New research on two fronts may bring significant changes to how physicians approach and manage hemangiomas in pediatric patients. Each represents an important advancement in hemangioma clinical research, but with different kinds of impact. This article explores the extent to which research may affect the trajectory of the standard of care for hemangiomas.

About PHACE
PHACE Syndrome was initially described in 1996, defining a set of findings in some children with hemangiomas of infancy that were found to have associated structural anomalies. PHACE is an acronym for Posterior fossa anomalies, Hemangioma, Arterial Lesions, Cardiac Abnormalities/aortic coarctation and Eye abnormalities. It had been suggested that infants with large facial or scalp hemangiomas be considered for the syndrome, but there had been no organized study of specific diagnostic criteria and limited study of associated problems. Two recent publications help to elucidate more details about the syndrome, greatly strengthening our ability to appropriately diagnose and manage these infants.

The first is a summary of the collective knowledge about PHACE syndrome with the consideration of future directions. Metry, et al. organized a multidisciplinary, collaborate research group, reporting findings and summarizing state of the art knowledge of the syndrome, including cerebral, vascular, and cardiac abnormalities. While PHACE syndrome is uncommon, it appears that it is probably much more common than Sturge-Weber syndrome, which is the association of port-wine stains (not hemangiomas) with ophthalmologic and central nervous system disease, even though SWS has been better studied and characterized. The paper discusses the findings of retrospective studies and expert experience with the hemangiomas and systemic associations.

The paper presents the most complete set of data on the findings that may be seen with the syndrome and is a useful reference to give to other specialists to assist them with “what they should be looking for” in evaluating a patient with possible PHACE syndrome. The authors conclude that infants with large facial hemangiomas should undergo magnetic resonance imaging/magnetic resonance angiograms (MRI/MRAs) of the brain and great vessels, echocardiograms, and ophthalmologic evaluations. Given the number of abnormalities and conditions associated with PHACE syndrome, the authors recommend ongoing research into the genes/pathways that may underlie the disorder. They argue that this may lead to a greater understanding of broader embryologic developmental pathways.

The second article, “Consensus Statement on Diagnostic Criteria for PHACE syndrome,” delineates the diagnostic criteria for PHACE syndrome. Based on the multidisciplinary expertise of diverse specialists, diagnostic criteria are broadly inclusive, with the definition of a facial hemangioma plus one or more extracutaneous feature defining either the PHACE syndrome diagnosis, or “Possible PHACE syndrome” label. A facial hemangioma greater than 5cm should prompt consideration of the syndrome. This plus one major criteria (a subset of cerebrovascular, structural brain, cardiovascular, ocular, or
ventral/midline anomalies) is considered diagnostic. Facial hemangiomas >5cm and one minor criteria, or neck or upper torso hemangiomas plus one major criteria or two minor criteria, or no hemangioma plus two major criteria are proposed to be “possible PHACE syndrome.”

The list of criteria also includes a vast number of associated abnormalities, including anomalies of major cerebral arteries, posterior fossa brain anomalies, aortic arch anomalies, specific eye findings, and sternal cleft malformations, as well as endocrinologic anomalies. These criteria help to establish a standard of care that will likely continue to evolve in coming months and years as more data on more specific elements become available.

Recommendations for evaluation are as listed above, though the authors have also left open the possibility of the need for endocrinologic evaluation of a subset of patients. While the standard of care is evolving, these papers are both a resource for healthcare professionals and a blueprint for appropriate evaluation and management.

A New Approach to Treatment?
The other substantial development in hemangioma research and care concerns the treatment of hemangiomas of infancy with propanolol and perhaps other beta blockers. The first documented use of propanolol for infantile hemangioma patients was published in June 2008.3 Initially using propranolol for cardiac and blood pressure changes secondary to systemic corticosteroids, the remarkable response in some patients to propanolol appeared much better than that to the corticosteroids. Some patients were treated with propranolol without prior glucocorticoid treatment, also showing excellent clinical response.

Since then, pediatric dermatologists have been abuzz about the possibility of this treatment in more severe cases of hemangiomas. Within the past year, clinical experience from around the world has indicated that patients have shown seemingly excellent response to the treatment.4,5 However, there have been some concerns about safety, and some significant adverse events have been observed.

One safety concern is that propanolol can lower blood pressure and have cardiac effects, such as hypotension and lethargy. Hypoglycemia has also been observed, as have seizures (perhaps secondary to hypoglycemia). Some cases have required emergency room care and resuscitation. As formal prospective studies have not been performed on hemangioma patients, the side effect profile in infants is unknown, and it is hard to counsel families about specific rates of adverse events. Although these instances are rare, they should be taken very seriously as researchers and clinicians begin to incorporate propanolol into the repertoire of treatment.

Importantly, there is a multi-center trial currently underway for propanolol to examine and hopefully establish efficacy, dosing, and a more defined side effects profile. This work may play a significant role in determining the role of propanolol in hemangioma therapy. In the interim, I recommended that physicians who are considering using propanolol in their practices use a standardized protocol and have a pediatrician or pediatric specialist share in patient care.

Experts in management of hemangiomas in children often consider propanolol as first-line therapy for functionally significant or deforming hemangiomas and may use it in “multi-modal therapy,” including systemic or intralesional corticosteroids, laser therapy, and other treatment modalities.

Ongoing Evolution
This is an exciting time in the evolution of the knowledge of hemangiomas, with new information that is very important in the diagnosis and management of a great number of children. As more data become available, there is no doubt that our collective understanding of hemangiomas will continue to improve as the standard of care evolves.

References: