What a useful tool the vascular anomalies classification described by Wassef et al\(^1\) would have been during my medical training! As a pediatric resident in the 1980s, I was frequently perplexed by the many red "birth marks" I was confronted with while performing newborn and well-child examinations. Despite a reassuring nod from attendings, who offered terms like "port wine stain" and "strawberry hemangioma," such gastronomic allusions did little to make sense of the nature of those unpredictable red vascular lesions. Most were red, flat "Angel's kisses", and faded with time, whereas a smaller percentage remained flat but darkened with age. Some presented as innocuous red spots in the first month or 2 of life, then mushroomed in color and size during early infancy. When queried by a concerned parent, I often felt unable to provide a clear diagnosis or prognosis.

At the same time, a conceptual breakthrough regarding pediatric vascular lesions was occurring in Boston. In 1982, Mulliken and Glowacki\(^2\) first proposed a more organized way of viewing "pediatric red spots." They elected to divide pediatric vascular lesions into 2 general categories: proliferative tumors and vascular malformations. Infantile hemangiomas fell into the former category, whereas port wine stains were thought to represent malformations of the cutaneous capillaries, resulting from inborn errors of vascular morphogenesis. This clarification of terms, and distinction between proliferative tumors and more static malformations, allowed us to provide families with a better sense of how their children's "red spots" might behave. Although hemangiomas might proliferate in a tumor-like fashion in early infancy, they would generally "burn out," involuting in early childhood. In contrast, the flat port wine stain might initially appear quiescent, but almost always persisted and darkened over time. A PWS in the forehead/V1 trigeminal area mandated a search for evidence of Sturge Weber syndrome. Port wine stains, in contrast to hemangiomas, often pose more of a problem with time, darkening, thickening, and sometimes developing small vascular papules during early adulthood.

This new understanding led to a breakthrough in our approach, as well as the first International Society for the Study of Vascular Anomalies (ISSVA) classification of vascular lesions in 1996.\(^3\) Experts in the field of vascular disease built on Mulliken and Glowacki's\(^2\) concepts, providing a more detailed approach to the classification and understanding of vascular anomalies. They noted that malformations could affect veins, arteries, or even lymphatics, and that some lesions were combinations of abnormalities of these vessel types. But rules (as well as classifications) were made to be broken (or amended), and Wassef et al\(^1\) have done just that with the latest ISSVA classification, summarized in this month’s journal. As our knowledge of the presentation, life cycle, histopathology, and radiologic characteristics of vascular lesions has grown, it has become clear that there are “exceptions and additions” to the 1996 classification. Not all vascular lesions are hemangiomas or malignancies; other tumors with borderline invasive or malignant qualities also have been identified. Port

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**Making Sense of “Red Birth Marks”**

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wine stains are better termed capillary malformations. They initially share clinical and histopathologic characteristics with the much more common (and less worrisome) nevus simplex (also known as Angel’s kiss), although their clinical course is quite different. More complex combinations of vascular malformations have been identified, as well as related syndromes involving diverse associated findings, such as macrocephaly or limb overgrowth. In addition, some lesions remain unclassifiable according to existing taxonomy, and the new classification acknowledges the limits of our understanding of these anomalies.

The new classification also addresses the most significant progress made in our understanding of vascular lesions: we now know the genetic mutations responsible for a number of vascular malformations, and often the molecular pathways affected. These include the genetic basis of heritable diseases such as capillary malformation–arteriovenous malformation RASA-1–related disease, as well as some sporadic overgrowth (PIK3CA) and vascular abnormalities that likely result from postzygotic somatic mutations. An appendix to the newest classification provides a list of all currently known mutations relating to vascular anomalies.

Wassef et al’s article is a useful new “guide” to the world of pediatric vascular lesions, and also serves as an excellent primer for anyone interested in this field. The new ISSVA classification is an interactive document available on the Web (www.issva.org) that provides clear discussions of the most common, as well as more esoteric vascular anomalies. The classification also uses hyperlink text to connect up-to-date terminology with the latest knowledge regarding known causal genetic abnormalities, as well as associated syndromes. It has helped transform a field previously mired in fuzzy terminology (no more strawberries or port wine!) into one that can now provide patients with a better chance at appropriate evaluation, diagnosis, and management. Weber et al’s article, with its description of the new ISSVA classification, is highly recommended reading for all of those pediatric residents currently wrestling with “red spots” in the neonatal nursery!

### ABBREVIATION

ISSVA: International Society for the Study of Vascular Anomalies

### REFERENCES


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