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AJNR Am J Neuroradiol 1980, 1 (3) 271-273
http://www.ajnr.org/content/1/3/271.citation

Editorial

A New Image For the Neuroradiologist

Before the advent of transmission computed tomography (CT), the neuroradiologist needed only to view the human brain as a vascular tissue punctuated by ventricles and cisterns and wrapped in an envelope of gray matter. White matter diseases were of little practical consequence. Dr. Lucien Rubinstein's address on the pathology of white matter disease at the 1978 meeting of the American Society of Neuroradiology was testimony to the neuroradiologist's CT-inspired transformation into the complete cerebral morphologist. Now techniques for noninvasive diagnosis of carotid disease [1], CT measurement of cerebral blood flow (CBF) [2, 3], and positron imaging of brain circulation and metabolism [4]—and the potential physiologic applications of nuclear magnetic resonance [5]—challenge the neuroradiologist to be born again in yet another role, that of physiologist.

Physiology has always been a part of neuroradiology. Greitz [6] and Leeds and Taveras [7] studied the contrast arteriovenous circulation time as an index of cerebral blood flow. du Boulay et al. [8] investigated the effects of physiologic factors on angiographic findings. Davis et al. [9], Hilal [10] Taveras [11], and others have explored techniques for measuring regional CBF. And all neuroradiologists systematically examine the arteriogram for evidence of hemodynamic change as well as using contrast-enhanced CT scans to evaluate the integrity of the blood-brain barrier. However, in routine use the standard neuroradiologic tools are inefficient for providing physiologic information; physiologic data are secondary spin-offs of an exercise in structural imaging. Now, neuroradiology is faced increasingly with imaging techniques that primarily display physiologic data or that show structure, but are diagnostically inconclusive without additional information from a physiologic monitoring system.

How the neuroradiologist deals with these new techniques will help determine the shape that neuroradiology takes in the future. The common denominator of all previous neurologic tests has been that they largely facilitate in vivo clinicopathologic correlations, which serve as the basis for diagnosis. The next generation of testing will emphasize clinicophysiologic correlations, which are required for designing specific therapy for many neurologic disorders.

To place these trends in perspective this editorial will review some points in the development of neurologic testing. It will then discuss relevant aspects of positron imaging and noninvasive diagnosis of carotid disease to illustrate types of physiologic measurements that may be important to neuroradiologists. All clinical examples will relate to ischemic stroke disease, but the arguments should not be construed as being limited to this problem.

Until now, the history of the development of neurologic tests has been largely the history of neurodiagnosis, which is based on description of the pathologic features of a disease entity and of the clinical signs and symptoms that identify the pathologic process. Special diagnostic procedures have been extensions of the eyes, ears, and fingers, helping both to elucidate new diseases and aid in their clinical recognition. They have permitted clinical neuroscience to realize diagnostic goals that date back to the early 19th century. However, for treatment capability to match diagnostic capability, tools are required that provide physiologic data as efficiently as present tools give structural information.

In 1868, Sir William Gull wrote: "Diagnosis ultimately rests upon an exhaustive pathology. Without a *knowledge of what is possible in disease*, diagnosis must be defective . . . Moreover, a knowledge which seems exhaustive today may, in the changing circumstances of the world, be defective tomorrow" [12]. When the 19th century opened, effusion into the brain was the only recognized cause of neurologic disease. Hydrocephalus was an example of serous effusion and cerebral hemorrhage an example of sanguinous effusion. In 1820, Rostan [13] first disturbed this unified view by introducing the concept of brain softening (infarction) based on correlation of clinical deficits with

pathologic findings. In 1823, he suggested that ischemia might cause brain infarction because he frequently found that "the vessels destined to bring blood and life to the affected part, are ossified" [14].

Such advances in our "knowledge of the possible in disease" continue to come from correlations of clinical findings with postmortem examinations. The recent elaboration of the clinical syndrome of lacunar disease by Fisher [15] is based entirely on modern applications of this classic technique. But increasingly in the 20th century new neurodiagnostic tools have helped contribute to innovative clinicopathologic insights. For example, arteriography led to the recognition of carotid disease as a cause of stroke. Fisher [16] undertook the clinicopathologic correlations that resulted in his description of the clinical syndrome of carotid disease partly because: "Since the introduction of carotid arteriography many unexpected cases of occlusion of the internal carotid artery have been discovered."

Neurodiagnostic testing, which permits one to probe pathology in the intact patient, was born in the nineteenth century out of the marriage of clinical observation and pathologic examination of the brain. Its gestation was characterized by the quixotic activities of the phrenologists, who recognized the effects of the developing brain on the skull and tried to interpolate information about brain structure by palpating the bumps on the head. The early phrenologists were serious and highly respected scientists who were interested in how brain configuration related to intelligence, character traits, and behavior. Their comparisons of personal history and skull features with the results of pathologic dissections were tantamount to the first systematic neuroscience attempts at clinicopathologic correlation and at localization of brain function.

By palpating the skull the phrenologists were attempting to noninvasively *see* the brain in vivo, which has been the end-point of all neurodiagnostic endeavors ever since. The modern neurologic examination, which developed largely from 1850 to 1900, is a vehicle for noninvasively demonstrating disturbances in brain structure due to alterations in brain functions. The imaging modalities that preceded CT (table 1) demonstrate, often invasively, disturbances in brain structure due to alterations in tissues such as brain vessels, cisterns, or ventricles. With the advent of CT it finally became possible to directly image both normal and abnormal brain tissue.

Gull [12] would have approved of the technologic evolution of neurodiagnosis for he recognized that "the advancement of diagnosis depends upon the capacity of medicine to make *anticipations of the probable with increasing certainty*." Diagnosis is the identification of a disease process. A process is a dynamic phenomenon. One cannot diagnose a process by a single clinical fact, neurologic finding, or static image. The identifying temporal and spatial profile of a disease must be wrought from often nonspecific data by assembling a characteristic constellation of symptoms, signs, and special procedure results. Each new neurodiagnostic test listed in table 1 has vastly increased the neuroscience capacity to make such constellations more specific, permitting one to "anticipate the probable" with ever greater certainty.

TABLE 1: **Periods Neurodiagnostic Tests Came Into General Use**

Period	Test
1850–1899	Neurologic examination
1900s	Skull film
1910s	Lumbar puncture
1920s	Myelography and pneumoencephalography
1940s	Electroencephalography
1950s	Angiography
1960s	Radionuclide brain scan
1970s	Computed tomography

For diseases such as ischemic stroke it might be asked towards what end we continually increase our diagnostic accuracy. Stroke treatment today remains essentially preventive. Diagnosis of an acute stroke presents a paradox described (for other circumstances) by Gowers [17] in 1885: "Our knowledge of the cerebral structure is at once far more than we can use, and far less than we need." What is needed to make the diagnosis of a stroke lesion bear direct therapeutic benefit is information on tissue physiology.

In the hours or days after an ischemic insult, the patient's neurologic deficit may be relatively stable and the results of his special neurodiagnostic tests normal. Yet rapidly evolving changes occur in CBF, metabolism, and tissue water. Techniques such as positron imaging have the potential to display acute changes in blood flow and metabolism in transverse section. If one can use positron technology to stage the physiologic severity of the stroke one can begin to assess possible therapy for each stage and compare the blood flow and metabolic responses to clinical outcome. Such clinicophysiologic correlations would be as important to designing specific therapy for stroke disease as clinicopathologic correlations are to its diagnosis. Initial work suggests the feasibility of using positron imaging techniques to provide the physiologic data for such correlations [18].

For neuroradiologists to be active in the appropriate application of positron techniques they need to understand the biochemical pathways in which the tracer agents they use are involved and how these pathways may be modified in disease states. A working knowledge of the aerobic and anaerobic glycolytic pathways must be retrieved from the dusty garrets of the brain, even if with a grim sense of déjà vu.

The field of noninvasive diagnosis of carotid disease [1, 19] brings a physiologic challenge to the neuroradiologist's home ground of diagnosis. The introduction of carotid imaging systems has particularly stimulated neuroradiologic interest in noninvasive assessment. However, to be clinically meaningful the imaging results require complementary physiologic information that may be obtained, for example, by a direct Doppler examination of velocity characteristics at the common carotid bifurcation and/or an indirect measure of distal flow effects. With the B-mode real-time imaging systems some lesions will lie out of reach of the transducer,

be hypoechoic, and/or be obscured by shadowing [20]. In these situations the use of a physiologic monitor to assess focal and/or distal hemodynamics will prevent a hasty misimpression based on the imaging results. Use of the physiologic tests in turn requires an understanding of the physical principles on which they are based, their sensitivity and specificity in different pathoanatomic situations, and the physiologic anatomy of the vascular beds being examined. The periorbital Doppler, for example, is of diminished sensitivity in the presence of a common carotid or combined internal and external carotid lesion on one side; oculoplethysmography might show normal results in the presence of bilateral internal carotid lesions. The Doppler examination at the common carotid bifurcation can be difficult in the presence of a chronic internal carotid artery occlusion, when the external carotid takes on the flow characteristics of the internal and shows compensatory dilatation. Two external carotid branches then can be confused for the normal bifurcation.

Noninvasive diagnosis of carotid disease does not replace arteriography, but permits better patient selection for this procedure. No single test is sufficient for effective noninvasive diagnosis of carotid disease. However, a battery of tests, which includes both anatomic and physiologic monitoring systems, can make the management of the stroke-prone patient more rational and cost-effective, and allow one to make anticipations of the arteriographically probable with increased certainty [19]. In addition, such a battery provides the means to identify early structural lesions and trace their progression in relation to local and distal hemodynamic change. Such findings will provide new insights into the natural history of carotid disease and mechanisms of stroke in patients with carotid lesions.

In the past, pathophysiology of human nervous system disease has had to be inferred largely from changes in the arteriogram and the fixed brain, and more recently from sequential CT studies. Increasingly, electromagnetic radiations are being used to define not only structure, but also physiology. Access to in vivo physiology as well as pathology will markedly enhance the capability of neuroscience to understand and treat neurologic disease. If the neuroradiologist approaches physiologic problems with the enthusiasm that he has given pathoanatomic correlations, he will no doubt play a major role in helping to open clinical neuroscience frontiers.

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