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Revisiting the blood-brain barrier.

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Revisiting the Blood-Brain Barrier

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Why study the blood-brain barrier? Because there is nothing more fundamental to the practice of neuroradiology than an understanding of this concept. It can be defined anatomically, physiologically, and chemically, and its alteration by disease, drugs, and radiologic contrast materials is evident daily in both the imaging and interventional procedures performed by neuroradiologists.

The invited review by Sage and Wilson which appears in this issue of *AJNR* (1) was originally felt to be too long for one issue: the intent was to divide and spread it over several issues. After reading it, I felt that its message would be lost if it were not published in its entirety, so that it could be read at one sitting rather than over a period of several months. That is why it appears as it does.

Neuroradiologic investigations of the blood-brain barrier began with the development of contrast materials for arteriography and myelography. Radiologists conducted some of the earliest studies of the effects of osmolality of contrast materials on the blood-brain barrier; these contributions led to the improved safety of ionic contrast materials and the development of the non-ionics.

Neuroradiologists were also instrumental in the study of blood-brain barrier changes brought about by different disease states. The angiographic, computed tomographic, and magnetic resonance enhancement characteristics of a variety of neoplastic, inflammatory, and ischemic entities in the central nervous system have been extensively investigated and described in the neuroradiologic literature. This body of knowledge also contains many studies of the complications caused by the effects of intraarterially, intravenously, and intrathecally administered contrast materials, and specifically how these are mediated by disruption of the blood-brain barrier.

In the year 1994, the message of this article is that research into the many aspects of this phenomenon is still the next frontier of our specialty.

The importance of the blood-brain barrier in understanding adverse reactions to contrast media during angiography is yet to be defined. How such factors as age, systemic blood pressure, ischemia, intracranial pressure, drugs, and various disease states affect the permeability of the blood-brain barrier to intravascularly delivered contrast material is still incompletely explored but is potentially important for the safe conduct of cerebral and spinal angiography and noninvasive imaging. The development of drugs to seal the permeability of the blood-brain barrier and protect the central nervous system from toxic effects of intravenously administered contrast media and chemotherapeutic agents can result from further study of this elusive boundary. Conversely, development of intravenously administered agents that cross the blood-brain barrier in diagnostically significant amounts, without causing central nervous system toxicity, may enable opacification of the cerebrospinal fluid and, ultimately, noninvasive myelography.

The interventional neuroradiologist needs to understand how the blood-brain barrier operates, especially when it is intentionally disrupted for the intraarterial delivery of chemotherapeutic agents to highly selective areas by the endovascular route, or when various radiopharmaceuticals are used to measure regional cerebral blood flow during and after induced temporary vascular occlusion.

In an era when cost containment in medicine is so important, it is time to take the knowledge we have accumulated about the blood-brain barrier and apply it to the problem of achieving a diagnostic degree of contrast enhancement on a computed tomographic or magnetic resonance scan using less than the commercially recommended dose of contrast material. It may be that this can be achieved by administering intravenous contrast materials in conjunction with inexpensive agents that disrupt the barrier or delay the excretion of the contrast material. Perhaps adjusting the duration and rate of contrast-medium

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delivery, or the time interval between contrast administration and the acquisition of images, can produce this result. Permutations of all of the above suggest an infinite number of routes by which the study of this problem can be approached.

It is not difficult to imagine the impact on the global cost of imaging if the volume of contrast agents used for neuroimaging could be decreased without losing the sensitivity of lesion detection. Thorough understanding of the blood-brain barrier lies at the heart of such research.

These are a few of the ideas that are brought to mind by the review of Sage and Wilson. Their article is a fertile source of research ideas to be pursued by neuroradiologists, yet it deals with an area that is important to understand in order to direct and interpret neuroradiologic examinations effectively.

Twelve years ago this month, Dr Sage prepared a review on the same topic for this journal (2). This was at the start of the era of nonionic contrast materials and predated the era of magnetic resonance, paramagnetic contrast agents, and serious cost control in medicine. Therefore, for many reasons, it is an appropriate time for neuroradiologists to revisit the blood-brain barrier, and Sage and Wilson have helped us do this with a superbly organized, well-documented, timely, and readable manuscript.

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