Contents

Preface: Vascular Anomalies: Current State  xi
Marcelo Hochman and Lara Wine Lee

Vascular Anomalies: Nomenclature and Diagnosis  339
Laura Andrews, Chelsea Shope, Lara Wine Lee, and Marcelo Hochman

Before the development of the International Society for the Study of Vascular Anomalies (ISSVA) classification system in 1996, nomenclature used to describe vascular lesions was inconsistent and imprecise. This since widely adopted system stratifies vascular anomalies into vascular malformations and tumors. Vascular tumors involve abnormal proliferation of vascular cells and are further classified as benign, locally aggressive/borderline, or malignant. Vascular malformations are lesions of defective vascular morphogenesis with quiescent endothelium and are named according to their vessel composition, and subdivided into simple; combined, of major named vessels; and syndrome-associated malformations. The updated 2018 ISSVA criteria are referenced in this review.

Histopathology of Vascular Malformations  345
Thuy L. Phung

Vascular malformations are developmental disorders involving the blood and lymphatic vasculature. The study of vascular malformations is a complex and rapidly evolving field with new understanding and insights into the clinical, histopathology, and molecular basis of these lesions. Diagnostic classification of vascular malformations is based on their unique clinical, radiologic imaging, histologic, and molecular characteristics. This article follows the published classification of the International Society for the Study of Vascular Anomalies. It describes characteristic histopathologic findings in tissues of vascular malformations and information on known genetic causes.

Histopathology of Vascular Tumors  357
Thuy L. Phung

Vascular tumors are neoplasms of endothelial cell origin. These tumors comprise a broad and complex group of vascular anomalies. Diagnostic classification of these lesions is based on their unique clinical, radiologic imaging, histopathologic, and molecular characteristics. This article follows the published classification of the International Society for the Study of Vascular Anomalies. It describes characteristic histopathologic findings in vascular tumors and information on known genetic causes.

Diagnostic Imaging  367
John McAlhany and Ricardo Yamada

Vascular tumors and malformations encompass a spectrum of pathology that varies widely in presentation, severity, and treatments. Although typically a clinical diagnosis, accurate classification of lesions is often challenging. Imaging plays an integral role in confirming the clinical diagnosis, determining the extent of disease and
planning treatment strategies. Ultrasound and MRI constitute the backbone of diagnostic imaging in vascular anomalies; however, other modalities such as radiography, computed tomography, and conventional angiography can play a role in certain situations.

Timing and Rationale of Treatment: Achieving the “Best Result” 379
Marcelo Hochman

Various clinical disciplines defend the modality of therapy available to them (eg, medical vs surgery) when, in fact, multi-modality therapy is usually in the best interest of the patient. The aim of any modality of treatment is to obtain the best possible result for a given patient. To successfully achieve that aim for infantile hemangiomas (IH) and all vascular anomalies, defining what is meant by the best possible result and by when to achieve that, the result needs to be defined. Perhaps more important is to make a determination of what is an acceptable result. The impact of a 1-cm IH of the nasal tip is different from that of the same exact lesion on the thigh. The functional import of a 5-mm IH involving the lower eyelid is potentially very different from the same lesion involving the upper eyelid. These examples highlight that variables, such as size and location, are important. What is considered acceptable as a result of treatment of the nasal tip and upper eyelid IH is different from that for the corresponding thigh and lower lid lesions.

Infantile Hemangiomas 383
Divina Justina Hasbani and Lamiaa Hamie

Infantile hemangiomas (IHs) are the most common benign vascular tumors of childhood. They develop during the first few weeks of life and naturally progress by proliferating over several months before they involute and resolve South Carolina; this renders them inconsequential in many cases, but sometimes IHs can have detrimental consequences on function and disfigurement. Hence, systemic propranolol has become a crucial element in IH management, alongside various other medical, procedural, and surgical options that aim to promote their quicker resolution and prevent and alleviate complications.

Hemangioma Genetics and Associated Syndromes 393
Julie Luu and Colleen H. Cotton

This article explores what is known regarding infantile hemangioma (IH) genetics. Despite a great deal of research on this topic, the relationship between IH genetics and pathogenesis has yet to be understood. This article also outlines the appropriate work-up and management of syndromes associated with specific presentations of IH.

Vascular Anomalies: Other Vascular Tumors 401
Kelly Atherton and Harriet Hinen

Vascular tumors are classified into three categories by the International Society for the Study of Vascular Anomalies (ISSVA): benign, locally aggressive/borderline, and malignant. Many of these tumors are rare, cutaneous in nature, and present in childhood. The characterization and delineation of these distinct vascular tumors is an evolving area of clinical research. The diagnosis of these lesions relies on history and clinical presentation, location, histologic appearance, immunohistochemistry,
and more recently, associated genetic mutations. This article provides a brief, yet comprehensive overview of all cutaneous vascular tumors currently recognized by the ISSVA, including presentation, diagnosis, and treatment.

Capillary Malformations 425
Karla Escobar, Karan Pandher, and Marla N. Jahnke

Capillary malformations (CMs) are the most common vascular anomalies, composed of enlarged capillaries and venules with thickened perivascular cell coverage in skin and mucous membranes. These congenital anomalies represent an error in vascular development during embryogenesis. Most of the CMs occur without any syndromic findings; the association between CMs systemic anomalies in some patients, however, makes the recognition of additional syndrome features critical. Some genetic disorders discussed, which feature CMs, include Sturge-Weber syndrome, diffuse CMs with overgrowth, Klippel-Trenaunay syndrome, CLOVES syndrome, among others. This article can aid clinicians in better identifying CMs and associated syndromes and provide consistent terminology to facilitate interdisciplinary management.

Venous Malformations: A Journey Through Their Multifaceted Clinical Presentations 435
Maria Gnarra Buethe, Susan J. Bayliss, and Leonid Shmuylovich

Venous malformations are the most common congenital vascular malformations. Because venous malformations can be complex, difficult to treat, and associated with late complications, it is important to know the basics of the different types of venous malformations and clinical differential diagnosis. Patients with complex lesions may be best served by a specialty vascular anomalies clinic.

Arteriovenous Malformations 445
Shomoukh AlShamekh

Arteriovenous malformations (AVMs) are a group of high-flow congenital vascular malformations. They are characterized by abnormal shunting of the blood supply from fast-flow feeding arteries to low-resistance draining veins via a cluster of aberrant blood vessels termed a central nidus. They are often sporadic but can be associated with syndromes. AVMs are of the most challenging vascular malformations to diagnose and manage and often lead to significant morbidity and mortality. Early diagnosis by recognizing clinical features and experienced multidisciplinary team management is essential to minimize and avoid later complications. This article focuses on clinical findings and natural history of AVMs.

Genetic Causes of Vascular Malformations and Common Signaling Pathways Involved in Their Formation 449
Aubrey L. Rose and Sara S. Cathey

The identification of the genetic causes of vascular malformations is improving understanding of pathogenesis of these lesions and also informing potential opportunities for treatment. Somatic activating mutations affecting RAS/MAPK and PIK3/AKT/mTor pathways are implicated in all types of vascular malformations. Pathogenic variants associated with vascular lesions may be germline or somatic. Next-generation sequencing technologies allow identification of lower level mosaic mutations than was achievable with standard Sanger sequencing. Best practice
strategies to identify underlying genetic mutations in vascular malformations are influenced by the tissues involved and the type of vascular lesion.

Medical Treatment of Vascular Anomalies 461
Alexa DeMaio, Christina New, and Shayla Bergmann

The treatment of vascular malformations and vascular anomalies is often complex, combining various approaches in the art of medicine to provide best outcomes and quality of life for these patients. Treatment may include but is not limited to the following: local control with compression garments and attire, pain control, surgical procedures and debulking, laser therapy, sclerotherapy, and medical management. In this article, the authors discuss the aspects of medical management, visiting the history of medical treatment, and the recent utilization and success of enzymatic pathway inhibitors, specifically sirolimus and new therapies that hold promise for the future for these patients.

Surgical Treatment of Vascular Anomalies 473
Dov Charles Goldenberg and Rafael Ferreira Zatz

Recommendation for the surgical approach to vascular anomalies is rapidly evolving. From an isolated approach, surgery is best seen nowadays as an adjunctive tool in multidisciplinary management. Several studies focusing on targeted therapy based on genetic findings were published, and their use in clinical practice is on the way.

Laser Treatment of Vascular Anomalies 481
Austin N. DeHart and Gresham T. Richter

Lasers are a safe and effective tool for the treatment of vascular anomalies. There are many laser options available. Matching laser parameters with the characteristics of the vasculature in these lesions can selectively deliver energy to the abnormal tissue. This can lead to reduction in size and symptoms of vascular malformations and hemangiomas.

Interventional Treatment of Vascular Anomalies 489
Michael J. Waters, Jonathan Hinshelwood, and M. Imran Chaudry

Vascular anomalies are highly variable in their angioarchitecture, location, and flow dynamics. An individualized, multidisciplinary approach to treatment is required, focusing on improving patient quality of life. With appropriate percutaneous or endovascular treatment, patient satisfaction following interventional therapy is generally high, acknowledging that a complete cure may not always be possible.