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<p>An ambiguous pathologic report can present a clinical dilemma to the treating surgeon. We describe lesions ranging from the potentially benign to the likely malignant. Correctly identifying features associated with higher-risk lesions has proven challenging given the overall good prognosis and low rate of events. An appropriate treatment plan generally requires discussion between the surgeon and an experienced dermatopathologist. When clinically indicated, additional testing may be used to further support or refute a diagnosis of melanoma. The indications for these techniques, the data to support their use, and the strengths and weakness of each are reviewed.</p>	
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<p>Surgery with wide local excision is the mainstay of treatment for primary melanoma. Surgical margins differ depending on the depth of the primary lesion, subtype, and anatomic, cosmetic, or functional considerations. Adjuncts or alternative treatments to wide local excision are limited to specific patient populations and mainly experimental in nature.</p>	
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<p>Wounds resulting from wide local excision of melanoma vary in size and complexity, and require individualized solutions to achieve satisfactory closure. Goals of reconstruction include restoration of form, function, and aesthetics while minimizing donor site morbidity without compromising the effectiveness and safety of oncologic melanoma treatment. Optimal reconstruction relies on an in-depth understanding of the defect, locoregional anatomy and vasculature, available donor tissues, and basic wound healing and surgical principles. This article provides a broad overview of preoperative patient, timing, and wound considerations; various surgical techniques for complex reconstruction throughout the body; and postoperative care and complication management.</p>	

Age and Melanocytic Lesions

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Adrienne B. Shannon, Yun Song, Xiaowei Xu, and Giorgos C. Karakousis

Age plays a dynamic role in incidence, presentation, and extent of disease for cutaneous melanoma. Even within the spectrum of juvenile melanoma, there exists a range of spitzoid and nonspitzoid melanocytic and melanoma lesions. Spitzoid melanomas, a more favorable disease in juvenile patients, are malignant lesions and require treatment as such. Lymph node metastases in melanoma occur at lower rates in older patients compared with younger counterparts, yet the rate of metastases is still high. Age appears to play an important role in the development and progression of melanoma, and understanding the differences across age populations is important when counseling patients.

Management of Noncutaneous Melanomas

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Ann Y. Lee and Russell S. Berman

Noncutaneous melanomas are rare subtypes of melanoma with high rates of metastatic disease and poor overall survival. One-third to one-half of cases are amelanotic, which may contribute to a delay in diagnosis. Immunohistochemistry staining with typical melanoma markers helps confirm the diagnosis. There is no standard staging system across mucosal melanomas. Elective nodal dissection is not recommended and there is a paucity of data to support use of sentinel lymph node biopsy. Mutational analysis should be routinely performed. Systemic therapy options include targeted inhibitors, immunotherapy, and cytotoxic chemotherapy, although further studies are needed to confirm their efficacy.

Sentinel Lymph Node Biopsy: Indications and Technique

401

Jessica Crystal and Mark B. Faries

Sentinel lymph node biopsy is a key tool in the care of many patients with melanoma. The indications for the procedure have gradually become clearer over the 3 decades since the technique was developed. For appropriately selected patients, it carries enormous significance. Although it is a minimally invasive procedure, it does carry some risk. It is also a multidisciplinary procedure, requiring knowledge and experience from several specialties including nuclear medicine, surgery, and pathology.

Management of Regional Nodal Melanoma

415

Christina V. Angeles and Sandra L. Wong

Regional nodal melanoma management has changed substantially over the past 2 decades alongside advances in systemic therapy. Significant data from retrospective studies and from 2 randomized controlled trials show no survival benefit to completion lymph node dissection compared with observation in sentinel lymph node–positive melanoma patients. Observation is becoming the standard recommendation in these patients, whereas patients with clinically detected lymph nodes are still recommended to undergo lymph node dissection. Promising early results from a neoadjuvant approach inform the ongoing evolution of melanoma management. Recruiting patients to clinical trials is paramount to attaining evidence-based practice changes in melanoma.

- Injectable Therapies for Regional Melanoma** 433
- Norma E. Farrow, Margaret Leddy, Karenia Landa, and Georgia M. Beasley
- Patients with unresectable cutaneous, subcutaneous, or nodal melanoma metastases are often candidates for injectable therapies, which are attractive for ease of intralesional delivery to superficial metastases and limited systemic toxicity profiles. Injectable or intralesional therapies can be part of multifaceted treatment strategies to kill tumor directly or to alter the tumor so as to make it more sensitive to systemic therapy. Talmogene laherparepvec is the only Food and Drug Administration–approved injectable therapy currently in wide clinical use in the United States, although ongoing trials are evaluating novel intralesional agents as well as combinations with systemic therapies, particularly checkpoint inhibitors.
- Neoadjuvant Therapy for Melanoma** 445
- Michael C. Lowe and Ragini R. Kudchadkar
- With the universal adoption of immune checkpoint blockade and agents targeting BRAF-mutated melanomas in the metastatic setting, numerous clinical trials have evaluated these agents in the neoadjuvant setting. These smaller trials have shown promising results with high pathologic response rates and acceptable safety. Larger prospective randomized trials are under way to determine if all patients with resectable metastatic disease should be receiving neoadjuvant therapy.
- Adjuvant Therapy for Cutaneous Melanoma** 455
- Darryl Schuitevoerder, Charles C. Vining, and Jennifer Tseng
- This article presents the current data supporting adjuvant therapy for patients with cutaneous melanoma. With the recent development of novel immunotherapy agents as well as targeted therapy, there are strong data to support the use of these therapies in patients at high risk of developing recurrent or metastatic disease.
- Novel Targets in Melanoma: Intralesional and Combination Therapy to Manipulate the Immune Response** 467
- Alicia A. Gingrich and Amanda R. Kirane
- Clinical outcomes for metastatic melanoma have been dramatically altered by recent developments in immunotherapy and targeted strategies, but response to these therapies is not uniform, the majority of patients do not respond, and clinical response can be self-limited. Current directions in melanoma treatment aim to leverage a combination of therapies for tumors refractory to monoimmunotherapy, to include tumor-directed strategies, such as intralesional therapy and inhibitors designed for novel targets, which may augment current systemic agents when used in combination. Here, we summarize new classes of agents and emerging multimodal combination strategies that demonstrate significant promise in future melanoma management.

Role of Surgery in Stage IV Melanoma

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Conor H. O'Neill, Kelly M. McMasters, and Michael E. Egger

Stage IV melanoma has a 5-year survival rate of 6%, but considerable advances have been made in systemic therapies. Systemic immunotherapy has achieved durable responses in up to 40% of patients, with similar improvements with targeted therapies. This has reshaped the landscape for surgery in stage IV melanoma. Metastasectomy can be considered in patients on systemic immunotherapy or targeted therapy with responding, stable, or isolated progressing lesions, oligometastatic disease, or long disease-free intervals. Surgery plays a role in providing tumor tissue for preparation of tumor-infiltrating lymphocytes for adoptive cell therapy. Surgical palliation plays a role in patients with symptomatic metastases.