based his *De Humani Corpis Fabrica* on dissections of human cadavers. His work contained 15 diagrams of the brain. **Johann Jakob Wepfer** (1620–1695) wrote a popular treatise on apoplexy and showed that bleeding into the brain was an important cause. He described occlusive disease of intracranial arteries. **Sir Thomas Willis'** (1621–1675) dissections of the brain were drawn in detail by Sir Christopher Wren in his *Cerebri Anatome*. Willis was a busy clinician who described migraine and transient ischemic attacks.

1800–1925: Emphasis on pathology and disease

Giovanni Battista Morgagni (1682–1771) was the father of clinicopathologic explorations. His *De Sedibus et Causis Morborum per Anatomen Indagatis* (*On The Seats and Causes of Disease, Investigated by Anatomy*), published in 1769, contained 70 letters describing necropsied cases. The first volume was *Diseases of the Head*. Morgagni described diseased arteries and "serous" and "sanguinous" apoplexies.

John Cheyne (1777–1836) published *Cases of Apoplexy and Lethargy with Observations upon the Comatose Diseases*, which emphasized the pathology in the brain, including brain softenings and subarachnoid and intracerebral hemorrhages.

Richard Bright (1759–1858) in 1831 published an atlas that included a volume on brain and nervous system disease. He collected 200 neurological cases and specimens.

Rudolph Virchow (1821–1902) described the phenomenology of arterial thrombosis and embolism and recognized the important interaction between the blood and the arterial wall. Virchow clearly showed that vascular occlusions caused infarction.

Sir William Osler (1849–1919) began as a pathologist and recognized the clinical and pathologic features of bacterial endocarditis, cerebral palsy, aphasia, and brain infarcts and hemorrhages.

1850–1950: Focus on vascular anatomy and clinical-anatomic correlations

This period focused on how the brain works as seen from vascular cases. Vascular anatomy was explored by **Duret**, **Stopford**, **Foix**, **Duvorny**, and others. Brainstem syndromes were described by **Weber**, **Benedikt**, **Claude**, **Millard**, **Gubler**, **Babinski**, **Nageotte**, **Foville**, and **Wallenberg**.

Jules Dejerine (1849–1919) was a master of clinico-anatomic correlations and described the clinical findings in patients with various brainstem lesions. He also described the syndrome of alexia without agraphia in a patient with a posterior cerebral artery territory infarct.

Charles Foix (1882–1927) dissected and described the clinical features and usual anatomic

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distributions of *ramollissements* (brain softenings) caused by disease of the middle, anterior, and posterior cerebral arteries and the anterior choroidal arteries. He defined the blood supply of the brainstem and the arteries of the posterior circulation.

1927–1975: Interest in the pathology and pathophysiology of vascular lesions begins

Charles Foix and colleagues noted in 1927 that most arteries supplying infarcted brain regions were not completely obstructed; they posited embolism, insufficiency, and vasospasm as possible explanations.

Raymond Adams and **Charles Kubik** in 1946 described the clinical and pathologic findings in patients with basilar artery occlusions found at necropsy. They discussed the morphologic differentiation between in situ thrombosis and embolism.

C. Miller Fisher described the pathology in arteries underlying lacunar infarcts, brain hemorrhages, and carotid artery occlusions. Fisher also clearly described the clinical features in patients with carotid artery disease, lacunar infarcts, and brain hemorrhages at various sites.

1978 to today: Stroke registries and databases begin and flourish

Computers facilitated the collection of series of patients with cerebrovascular disease. The first published prospective registry, the Harvard Stroke Registry (Mohr and Caplan, 1978), was begun before CT scanning became available. The Stroke Data Bank (Mohr, Caplan, Hier, Wolf, Price) and the Lausanne Stroke Registry (Bogousslavsky) followed and represented experience at one or more hospitals. Now large stroke registries are available in nearly every country. More recently, the German Stroke Data Bank has come to contain a wealth of cases collected in an entire country.

■ THE PRESENT: Technology, epidemiology, treatment, and evidence-based medicine in a managed care environment

Technology is rapidly improving and still developing. CT and MRI allow delineation of the location and type of lesion, while CTA, MRA, and extracranial and transcranial ultrasonography (TCD) allow definition of arterial lesions. Echocardiography, cardiac rhythm monitoring, and blood analysis detect cardiac, aortic, and hematologic causes of stroke. Neurologists of today can quickly and safely define the cause and extent of cerebrovascular disease.

Epidemiologic studies worldwide define stroke risk factors and factors related to prognosis.

This is the era of therapy. The introduction of thrombolysis and endovascular treatments focused attention on rapid delivery and throughput of patients. Randomized therapeutic trials are considered essential to provide a true evidence base for treatment of stroke patients. Statisticians are kings. At the same time, managed care directors and insurers control the purse strings.

■ THE FUTURE: Predictions and wishes

- More hospital-based cerebrovascular disease and ICU-type neurology specialists will be trained. The need for rapid evaluation and treatment means that neurologists with experience and training in cerebrovascular disease must be in the hospital and available to accomplish optimal management. Community-based practitioners and non-neurologists cannot do it because of time constraints and lack of knowledge and experience with acute stroke cases.
- Endovascular interventions will become more and more prominent.
- Stem cells and other multipotential cells and growth factors will become important therapeutic tools.
- Use of genetic information will proliferate. Physicians will be able to study individual patients' genetic makeup to predict risks and to take measures to reduce those risks. Study of the genetics of vascular disease will identify new treatment strategies. Endovascular introduction of genetic materials may play an important role in treatment.
- The obsession of the past decades with randomized, double-blind trials as the only way to determine treatments will cool. Many conditions are too uncommon or too diverse to lend themselves to trials. In order to please statisticians, trials often lump together heterogeneous situations so that answers are not very helpful for physicians who must treat individual patients. Patients are complicated, and many psychological, social, personal, and other variables not studied in trials influence treatment decisions.
- Recovery and rehabilitation will be given more attention and will be based on a more solid sci-

entific foundation.

- Hopefully, the medical community will wake up to the fact that strokes are very complex. Whenever possible, stroke patients should be guided to facilities that have the following:
  1) Physicians available 7 days a week, 24 hours a day, who are trained and experienced in caring for stroke patients
  2) Advanced modern technology that can quickly and safely image the brain and causative vascular lesions
  3) Protocols for rapid throughput and treatment.

  Criteria should be published for categorizing stroke care facilities in a fashion similar to the present practice for trauma centers.
- As with coronary artery and peripheral vascular disease, physicians will begin to learn that stroke is a vascular disease. To care for stroke patients, the causative cardiac–cerebrovascular–hematologic causes need to be defined. This is not possible with only a CT scan. Vascular studies are required.