

**Overall 2020 Conference Needs Assessment**

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**Overall Conference Description**

Each year, nationally recognized leaders in medical and procedural and aesthetic medicine convene in Hawaii to discuss and review the current state of knowledge in their respective dermatologic specialties. We explore the latest advances in the treatment and management of common and complex diseases of the skin, both for adults and children as well as new developments in aesthetic medicine. Our exceptional faculty will present clinically relevant information that you will find immediately useful in the care of your patients. This six-day meeting provides interactive presentations, case studies in medical dermatology, live-patient injection sessions and multiple workshops. Learn from the experts about acne, actinic keratoses, atopic dermatitis, melanoma and non-melanoma skin cancers, nonsurgical facial rejuvenation, psoriasis, rosacea, and much more.

Skin Disease Education Foundation’s (SDEF) 44rd Annual Hawaii Dermatology Seminar’s comprehensive agenda addresses cutting-edge innovations and explores current issues relevant to practicing physicians and healthcare providers who treat diseases of the skin. Our scientific program has been designed to keep the clinician up to date on new developments within the field of dermatology. This year we are offering an interactive workshop on Dermoscopy.

In addition, SDEF’s 44rd Hawaii Dermatology Seminar will offer attendees American Board of Dermatology **Maintenance of Certification (MOC-D)** via self-assessment modules. At the conclusion of the meeting, physicians will receive a web link to the transcript of the MOC-D self-assessment discussions as well as certification.

***“****In 2019, SDEF’s Annual Hawaii Dermatology Seminar celebrates 43*

*years of excellence in providing CME/CE to dermatologists and all the*

*healthcare professionals who treat skin diseases. For six days you’ll*

*have the opportunity to learn from the experts and mix with your peers. We*

*provide medical and aesthetic sessions focusing on serious science and the*

*latest developments. Add that to our engaging interactive discussions and*

*you’ll know that your time with us was productive and well spent.”*

-SDEF’s 44rd Annual Hawaii Dermatology Seminar Conference Directors

**Learning Objectives**

At the conclusion of this live conference, participants should be able to:

• *Discuss the use of currently recommended diagnostic and treatment approaches for specific dermatologic conditions and match patients with the most appropriate interventions.*

*• Apply evidence-based pharmacologic and nonpharmacologic strategies to the management of patients with acne.*

*• Review current scientific findings that demonstrate the underlying pathophysiology of, and the treatment targets for, acne vulgaris.*

*• Discuss the factors that increase a patient’s risk for developing actinic keratosis.*

*• Design a treatment strategy for actinic keratosis that improves outcomes while minimizing the*

*potential risk of complications.*

*• Discuss the benefits and risks of current agents and techniques commonly used in aesthetic and procedural dermatology.*

*• Select filler agents suitable for use in treating different facial areas.*

*• Design a nonsurgical treatment strategy, including potential use of neuromodulators, to address patient concerns about facial aging.*

*• Develop a treatment approach for atopic dermatitis that achieves the goal of clear or almost clear skin.*

*• Review safety and efficacy data on therapies that target the inflammatory component of atopic dermatitis.*

*• Compare and contrast the symptomatology of atopic dermatitis and the differences in the*

*approach to treatment for adults vs pediatric patients.*

*• Recognize the role of dermoscopy in diagnosis and management of various skin lesions.*

*• List signs, symptoms, and diagnostic indicators of hidradenitis suppurativa severity levels and describe initial steps for treatment.*

*• Identify the conditions under which patients with hidradenitis suppurativa would be eligible for treatment with biologic therapies.*

*• Describe recent scientific findings that explicate the inflammatory basis of psoriasis.*

*• Discuss current clinical guidelines for optimal diagnosis and treatment of psoriasis.*

*• Review safety and efficacy data on new and emerging therapies for psoriasis.*

*• Implement a strategy for stepwise management of psoriasis with topical and biologic agents, including the use of treat-to-target goals.*

*• Apply current strategies for assessing and treating dermatologic conditions in pediatric patients, including acne, atopic dermatitis, birthmarks and scar management.*

*• Identify when epicutaneous patch testing is appropriate in pediatric patients.*

*• Discuss safety and efficacy data on current and emerging therapies for rosacea.*

*• Define appropriate goals and strategies for the optimal management of patients with rosacea.*

*• Distinguish between benign nevi and suspicious neoplasms.*

*• Discuss available treatment strategies for melanoma at various stages of its progression.*

*• Identify high-risk tumor characteristics and indications for Mohs surgery and the impact of patient characteristics and expectations on the results of the procedure.*

*• Recognize the need for increased vigilance for the development of skin cancer in immunocompromised patients.*

*• Explain available methods for assessing and monitoring Spitz nevi.*

*• Describe available nonsurgical options for managing superficial nonmelanoma lesions.*

*• Define the underlying processes that lead to Merkel cell carcinoma, how recurrences can be diagnosed early, and resources for management.*

*• Discuss NCCN guidelines on melanoma surveillance, diagnostic tests and recurrence risk calculators.*

*• Describe techniques for managing keloids that offer the greatest benefits with minimal risk of*

*scarring.*

*• Diagnose and develop treatment strategies for hypopigmentation disorders.*

*• Discuss the latest data on the prevalence, severity, and impact of primary axillary hyperhidrosis and other common forms of hyperhidrosis.*

*• Outline strategies for diagnosing primary axillary hyperhidrosis and other forms of hyperhidrosis, including the use of validated instruments to assess the impact of the condition on affected patients.*

*• Review the evidence regarding the efficacy and safety profile of various first line and subsequent therapies for various types of hyperhidrosis, as well as patient candidacy for*

*the different treatments.*

*• Counsel patients about effective strategies for photoprotection.*

**Evaluations From the 43nd Annual Hawaii Dermatology Seminar**

**1. Participating in this educational activity changed my knowledge. N=276**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strongly Agree | Agree | Somewhat Agree | Disagree | Strongly Disagree |
| 59% | 29% | 10% | 2% | <1% |

**2. Participating in this educational activity changed my COMPETENCE. N=276**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strongly Agree | Agree | Somewhat Agree | Disagree | Strongly Disagree |
| 50% | 33% | 14% | 2% | <1% |

**3. Participating in this educational activity changed my PERFORMANCE. N=256**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strongly Agree | Agree | Somewhat Agree | Disagree | Strongly Disagree |
| 47% | 33% | 17% | 3% | <1% |

**4. Based on the content of the activity, what will you do differently in the care of your patients and/or regarding your professional responsibilities? N=212**

|  |  |
| --- | --- |
| **Statement** | **% Responding** |
| Implement a change in my practice/workplace. | 27% |
| Seek additional information on this topic. | 24% |
| Implement a change in my practice/workplace and seek additional information on this topic. | 31% |
| Do nothing differently. Current practice/job responsibilities reflect activity recommendations. | 15% |
| Do nothing differently as the content was not convincing. | <1% |
| Do nothing differently. System barriers prevent me from changing my practice/workplace. | 3% |

**Performance Changes from 2019 Conference**

The following comments were provided in response to the request, “If you anticipate changing one or more aspects of your practice and/or professional responsibilities as a result of your participation in this activity, please describe how you plan to do so?”

* Incorporating new techniques when treating patients with dermatology-related issues.
* Evaluate patients with non-cutaneous findings more diligently.
* Medical management of rosacea.
* Implement different medications and management strategies for acne, sunscreen, and other derm conditions.
* May be able to reduce biopsies with my dermoscopy.
* Understanding comorbidities in psoriasis.
* Discuss newer safer medication for the treatment of severe psoriasis.
* Different first choices for biologics for psoriasis. Change diagnostic testing for onychomycosis. Understand spitz nevi.
* Understand risks and benefits and strength and weaknesses of each of the biologics.
* Assessing PASI and DLQI scores on patients; improving methods of dermoscopy; changing approach to AD; implement better PsA clinical evaluations.
* Management of acne based on current evidence.
* Increase counseling and patient education on sun protection; manage spitz Nevi with excision up front; purchase Dermascope.
* Biopsy nails suspicious for melanoma.
* Using different pharmacological and non-pharmacological therapies to treat patients with Acne and psoriasis. Also, I am more confident in treating nail disease and melanochyia.
* The aesthetics conference days were highly valuable to me and I plan on including more and updating my techniques and possibly adding filler.
* Try to obtain the most effective treatment options for my patients who do not achieve acceptable results with the most commonly used treatments.
* More strongly consider acne therapies based on alternate needs vs. using antibiotics.
* I will be more aware of filler complications and do everything I can to prevent them but also be ready with a protocol for when things do not go as planned. I will adjust my monitoring of Isotretinoin labs for acne patients. I will also spend some time educating my patients on skin care and sun protection.

**Acne**

**Gap: Many clinicians treat acne without having a complete understanding of the most recent guidelines for its diagnosis and management in pediatric, adolescent, and adult populations.**

*Learning objective: Apply evidence-based pharmacologic and nonpharmacologic strategies to the management of patients with acne.*

Acne is one of the most common skin conditions treated by physicians, affecting 40 to 50 million people in the United States. Although the disease can affect patients at any age, from newborns to the elderly, acne occurs most commonly during the adolescent years, with a prevalence as high as 85%. In 20% of cases the acne is severe, resulting in permanent physical scarring, poor self-image, depression, and anxiety. For this reason, experts recently have broadened the scope of their research, clinical discussions, treatment focus, and guidelines for management to encompass the complete spectrum of the disease.[Zaenglein 2016]

For effective management, all patients with acne, regardless of age, gender, or skin type, need early recognition, accurate diagnosis, and prompt initiation of treatment. Despite the high prevalence of this disease, until recently, guidelines addressing standard management were lacking and approaches to treatment varied widely among clinicians. The situation changed with the publication in 2013 of evidence-based recommendations for the diagnosis and treatment of pediatric acne, developed by a panel from the American Acne and Rosacea Society (AARS) and approved by the American Academy of Pediatrics.[Eichenfield 2013] These comprehensive guidelines are the first to specifically address acne in the pediatric population.

In 2016 the American Academy of Dermatology (AAD) published its guidelines of care for acne vulgaris management in adolescents and adults.[Zaenglein 2016] The guidelines discuss topical and systemic therapies as well as physical modalities, including lasers and photodynamic therapy. In addition, a grading/classification system, microbiology and endocrinology testing, complementary/alternative therapies, and the role of diet are reviewed.

Many clinicians are not sufficiently knowledgeable about the new guidelines to effectively apply them in clinical practice. A recent survey revealed that only 41% of respondents correctly stated that pustular acne was the form of acne that may respond quickly to drying therapy with a combination of benzoyl peroxide and sulfacetamide and sulfur lotion. In the same survey, only 13% of respondents knew that some form of facial scarring has been reported in up to 95% of acne patients. Similarly, only 25% of respondents believed that patients with acne fulminans, and without systemic symptoms, should be treated with prednisone for 2 weeks, according to the guidelines; most would apply this treatment for 4 weeks.[Frontline Medical Communications, MD-IQ quiz, 2016]

Clinicians should also take into account the needs of special populations. For example, challenges in managing acne in adult women include patient preferences, pregnancy, and lactation. Treatments vary widely and treatment should be tailored specifically for each individual woman.[Tan 2017] Similarly, topical retinoids are effective but are nonetheless underutilized among patients of Asian descent, due in part to the perception that Asian skin is more sensitive to these agents than is Caucasian skin.[See 2018] As a result, such agents may be underutilized in this population.

**Gap: Due to an incomplete understanding of the basic etiologies for acne and lack of confidence in prescribing, many clinicians fail to use advanced or appropriate treatment modalities in acne patients.**

*Learning objective: Review current scientific findings that demonstrate the underlying pathophysiology of, and the treatment targets for, acne vulgaris.*

The AAD guidelines [Zaenglein 2016] and those from the European Dermatology Forum (EDF) [Morton 2015] agree that retinoids have an essential role in treatment of acne. The AAD states that retinoids are the core of topical therapy for acne because they are comedolytic and anti-inflammatory, and they help maintain clearance.[Zaenglein 2016]

Despite uniform recommendation for use of topical retinoids, a recent study of prescribing practices from 2012 to 2014 indicated that dermatologists prescribed retinoids just 58.8% of the time while non-dermatologists prescribed them for only 32.4% of cases.[Leyden 2017] Another report suggested that fewer than half of clinicians treating pediatric patients self-reported confidence in prescribing according to the AARS guidelines, particularly in selecting combination therapy for patients with moderate to severe acne.[Feldstein 2016]

Fortunately, many effective treatment strategies are now available to manage acne vulgaris in younger patients. Safe and effective topical and oral therapies are approved for patients as young as 12 years of age. In 2014, the FDA approved clindamycin phosphate and benzoyl peroxide 1.2%/3.75% for once-daily treatment of comedonal and inflammatory acne in patients 12 and older.

The common perception among clinicians is that the microcomedone is the initiating event in the development of all acne lesions. However, technically speaking, all lesions are inflammatory lesions; inflammation may be a primary event in acne, and may persist throughout the lesion lifecycle, even beyond the disappearance of visible lesions.[Stein Gold, 2017] Emerging therapies and regimens offer clinicians an enhanced range of options to improve tolerability, sustain positive clinical outcomes, and effectively treat diverse patient populations. For patients with moderate-to-severe and persistent acne, oral and topical antibiotics have been the therapies of choice. Recent reports have suggested the superiority of combination therapy with topical treatments (such as tretinoin and other retinoids, benzoyl peroxide, and salicylic acid), for mild-to-moderate comedonal lesions, superficial inflammatory (papular or pustular), and nonscarring acne.[Stein Gold2016]

Photodynamic therapy (PDT) is an effective adjunctive treatment for mild to severe acne, especially in patients who have not responded to topical therapy and oral antibacterials and who are not good candidates for isotretinoin, according to a recent review.[Boen 2017] The most common photosensitizers used in this report were 5-aminolevulinic acid and methyl aminolevulinate, and red light plus intense pulsed light was the most common light source. Inflammatory and non-inflammatory lesions both responded to the treatment, with inflammatory lesions showing greater clearance in most studies. The use of newer types of lasers, such as those used to remove tattoos (picowavelength lasers) in acne scar removal, is under study.[Mechcatie 2017]

Systemic treatments (such as the tetracycline class of oral antibiotics) are indicated for moderate to severe manifestations (scarring or nonscarring) and patients with persistent hyperpigmentation. However, emerging data suggest limiting the use of oral antibiotics in patients with acne, particularly children.[Stein Gold2016] Other treatments, including oral isotretinoin, light-based phototherapy, and laser therapies, may be as effective for carefully selected patients.[Zaenglein 2016]

Other therapies have shown efficacy in adult women with acne. A 4-year retrospective study reported that up to 95% of adult women with acne improved on spironolactone alone or in combination with a topical agent.[Grandhi 2017] In another study, topical spironolactone gel improved the noninflammatory elements of mild to moderate acne in adult women.[Bagherani 2014] Oral contraceptives have also shown efficacy in treating acne in adult women.[Harper 2015]

Several new agents are under investigation that address at least one of the 4 factors of acne pathophysiology, including sebum production, altered keratinization of the pilosebaceous duct, *C. acnes,* and inflammation.[Cong 2019] Agents that may reduce sebum production include SB204, a topical agent, releases nitric oxide, which has antimicrobial and anti-inflammatory activities, and DRM01, which targets acetyl coenzyme-A carboxylase (ACC), a key regulator of sebum production. A third topical agent is a potent antiandrogen, cortexolone 17α-propionate 1%, which has shown at least comparable efficacy to tretinoin.[Rosette 2019]

Ongoing education of clinicians is needed with respect to new research findings on acne pathogenesis, disease course, and current treatment guidelines. Clinicians also must be kept up to date as new agents and newer formulations and delivery routes for existing medications are developed. Antimicrobials, including modified diallyl disulfide oxide and nitric oxide, are under investigation as potential acne therapies.[Trivedi 2018] Also being studied are anti-inflammatory phytochemicals; small molecule inhibitors targeting sebaceous glands and enzymes; laser light therapy in combination with metal nanoshells and vacuum assistance; and probiotics that alter the microbiome.[Trivedi 2018]

Clinicians would benefit from education that keeps them abreast of scientific developments and their potential application in the management of acne.

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**Actinic Keratosis and Nonmelanoma Skin Cancer**

**Gap: Dermatologists must be able to recognize and treat nonmelanoma skin cancers and actinic keratoses as early as possible, including appropriate follow-up care, to minimize the risk for developing skin cancers.**

*Learning objective: Discuss the factors that increase a patient’s risk for developing actinic keratosis.*

Actinic keratosis (AK) – a skin lesion resulting from sun exposure – is the second most common diagnosis in dermatologic practices, affecting more than 58 million Americans. Despite its prevalence, there is no universally accepted definition of AK and thus it may be difficult to identify reliably.[Siegel 2017] The condition is especially prevalent among patients with skin phototypes I or II, or with specific genetic factors and who are exposed to prolonged ultraviolet radiation.[Arenberger 2017] AK poses a significant risk of progressing to squamous cell carcinoma (SCC). The rate of progression from AK to cutaneous SCC is estimated to be between 0.025% and 16% per year for an individual lesion; however, because a person with AK typically has 6 to 8 lesions, the inherent risk of progression is between 0.15% and 80%. It is still not possible to predict which AK lesions will progress to SCC.[Arenberger 2017] For this reason, both clinically visible lesions and subclinical, non-visible lesions (ie, the entire area affected by AK/field cancerization) should be treated.[Goldenberg 2017] An estimated 700,000 cases of SCC are diagnosed each year in the United States, resulting in approximately 2,500 deaths. Well-established clinical criteria are lacking that would help clinicians determine which specific AK lesions are most likely to undergo malignant transformation.

About 90% of nonmelanoma skin cancers (NMSCs) are associated with exposure to ultraviolet radiation from the sun. Despite widespread and ongoing educational efforts about this risk, at least 50% of children and adults still do not adequately protect themselves from exposure, failing to use simple measures such as wearing proper clothing and applying sunscreen. It has been estimated that regular application of sunscreen with a sun protection factor of 15 or greater for the first 18 years of life would reduce the lifetime incidence of NMSC by 78%. Other risk factors for NMSCs include having a fair complexion, genetic and molecular alterations, and immunosuppression.[Didona 2018] Awareness of these factors can lead to more effective prevention of NMSC.[Didona 2018]

**Gap: Clinicians must be aware of the new formulations of existing treatments for actinic keratosis and squamous cell carcinoma, as well as new compounds—in particular, biologic agents—that currently are being evaluated in clinical trials and should be prepared to assess the emerging data on these new therapies.**

*Learning objective: Design a treatment strategy for actinic keratosis that improves outcomes while minimizing the potential risk of complications.*

The major treatment options for AK include destructive therapies (eg, cryotherapy, surgery, dermabrasion), topical medications (eg, 5-fluorouracil [5-FU], imiquimod, ingenol mebutate, diclofenac), chemical peels (eg, trichloroacetic acid), and photodynamic therapy (PDT). Given that multiple effective treatment options are available for AK, the choice of therapy is influenced by several factors, including the number and distribution of lesions, lesion characteristics, patient preference for the mode of treatment (eg, office-based versus home administered, duration of therapy), patient tolerance for side effects (eg, pain, inflammation, hypopigmentation, scarring), treatment cost, and treatment availability.[Goldenberg 2017] A recent meta-analysis found that PDT combined with  5-aminolevulinic acid nanoemulsion (BF-200 ALA) was more effective in providing complete clearance than PDT combined with methyl-5-aminolevulinate (MAL).[Fu 2019]

Recent research has identified several promising approaches to treating AK and SCC. A steroidal alkaloid extracted from the corn lily *Veratrum californicum* inhibits the hedgehog signaling pathway, mediated by the tumor suppressor patched (PTCH) and the proto-oncogene smoothened (SMO) genes. Nicotinamide (vitamin B3 or niacinamide) is a substrate and inhibitor of poly-ADP-ribose polymerase and a precursor of nicotinamide adenine dinucleotide, both of which are involved in DNA repair. Orally administered nicotinamide has shown to significantly reduce rates of new NMSC and AK in high-risk patients.[Arenberger 2017]

A new formulation containing a low dose of fluorouracil (0.5%) to decrease adverse events and salicylic acid (10%) to reduce hyperkeratosis and increase penetration of fluorouracil through the skin is currently being marketed in several European countries for the topical treatment of slightly palpable and/or moderately thick hyperkeratotic actinic keratosis in immunocompetent adult patients. Further larger studies are needed before considering any of these new options as an effective agent for the reduction of AKs.

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**Aesthetic and Procedural Dermatology**

**Gap: Clinicians are not adequately trained on the benefits and limitations of surgical and nonsurgical techniques as well as nonsurgical treatment options for aesthetic dermatology. The rapid rate of change within the field of procedural and esthetic dermatology, and increasingly, demands from patients, suggest the need for improved, increased, and more accessible training for clinicians.**

*Learning objectives:*

* *Discuss the benefits and risks of current agents and techniques commonly used in aesthetic and procedural dermatology.*
* *Select filler agents suitable for use in treating different facial areas.*
* *Design a nonsurgical treatment strategy, including potential use of neuromodulators, to address patient concerns about facial aging.*

According to the American Society of Plastic Surgeons, more than 17.7 million cosmetic procedures were done in 2018, an increase of 2% from 2017.[ASPS 2018] The overall growth in cosmetic surgery continues to be driven by a significant rise in minimally invasive procedures: 15.9 million of the 17.7 million procedures were minimally invasive. In contrast to a 3% drop in facelifts, there was a 2% increase in neurotoxin injections and a 3% increase in procedures involving soft tissue fillers. In fact, neurotoxin injection procedures have increased 845% from 2000 to 2018.[ASPS 2018] The ASPS identified the top three procedures as:

* Botulinumtoxin (BoNT) type A injections: 7.4 million procedures
* Soft tissue fillers: 2.6 million procedures
* Chemical peel: 1.38 million procedures

Data from the American Society of Aesthetic Plastic Surgeons (ASAPS) identified the top 3 minimally invasive cosmetic procedures in women as BoNT injections, hyaluronic acid (HA) injections, and laser hair removal; in men, the most common procedures were BoNT injections, HA injections, and nonsurgical fat reduction procedures.[ASAPS 2018]

In the first of 3 recent articles by the Aesthetic Leaders in Facial Aesthetics Consensus Committee, the authors noted that “as the number of physicians with limited experience in providing aesthetic treatment expands, the need for guidance and training from more experienced injectors has become apparent.”[DeMaio 2017a] There has been rapid development of new devices and procedures, as well as new agents, often in the absence of comparative effectiveness research and patient-reported outcomes, making it challenging for clinicians to develop optimal cosmetic/aesthetic strategies.[Waldman 2017] In addition, dermatologists are now seeing more patients who are requesting these less invasive treatments, either as precursors to or instead of plastic surgery. Further, aesthetic dermatology is no longer limited to rejuvenating women’s faces – there is a growing interest among male patients, and there are procedures that address the neck, décolletage, hands and arms. Dermatologists need to remain current with the various approaches and techniques for each of these concerns, Facial rejuvenation is clinically challenging but also can result in positive outcomes when clinicians are prepared and skilled at using procedures that result in age-appropriate aesthetic improvements.

*Facial assessment:* Traditionally the face is divided into three horizontal sections: upper face, midface, and lower face/chin. The neck has recently been added as a fourth potential section to be addressed. As rejuvenation approaches differ for each of these areas, it is imperative that cosmetic dermatologists consider the entire face before determining an appropriate rejuvenation strategy.[Sundaram 2015] In addition, dermatologists must be knowledgeable regarding the underlying facial anatomy, the structural and physiologic changes in the face associated with the aging process – including a loss of volume and a redistribution of fat – and the visible consequences of photoaging.[Dhir 2016; Lambros 2007] Specifically, not all agents or techniques are appropriate – or safe – for all facial sections.

Volume loss is considered to be on the of the major contributors to facial aging, in turn, restoration of facial volume and contour changes has become an important treatment approach in the aesthetic field. The concept of gravity as the cause of facial aging has been gradually revised over the past 4 decades. During this time, pioneering research by investigators in the fields of plastic and reconstructive surgery and dermatology has consistently demonstrated facial aging involves changes on many levels, including bone structures, muscle strength, fat, and skin integrity. These changes, resulting from both intrinsic (age-related) and extrinsic (“environmental”) factors, lead to modifications in the contours, shape, balance, and proportions of the face.

Generally, the upper face is considered a ‘basic’ area for neuromodulators, but an ‘advanced’ area for fillers.[De Maio 2017a] In contrast, fillers are considered ‘basic’ for the midface area, to provide volumizing and contouring.[De Maio 2017b] However, both the midface and lower facial areas require more knowledge and skill to address than the upper face, as there are increased risks of serious complications in these areas.[De Maio 2017b, 2017c]

*Neurotoxins:* Neurotoxin injections with botulinumtoxin type A are undeniably the most popular of all minimally-invasive cosmetic procedures.[ASPS 2017] Botulinumtoxin (BoNT) type A includes three distinct formulations: onabotulinumtoxin, abobotulinumtoxin, and incobotulinumtoxin. These 3 agents are not interchangeable -- each has distinct indications, and recommended doses and number of injections differ by agent and by injection location.[Carruthers 2018; Sundaram 2015] Further, there has recently been a move away from muscle paralysis towards neuromodulation through lower dosing and more frequent combinations with facial fillers.[Sundaram 2015] The effects are transient, lasting a few months.[Carruthers 2018] Cosmetic BoNT injections are predominantly used to address cosmetic concerns caused or exacerbated by muscle contractions – such as glabellar rhytides. Among the many other target areas are horizontal lines on the forehead, lateral canthal lines, and marionette lines.[Carruthers 2018] It is very important for clinicians to carefully screen potential candidates prior to treatment. Common complications include headache and transient bruising/swelling at the injection site(s); rare but potentially serious adverse effects include dysphagia, anaphylaxis, aspiration, pneumonia, and death.[Carruthers 2018]

*Facial fillers:* Whereas BoNT injections relax the underlying muscles that cause facial wrinkles, fillers are used to decrease the depth of lines or increase the size of specific facial structures. As such, BoNT is more often used in the upper third of the face, and fillers in the lower two-thirds. The last decade has seen the introduction of a multitude of new stimulatory and non-stimulatory soft tissue fillers for facial rejuvenation. Nonstimulatory fillers are more temporary, and do not stimulate collagenesis – whereas stimulatory fillers stimulate collagenesis and are thus considered to be permanent. Nonstimulatory fillers are generally comprised of hyaluronic acid (HA) or non-animal stabilized HA (NASHA). The non-HA fillers are comprised of calcium hydroxylapatite, poly-L-lactic acid (PLLA), poly-methyl methacralate microspheres (PMMA), or polyalkylimide (considered a semi-permanent filler that can be removed). Some of these formulations also contain lidocaine to limit injection site pain.

The increased availability of dermal filler options carries with it the inherent challenge of choosing the most appropriate agent (or combination of agents), including which agents are most appropriate to use to complement plastic surgery (when appropriate). As with the different formulations of BoNT, it can be challenging to remain current regarding the benefits, indications, facial locations, and techniques unique to the different fillers. Although not a new concept, the use of blunt cannulas to deliver fillers is on the rise due primarily to the fact that the filler can be injected with great precision with minimal bruising and bleeding as well as offers little downtime and discomfort.

Platelet-rich plasma (PRP) was originally used to address musculoskeletal and maxillofacial concerns, and its use was expanded to include dermatologic concerns such as wound healing, fat grafting, alopecia, and scar revision. It has recently begun to be used in aesthetic dermatology for dermal volume augmentation.[Leo 2015; Lynch 2016] While the literature suggests there may be a modest benefit for specific indications, the current evidence does not support the efficacy of PRP in routine aesthetic dermatology. However, future investigation is warranted in light of the high tolerability and general lack of complications.[Leo 2015; Lynch 2016]

*Cosmeceuticals:* Cosmeceuticals are defined as a “cosmetic that has medicinal or drug-like (pharmaceutical) properties.” Cosmeceutical products typically target skin aging and/or pigmentation concerns, but may also be used as adjuvant therapies in combination with traditional medications for issues such as rosacea.[Draelos 2017; Zenker 2017] Cosmeceutical products encompass cleansers, moisturizers, cosmetics, and sunscreens, and may include anti-inflammatory agents, retinoids, and anti-oxidants, among other ingredients. Products may be sold on-line, in dermatology offices, or possibly in retail stores. However, although patients seek skin care recommendations from their dermatologist, a recent survey of dermatology residents and faculty noted that 75% of residents reported their education regarding skin care and cosmeceutical education has been “too little or nonexistent” during residency.[Feetham 2018] Ironically, 60% of the responding faculty reported the resident education on these topics is either “just right or too much.”[Feetham 2018] As the go-to source for information on cosmeceutical products, dermatologists would benefit from greater understanding of these products.

*Skin rejuvenation/resurfacing procedures:*In addition to the improvement of age-related structural changes, facial rejuvenation also may require improvements in minor to major surface skin abnormalities or skin quality. Improvements of many superficial flaws may be accomplished nonsurgically with any of a number of topical medications (ie, retinoids and hydroquinone) and/or resurfacing procedures (such as acid peels, dermabrasion, or laser resurfacing). Other patients require correction of more severe defects —particularly scarring from surgical or accidental wounds or burns, or those that occur as sequelae of skin disorders (especially severe acne). Consensus guidelines from the American Society for Dermatologic Surgery advise that dermabrasion, chemical peels, and most laser treatments are safe within 6 months after isotretinoin therapy.[Waldman 2017] Although the desire for improved appearance motivates many patients to consult a practitioner for facial scar revision, others seek such treatment because of diminished function of the eyes, mouth, or nose. Effective and safe surgical and nonsurgical techniques are available, and chosen according to the cause, type, location, and pigmentation of the scar(s).[Zachary 2016] Various laser types and non-laser ablative therapies differ in the type of injury produced in the skin and therefore the potential application, efficacy, and recovery of patients.[Zachary 2016]

*Body shaping/contouring:*As newer treatments become available, dermatologists are also seeing the expansion of aesthetic medicine beyond the face to other parts of the body. Clinicians are now seeing more patients who seek body contouring and body rejuvenation through nonsurgical fat reduction.[Kilmer SL 2015] Cryolipolysis and ultrasonic energy both are non-surgical body shaping/contouring procedures that are on the rise. Cryolipolysis destroys subcutaneous fat cells by freezing them; therefore, cause cell death of subcutaneous fat tissue without apparent damage to the overlying skin.[Kilmer 2015] Cryolipolysis has been shown to safely and effectively reduce subcutaneous fat on the body, and previously had FDA clearance for treatment of the flanks, abdomen, and thighs.[Kilmer]

Other lipoplastic techniques currently are in development. One of these, known as focused ultrasound body contouring, uses low-intensity ultrasonic waves delivered across the surface of the skin. The device is said to work by destroying the membranes of subcutaneous fat cells. The device is said to work by destroying the membranes of subcutaneous fat cells.[American Society for Dermatologic Surgery] Ultrasound technology is a safe and efficacious approach for skin laxity, lipolysis, and cellulite, with minimal adverse effects.[Juhasz 2018] Microfocused ultrasound (MFU), alone or in combination with high-resolution imaging (MFU-V) is being used to tighten sagging facial and neck skin in patients with mild-to-moderate tissue laxity complaints.[Fabi 2015] Generally considered safe and effective, with mild and transient adverse effects, rare cases of serious adverse events, including cutaneous necrosis, have been reported.[Friedmann 2018]

An emerging technology combines radiofrequency with ultrasound for lipolysis, skin tightening and cellulite treatment; combining hot and cold technologies appears safe and effective.[Kapoor 2017] Diluted calcium hydroxylapatite (CaHA) is a growing option for skin tightening in the neck and décolletage; [De Almeida 2019; Yutskovskaya 2017] Typically used as a volumizing agent, hyperdilution facilitates neocollagenesis and is thus a very effective option for multiple body areas.[De Almeida 2019]

Patients with older skin and those who have previously undergone prior procedures may not be appropriate candidates for all options.[Dayan 2019] The use of radiofrequency microneedling in combination with bipolar radiofrequency may optimally address the needs of these patients who desire nonsurgical tissue tightening. Understanding the limitations and appropriate candidates for each technique is imperative to provide optimal individualized outcomes. Clinicians must stay abreast of the latest body shaping/contouring techniques as new options continue to become available.

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**Atopic Dermatitis**

**Gap: Clinicians need to improve their knowledge of current diagnostic guidelines and treatment paradigms for atopic dermatitis (AD) and to develop strategies for incorporating these approaches into their clinical practice.**

*Learning objective: Develop a treatment approach for atopic dermatitis that achieves the goal of clear or almost clear skin.*

Atopic dermatitis (AD), also called eczema, is a chronic, relapsing inflammatory skin disease that is associated with significant morbidity and costs to patients and their families. The prevalence of AD in the United States is 3%-5% overall, with a higher prevalence in children (10%-15% lifetime), varying by geographical location. The prevalence in children has increased by as much as 30% in recent decades.[Eichenfield & Stein Gold 2017] Adult-onset AD is also on the rise, with a current prevalence in the United States as high as 7%-10%.[Splete 2017]

The evidence-based guidelines for the diagnosis and assessment of AD, published in 2014, provide criteria for accurately diagnosing and differentiating AD from other conditions with similar characteristics.[Eichenfield 2014] Clinicians need to become aware of these guidelines so as to be better able to recognize AD, distinguish it from other conditions with similar appearance, and initiate effective treatment at the earliest opportunity.

Diagnosis of AD is based on typical findings including pruritus, erythema, papules/vesicles, xerosis, excoriations, erosions, and often lichenification and dyspigmentation. In infants, the face (particularly the cheeks and chin), trunk, and extensor extremities are the most common sites of involvement, with sparing of the diaper area. In toddlers and older children, the most commonly affected sites are the flexoral areas of the wrists, ankles, and antecubital and popliteal fossae. In adolescents and adults, the wrists, hands, neck, and ankles are typically affected.[Eichenfield 2017]

Clinicians need to be alert to potential misdiagnosis of adult AD as contact dermatitis. Differential diagnosis includes ichthyosis vulgaris, keratosis pilaris, nummular dermatitis, psoriasis, scabies, seborrheic dermatitis, and tinea corporis. Findings that should prompt reconsideration of the diagnosis of atopic dermatitis in infants and young children include failure to thrive; multiple cutaneous and/or systemic infections; unusual morphology or distribution of rash; poor response to typical atopic dermatitis treatments; fixed-plaque hypopigmentation; and late onset AD signs and symptoms.[Eichenfield and Stein Gold 2017]

Pruritus and other signs and symptoms associated with the disease can be severe and their impact on quality of life significant, particularly in those with moderate to severe disease. Coping with AD can lower self-esteem, negatively affect school performance and social interactions, disrupt sleep, and generally increase day-to-day stress experienced by patients and their families.[National Eczema Association] Although AD is common and relatively easy to identify, clinicians should avoid being complacent about the disease and its management. Additionally, there are often gaps between evidence-based guidelines in AD management, what the clinician recommends, and what the patient does.[O’Toole 2013]

Before seeking evidence of concomitant sensitivities such as foods and environmental allergens, clinicians can better identify the diagnostic and therapeutic path in AD by closely questioning patients and their families about the lesions, symptoms, and impact of their condition.[Eichenfield 2017] Indeed, specialized testing for sensitivities or blindly eliminating common allergenic foods from the diets of all patients with AD is generally not effective in modifying disease course. Nevertheless, some patients may have comorbid food allergies, and referral to a pediatric allergist is appropriate when skin disease is recalcitrant and the patient has a history of exacerbation after exposure to certain foods. [Stein Gold and Eichenfield 2017]

Clinicians need to become more conversant with the growing armamentarium of available therapeutic agents, their indications, and their appropriate use to achieve optimal clearing of skin lesions. Well-established treatment options such as emollients, corticosteroids, and topical calcineurin inhibitors will continue to play a role in treating AD of all severity levels. The use of topical corticosteroids to bring an acute flare under control is an established strategy, and research supports corticosteroid maintenance after clearing. In one study, ongoing maintenance with low-dose fluticasone propionate plus moisturizers for 4 weeks reduced the risk of relapse at 20 weeks.[Hanifin 2002] Another option is the use of the topical calcineurin inhibitors (TCIs) pimecrolimus and tacrolimus – corticosteroid-sparing agents that have been safely used for many years. Unlike corticosteroids, these agents can be used on any affected body surface including the face. Studies report short- and long-term efficacy of pimecrolimus, which has been approved for use in patients <15 years of age at the 0.03% concentration.[Afshar 2013; Eichenfield J Pediatr 2015; Luger 2015; Stein Gold/Eichenfield 2017]

Recent research into the pathophysiology of AD has revealed a complex etiology involving multiple immunologic and inflammatory pathways. Advances in the understanding of the roles of filaggrin and ceramides (waxy lipid molecules) has led to the theory of barrier therapy and the development of new moisturizers and topical skin therapies that are targeted to increase the levels of ceramides and natural moisturizing factors in the skin.[Miyagaki 2015; Irvine and McLean] The early identification of susceptible patients suggests the possibility of preventing or minimizing the risk for the development of AD. In one report, daily emollient use in susceptible infants beginning at age 3 weeks produced a 50% relative reduction in the risk of AD at age 6 months.[Simpson 2014]

With the increasing understanding of the role of epidermal skin barrier defects in AD pathogenesis, moisturization alone has become an option in treating mildly infected eczema. A recent study found rapid resolution in response to topical steroid and emollient treatment and ruled out a clinically meaningful benefit from the addition of either oral or topical antibiotics in children with mild clinically infected eczema.[Francis NA et al. 2017] Also, dilute bleach baths followed by application of a moisturizer and/or emollient ointment confers anti-inflammatory and anti-infective properties.

A recent review of studies investigating the effectiveness of bleach baths found that they improve the clinical symptoms of atopic dermatitis and restore surface microbiome by eradicating *Staphylococcus aureus* and other bacteria.[Maarouf 2018] This benefit appears to reduce the need for topical corticosteroids or topical antibiotics. Bleach baths do not disrupt the epidermal barrier function, and have strong anti-inflammatory and anti-pruritogenic effects.[Maarouf 2018] However, it is not yet known whether bleach baths, as monotherapy, are sufficient to manage AD.

To address the role of barrier dysfunction in the pathogenesis of AD, therapies that address the underlying lipid biochemical abnormality may be needed. These lipid-based forms of barrier repair therapy have been shown to be as effective as topical mid-potency corticosteroids.[Elias 2018] A novel addition to the topical armamentarium that appears to be gaining momentum involves the application of topical antioxidants (such as furfuryl palmitate) or ceramides.[Draelos 2018; Pigatto 2018] A review of studies regarding the beneficial effects of the new antioxidant molecule furfuryl palmitate (and its derivatives) indicates it is safe and effective in ameliorating the signs and symptoms of mild-to-moderate AD, along with other cutaneous skin disorders.[Pigatto 2018] Similarly, a recent study reported on the benefits of a proprietary therapeutic cream containing ceramides in the management of signs and symptoms of mild-to-moderate AD and other pruritic dermatoses.[Draelos 2018] These agents have no side effects and thus are safe to use in all patient populations.

**Gap: Clinicians need guidance to understand the role of inflammation in the pathogenesis of AD and in the use of current and emerging therapies designed to block the inflammatory activity that produces AD symptoms.**

*Learning objective: Review safety and efficacy data on therapies that target the inflammatory component of atopic dermatitis.*

The rationale for the development of new and emerging therapies for AD is the blockade of specific inflammatory mediators. The type 2 cytokines interleukin (IL)-4 and IL-13 appear to be key drivers of atopic dermatitis and are likely important drivers of atopic or allergic diseases in general.[Simpson NEJM 2016] Two new medications targeting these mediators were approved by the FDA in 2016 and 2017, and many others are under development.[Eichenfield and Friedlander 2016]

Crisaborole, a boron-based phosphodiesterase (PDE)-4 inhibitor, was approved in 2016 for the topical treatment of AD. The safety and efficacy of crisaborole ointment 2% were evaluated in 2 vehicle-controlled phase 3 trials in >1500 patients with mild or moderate AD.[Paller 2016] Significantly more crisaborole-treated patients achieved the study endpoints (ISGA of 0 or 1) by day 29 compared to those on vehicle. Treatment-related adverse events included AD and pain at the application site. In an open-label extension, severity of treatment-emergent adverse events was mild or moderate. No cases of application site atrophy, telangiectasia, or hypopigmentation were reported.[Paller et al 2016]

The systemic agent dupilumab was approved for treatment of AD in 2017. An inhibitor of the IL-4 receptor alpha subunit, dupilumab was evaluated in 2 16-week phase 3 placebo-controlled trials in adult patients whose AD was not adequately controlled with topical agents or who were not candidates for topical medication. In both trials, dupilumab produced an improvement of at least 75% on the EASI (EASI-75) at week 16 in significantly more patients compared with placebo (*P*<0.001 for all comparisons). Also in the 2 trials, dupilumab significantly reduced patient-reported symptoms of atopic dermatitis and its effect on sleep, symptoms of anxiety or depression, and quality of life.[Simpson NEJM 2016] A recent 16-week, double-blind, randomized, placebo-controlled phase III trial reported that significantly more adult patients receiving dupilumab 300 mg weekly (qw) or every 2 weeks (q2w) in conjunction with topical corticosteroid (TCS) treatment achieved >75% improvement from baseline in the EASI at week 16 compared with patients receiving placebo with TCS (P<0.001 for both doses vs placebo).[de Bruin-Weller 2018] In addition, patients receiving dupilumab with TCS demonstrated significant improvements in other clinical manifestations – including pruritus, pain, sleep disturbance, psychiatric symptoms (anxiety and depression), and quality of life. Further, no new safety signals were identified, and no significant differences in overall rates of adverse events between the groups.[de Bruin-Weller 2018] A long-term (120 weeks), phase 3 open-label extension study in pediatric patients with AD is underway.

A topical PDE-4 inhibitor, OPA-15406, produced promising results in an 8-week vehicle-controlled phase 2 study in patients 10 to 70 years of age with mild or moderate AD.[Hanifin 2016]. The primary end point, IGA of 0 or 1 with ≥2-grade reduction, was met at week 4 in the group receiving 1% concentration. Mean percentage improvement from baseline EASI score was notable in week 1 (31.4% vs 6.0% for vehicle; *P*=0.0005), was larger in week 2 (39.0% vs 3.0%; *P*=0.0001) and persisted for 8 weeks. Other clinical trials are under way to determine efficacy of OP-15406 compared with vehicle in adult patients with atopic dermatitis syndrome [ClinicalTrials.gov NCT03908970] and to establish safety of the 0.1% and 0.3% formulations in adults and children with atopic dermatitis.[ClinicalTrials.gov NCT03961529]

The therapeutic pipeline for atopic dermatitis is rapidly expanding, with a large number of agents currently in phase 2 or 3 clinical trials.[Paller 2017] Current trials include biologics that inhibit Th2 cytokines (thymic stromal lymphopoietin, IL-4, IL-5, IL-13, and IL-31 and their receptors), or Th22/Th17 cytokines.[Paller 2017; Simpson 2017] In addition, orally administered Janus kinase inhibitors- including tofacitinib and PF-04965842- have demonstrated initial benefit,[Cinats 2018; Cotter 2018; Jancin 2015; Paller 2017; PfizerNews 2018] but long-term studies are needed. Agents that address itching (NK1R inhibitors) are also being studied.[Paller 2017] Studies on the leukotriene mediator montelukast have not been consistent, offering only limited evidence of efficacy in treating moderate-to-severe AD.[Chin 2018]

Although AD has no cure, the current consensus suggests that, with the availability of new medications and better strategies for use of traditional therapies, signs and symptoms of AD can be significantly reduced and flares effectively controlled or even prevented. With the rapid growth of emerging biologic therapies for AD, it is imperative that clinicians remain current on their knowledge of ongoing clinical trials for their patients, as well as new and emerging agents in order to provide optimal care.

**Gap: Clinicians may not recognize the differences between adult and pediatric patients that affect the etiology, symptomatology, and management of atopic dermatitis.**

*Learning objective: Compare and contrast the symptomatology of atopic dermatitis and the differences in the approach to treatment for adults vs pediatric patients.*

Atopic dermatitis is increasingly recognized as a disease not only of children but also of adults who may have a persistent or relapsing course from childhood or who develop new-onset adult disease.[Boguniewicz 2017] The point prevalence estimates for AD in the United States are 11% to 13% for children compared with 7% for adults.[Paller 2017]

One factor that drives pathogenesis of AD is disruption of the skin barrier. Having high transepidermal water loss, a measure of barrier dysfunction, at 2 days of age is associated with a 7-fold higher risk of developing AD.[Kelleher 2015] A deficiencies in epidermal barrier proteins, notably filaggrin, increases the risk for AD, presumably by attenuating the skin barrier, which facilitates the interaction of external antigens with skin-resident immune cells and driving the cutaneous inflammation that leads to systemic immune response. Deficiency in filaggrin can be inherited and can manifest in early infancy. However, even in the absence of mutations, filaggrin expression in adults with AD is reduced, which in turn can affect the chronicity of the disease.[Egawa 2016]

In children, the pathology of atopic dermatitis is driven more by Th2-cell activity (which activates the cytokines IL-4 and IL-13) than it is in adults.[McKnight] Dupilumab, a fully human monoclonal antibody targeting the IL-4 Rα subunit, blocks signaling of both IL-4 and IL-13 and is the first biologic to be approved for the treatment of moderate-to-severe AD in adult patients. A recent open-label trial looked at the treatment with dupilumab in 38 children (aged 6 to 11 years) and 50 adolescents (aged 12 to 17 years) with moderate to severe AD who had all failed topical corticosteroid therapy; some had also failed at least one systemic therapy.[Cork 2017] At week 12, mean scores in the younger cohort given either 2 mg/kg or 4 mg/kg had improved by 76.2% and 63.4%, respectively, from baseline. In the adolescents, EASI scores at week 12 had improved by a mean of 66.4% in the 2-mg/kg group and 69.7% in the 4-mg/kg group.[Cork 2017] Itch also improved remarkably.

Emerging evidence suggests that pediatric patients with AD may benefit more than adults from treatment that targets the IgG component.[Paller 2017]

These and other findings support the notion that AD may have different causes and effects depending on the patient’s age, and that diagnosis and treatment should be personalized to address the needs of the individual.

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**Dermoscopy**

**Gap: Dermoscopy is often underused or misused, leading to missed diagnosis or misdiagnosis.**

*Learning objective: Recognize the role of dermoscopy in diagnosis and management of various skin lesions.*

Noninvasive imaging technologies have been found to improve diagnostic accuracy, detect earlier stage melanomas, and reduce costs. Total-body photography and sequential digital dermoscopy imaging, in combination with direct-to-consumer applications and teledermatology, are already revolutionizing the ways in which physicians and patients partner to enhance dermatologic assessment and management. Dermoscopy (also known as dermatoscopy, epiluminescence microscopy, incident light microscopy, and skin-surface microscopy) is a noninvasive, in vivo technique that can enhance the diagnosis of numerous skin conditions; it is particularly beneficial in determining whether or not to biopsy pigmented lesions to distinguish malignancies (melanoma and pigmented basal cell carcinoma) from benign nevi or seborrheic keratoses.[Marghoob 2018; Wachter 2010]

Dermoscopy requires a high-quality lens for significant magnification along with a lighting system to visualize subsurface structures and patterns. Hand-held devices, fluid immersion and polarized dermatoscopes are also available. Studies have identified numerous benefits of dermoscopy, including enhanced accuracy versus clinical diagnosis.[Sinz 2017; Berk-Krauss 2017; Carrera 2017] It can improve diagnostic accuracy by as much as 30% over unaided visual clinical inspection alone.[Braun 2009] Factors that determine the diagnostic accuracy of dermoscopy include experience of the practitioner, diagnostic algorithm and threshold for a positive test, and clinical context/patient-related factors.[Argenziano 2011; Marghoob 2018; Zalaudek 2009]

A variety of evaluation tools are available to aid in the use of dermoscopy. The two-step pattern recognition method requires the dermatologist to first determine if the neoplasm Is a melanocytic proliferative one (eg, nevus or melanoma) and to then use pattern recognition or an algorithm to confirm a diagnosis. The “3-point rule” requires a lesion with any 2 of the 3 criteria (atypical asymmetry, atypical pigment network, or blue-white structures) to be biopsied, because there is a higher likelihood of melanoma. The 7-point algorithm integrates the above 3 criteria with 4 minor criteria: streaks, regression pattern, irregular diffuse pigmentation, and irregular dot and globules in the decision-making process for biopsy. Use of dermoscopy can thus reduce the number of benign lesions excised. With proper training, dermoscopy may eventually result in the referral of fewer benign lesions from primary care physicians, although it may initially increase the number of unnecessary excisions without sufficient training on its use and interpretation of results. Notably, “false positive” results can lead to unnecessary excisions, and “false negative” results might result in overlooking a cancer.[Kamińska-Winciorek 2015; Papageorgiou 2018] Clinicians need training on the use of dermoscopy and interpretation of the findings, including the clues that indicate dermoscopic variations of malignancies versus benign tumors.[Papageorgiou 2018]

According to David L. Swanson, MD, chief of medical dermatology at the Mayo Clinic in Scottsdale, Arizona, “Patients are becoming aware of the technique and more and more are expecting their dermatologists to be skilled in its application.”[Wachter 2010] While dermoscopy is routinely taught to primary care physicians outside the US, such as in Europe and Australia, surveys of US dermatologists (predominantly those in academic medical centers) estimate that dermoscopy training has been provided to anywhere from 17% to 84% of residents.[Charles 2005; Terushkin 2010] A survey of practicing US dermatologists reported that only 48% were using dermoscopy; factors associated with increased use included younger versus established dermatologists, female sex, dermoscopy training, and involvement in resident teaching.[Engasser 2010] The study noted that barriers to dermoscopy use included lack of training, lack of interest, time required for dermoscopic examination, and a belief that dermoscopy would not affect clinical decisions.[Engasser 2010] However, a recent survey found that nearly 81% of participating dermatologists have used dermoscopy, and 83% were trained in it. Notably, about 98% of dermatologists with ≤5 years in dermatology practice used dermoscopy, and 100% of them had received training in dermoscopy.[Murzaku 2014] However, fewer than one-third of responding dermatologists perform dermoscopy on all pigmented lesions, and just under 50% use sequential dermoscopy imaging with baseline dermoscopy to follow changes in individual lesions.[Murzaku 2014]

In addition to its value in recognizing potentially malignant lesions, use of dermoscopy has been expanding to evaluation of other more general dermatologic conditions, including scalp and hair disorders, onychomycosis, skin infections/infestations (eg scabies), and cutaneous inflammatory diseases.[Errichetti 2015; Micali 2016] The usefulness of dermoscopy in inflammatory dermatoses is particularly promising because it offers a cost-effective, noninvasive tool with rapid results.[Micali 2016]

Integrating dermoscopy into routine clinical practice can enhance diagnostic accuracy of melanoma and other malignancies, as well as other common dermatologic conditions. To achieve these results, and to minimize the risk of inter-individual variability that is inherent to the technique, clinicians need practical education on dermoscopy training.[Marchionda 2010; Marghoob 2018; Halani 2018]

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**Hidradenitis Suppurativa**

**Gap: The differential diagnosis of hidradenitis suppurativa is challenging, so much so that many patients remain undiagnosed for an average of 7 years.**

*Learning objective: List signs, symptoms, and**diagnostic indicators of HS severity levels, and describe initial steps for treatment.*

Hidradenitis suppurativa (HS), a disease of the hair follicles that involves follicular occlusion and hyperkeratosis, is an uncommon disorder that disproportionately affects female patients, young adults, and African American and biracial patients in the US.[Barg 2017] A recent retrospective analysis found a prevalence of 0.10%, or 98 per 100,000 persons, with an adjusted prevalence in women more than twice that of men. The prevalence of HS was highest among patients aged 30 to 39 years (172 per 100,000) compared with all other age groups (range, 15-150 per 100,000), with a 3-fold higher prevalence among African Americans and 2-fold higher prevalence among biracial individuals than among white patients.[Barg 2017] An article in press from the Journal of the American Academy of Dermatology notes that HS “has an enormous impact on patients’ lives.”[Kolli 2019]

Patients with HS have painful, inflammatory papules and nodules which frequently progress to form abscesses, sinus tracts and hypertrophic scars. Bacteria are not thought to have a primary role in lesion formation, and abscesses are often sterile. The diagnosis of hidradenitis suppurativa is clinically based, without a specific diagnostic test. The 3 key elements required to diagnose HS are typical lesions, characteristic distribution, and recurrence. All 3 criteria must be present for the definitive diagnosis.[Zouboulis 2015] The most important nongenetic factors implicated in HS are obesity and smoking.[Ball 2016]. Causal risk factors include friction in areas of the body such as the armpits, use of medications such as lithium, and (somewhat more controversially) hormonal factors. Associated risk factors include obesity, smoking, and genetic predisposition. Patients with HS remain undiagnosed for an average of 7 years.[Micheletti 2017]

HS, especially when severe, can profoundly affect patients’ quality of life. In severe, recurrent, and/or recalcitrant cases, depression and other psychosocial effects (including withdrawal from social activities and impaired work performance) frequently are seen as well. Medical complications include anal, urethral, and rectal strictures and fistulas; contractures and limitations of limb mobility; an increased risk for Crohn’s and ulcerative colitis; squamous cell carcinoma and other malignancies; kidney disease; and the metabolic syndrome.[Micheletti 2017; Zouboulis 2015]

Specialists in dermatology and women’s health practitioners are the clinicians most likely to see patients with HS. Patients with severe cases often seek relief in hospital emergency departments; therefore, it is also important for emergency medicine clinicians to be able to readily recognize the manifestations of this disease, institute palliative therapy, and refer patients to the appropriate specialists for prompt attention and follow-up care.

**Gap: Because HS has many clinical “mimickers,” clinicians often treat patients erroneously – and sometimes harmfully – for an incorrect diagnosis.**

*Learning objective: Selectively treat patients based on an accurate diagnosis or refer patients for specialty care.*

Clinicians have many options to treat and help people manage HS, but for most patients, an early and accurate diagnosis remains elusive.[McNamara 2017] Treatment is based on the severity, duration, and morphology of characteristic lesions, as determined by the Hurley staging system.[Hurley 1989] Most patients with HS—an estimated 75%—have isolated lesions (Hurley stage 1); about 24% have some confluence of lesions (stage 2); and less than 1% have full confluence of lesions (stage 3). Early diagnosis of this disease can lead to better symptom management, prevention of lesion progression, and reduced risk for development of new lesions.[Zouboulis 2015]

More than 50 interventions have been used in the management of hidradenitis suppurativa.[Ingram 2016] For mild to moderate cases, lifestyle changes are recommended. For disease of any severity in patients with excess weight, weight reduction is a primary focus. Other measures to reduce skin-on-skin friction in intertriginous areas also are helpful, including wearing loose undergarments and using antiseptic soaps and absorbent powder.

Medical treatment options for mild or moderate cases include a variety of topical and systemic antibiotics, used alone or in combination, as well as intralesional injections of triamcinolone for early lesions. Other off-label treatments commonly used in hidradenitis suppurativa include oral dapsone, zinc, acitretin, hormonal therapy (eg, oral contraceptive pills and spironolactone), cyclosporine, and oral prednisone. Results with such approaches are mixed.[Micheletti 2017]

Locally recurring lesions are sometimes treated with surgery; techniques commonly used include excision, unroofing, and drainage. Surgery is not curative; approximately one in ten patients will need a reoperation.[Kohorst 2016] Pharmacologic and surgical therapies can reduce lesion activity and inflammation, but may be only modestly effective in preventing future recurrences and disease progression.[Hamzavi 2015] Adjunctive therapies such as laser and light-based therapies work by decreasing the number of hair follicles, sebaceous glands, and bacteria in affected areas, and by ablatively debulking chronic lesions.[Hamzavi 2015] The use of carbon dioxide lasers and Nd:Yag lasers has shown beneficial effects.[Jovanovic 2016]

**Gap: Many clinicians are unsure when and whether to initiate biologic therapies for HS.**

*Learning objective: Identify the conditions under which patients with HS would be eligible for treatment with biologic therapies.*

The discovery that hidradenitis suppurativa lesions contain elevated levels of cytokines, including TNF-alpha, has led to research on the potential role of TNF inhibitors as a treatment option. Results from randomized trials led to FDA approval of adalimumab in 2015, making it the first medication specifically approved for treatment of HS. In these studies, use of adalimumab led to significant reduction in symptoms at 12 weeks and sustained response at up to 72 weeks of follow-up. The incidence of adverse effects was low and was similar to the rate seen with placebo.[Kimball 2015] Some data support the use of another TNF inhibitor, infliximab, [Machet 2013] while etanercept has not been found to be effective. Evidence reported by a Cochrane meta-analysis suggests that adalimumab given weekly and infliximab are effective.[Ingram 2016] A video roundtable summarized the problems facing clinicians and proposed solutions in the diagnosis and treatment of HS.[Micheletti 2017] Participants suggested that biologic therapy is appropriate for patients who have severe disease or have failed on other HS therapies.[Micheletti 2017] They also reminded clinicians that, when prescribing adalimumab to a patient with HS, dosing regimens are different from those used in treating other skin diseases such as psoriasis,

Clinicians need to keep up to date about approved treatment options for management of their patients with hidradenitis suppurativa and must be prepared to counsel their patients that current treatments, while sometimes effective, are not curative.

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**Hyperhidrosis**

Hyperhidrosis – excessive sweating – significantly diminishes quality of life for the millions of people affected by the condition. [Doolittle 2016; Kamudoni 2017; Augustin 2013; Stolman 2008; Bahar 2016] In about two-thirds of cases, patients experience axillary hyperhidrosis, or excessive sweating in the underarms. [Doolittle 2016] Palmar hyperhidrosis (sweaty palms) is another common form of the condition.

In a recent report, Doolittle and colleagues concluded that previously published estimates of the prevalence of hyperhidrosis are outdated and underestimate the true prevalence of the condition. [Doolittle 2016] According to their survey of a nationally representative sample of 8160 individuals, those researchers estimate that the actual prevalence of primary hyperhidrosis (that is, excessive sweating that is not a secondary result from another medical condition) in the US population is 4.8% (15.3 million people), almost double the 2.8% rate for hyperhidrosis reported in a major study published 12 years earlier. [Doolittle 2016] Although numerous medical conditions and medications can cause excessive sweating, secondary hyperhidrosis is relatively uncommon, affecting only about 7% of patients. [Moraites 2014] Thus most patients will present with primary axillary hyperhidrosis.

**Gap: Physicians do not appreciate the prevalence of primary axillary hyperhidrosis and other forms of hyperhidrosis and may be unaware of the impact these conditions can have on a patient’s quality of life.**

*Learning objective: Discuss the latest data on the prevalence, severity, and impact of primary axillary hyperhidrosis and other common forms of hyperhidrosis.*

The key gap to emerge from an extensive assessment of the evidence is clinicians’ frequent failure to appreciate both the extent of hyperhidrosis and the impact it can have on an individual patient. [Doolittle 2016; Glaser 2007; Kerdel 2018; Pieretti 2014]

Patients and physicians alike contribute to the underrecognition of hyperhidrosis. According to Doolittle et al, only 51% of patients with hyperhidrosis have discussed their excessive sweating with a health care professional, mainly because they believe that hyperhidrosis is not a true medical condition and that no treatment options exist. [Doolittle 2016] Those attitudes may explain why, in a separate study involving 1,985 self-identified individuals with hyperhidrosis, 85% waited at least 3 years before seeking medical help for their condition, and 48.9% waited 10 years or more. [Glaser 2018]

However, physician attitudes constitute another major barrier to effective management of hyperhidrosis. In one report, patient who are members of a hyperhidrosis support group told researchers that their experience of receiving a diagnosis had been “humiliating” and “belittling.” [Kamudoni 2017] As these investigators report, “This was especially because the sweating problem was not taken seriously by the clinicians. For example, some participants reported being told that they were wasting their [clinicians’] time.”

A self-fulfilling dynamic – in effect, a negative feedback loop – contributes to underrecognition hyperhidrosis, says Francisco Kerdel, MD, a dermatologist practicing in Coral Gables, Florida. “We don’t appreciate the prevalence of hyperhidrosis, and thus we don’t look for it or ask about in when evaluating patients,” he explains. “Not spotting signs of hyperhidrosis or hearing patients report it contributes to our sense that it is uncommon.” [Kerdel 2018] He notes that this complacent approach to hyperhidrosis may have its origins in medical school; dermatology residency programs devote scant attention to hyperhidrosis, and primary care training devotes little – if any – time to the condition. [Kerdel 2018]

In addition to underestimating the prevalence of hyperhidrosis, clinicians often fail to appreciate its impact on patients. [Doolittle 2016] “Current findings suggest that the severity and prevalence [of hyperhidrosis] are both higher than previously thought, indicating a need for greater awareness of the condition and its associated treatment options among medical professionals,” note Doolittle and colleagues. [Doolittle 2016]

Those researchers found that 52% of patients reporting axillary hyperhidrosis said that their underarm sweating was barely tolerable or intolerable, and that it frequently or always interferes with daily activities. [Doolittle 2016] Patients also report significantly severe palmar hyperhidrosis. [Doolittle 2016] Because the mean age of onset of axillary hyperhidrosis among study subjects was 19 years, the effects of the condition can affect patients throughout their adult life. [Doolittle 2016]

In another study, interviews and online surveys with 71 people with hyperhidrosis found that:

* Nearly three-quarters reported an impact on lifestyle;
* 41% reported an adverse effect on leisure activities;
* One-third reported hyperhidrosis-related problems with performing daily household chores;
* 64% had concerns regarding other people’s negative reactions to them; and,
* 69% said they had experienced embarrassment, anxiety, sadness, anger, or hopelessness as a result of their hyperhidrosis. [Kamudoni 2017]

That last finding, reflecting the psychological sequelae of hyperhidrosis, confirms other research showing that people with hyperhidrosis are roughly 3 times as likely as dermatology patients without hyperhidrosis to have anxiety and depression. [Bahar 2016] A study of more than 2000 consecutive patients presenting to dermatology clinics found that 21.3% of those with hyperhidrosis had anxiety and 27.2% had depression, compared with 7.5% and 9.7%, respectively, of patients without hyperhidrosis. [Bahar 2016] Multivariate analysis showed a positive correlation between the severity of hyperhidrosis and the prevalence of anxiety and depression prevalence. [Bahar 2016] Other research has shown elevated social stress levels and depressive symptoms in patients with primary hyperhidrosis relative to age- and sex-matched controls from the general population, with a subgroup of patients with axillary hyperhidrosis being most adversely affected. [Gross 2014] While the concomitant presence of hyperhidrosis and anxiety raises a “chicken-or-the-egg” question, several experts consider anxiety and depression to be sequelae of hyperhidrosis, while acknowledging that there also can be a vicious cycle of sweating prompting stress or anxiety, which prompts further sweating. [Gross 2014, Bahar 2016]

As Dr Kerdel states, “Dermatologists, primary care physicians, and also pediatricians have many educational needs related to hyperhidrosis, but the first and most important thing is recognizing how prevalent it is, and how deeply it can affect our patients.” That awareness, he adds, is the key to setting an appropriate index of suspicion and to broaching the subject with patients in a manner that encourages candor. [Kerdel 2018]

**Gap: Physicians face challenges in diagnosing hyperhidrosis, correctly identifying the various forms of the condition, and assessing the extent to which HH affects patients’ daily activities and quality of life.**

*Learning objective: Outline strategies for diagnosing primary axillary hyperhidrosis and other forms of hyperhidrosis, including the use of validated instruments to assess the impact of the condition on affected patients.*

Beyond recognizing sweating that exceeds the norm and then empowering patients to discuss their symptoms, perhaps the most difficult aspect of diagnosing hyperhidrosis may be the differential diagnosis. Dozens of medical conditions can cause secondary hyperhidrosis, ranging from the commonplace, such as acute febrile illness, diabetes, and menopause, to the rarely seen, such as pheochromocytoma, rickets, and Klippel-Trenaunay syndrome. [Moraites 2014]

Similarly, many medications can cause secondary hyperhidrosis as an adverse effect, including those that are used to treat pain, hypertension, endocrine disorders, erectile dysfunction, asthma, psychiatric conditions and other diagnoses. [Moraites 2014] Despite that laundry list of possible causes, however, a retrospective chart review examining the records of 415 hyperhidrosis patients seen at university-based dermatology department found that more than 93% had primary hyperhidrosis. [Walling 2011]

In practical terms, the diagnosis of hyperhidrosis is not necessarily complicated. Statistical analysis has shown that when a patient had excessive sweating of at least 6 months’ duration, the presence of 4 or more of the following characteristics allows the diagnosis of primary hyperhidrosis to be made with 99% sensitivity and 82% specificity:

* Primary involvement of eccrine-dense (axillae/palms/soles/craniofacial) sites
* Bilateral and symmetric sweating
* Absence of nocturnal sweating
* Episodes at least weekly
* Onset at 25 years of age or younger
* Positive family history
* Impairment of daily activities [Walling 2011]

Some experts believe the diagnosis can be streamlined even further. One recent approach holds that only at least 2, rather than at least 4, of these characteristics must to be present to fulfill the criteria for primary hyperhidrosis when secondary causes have been excluded. [Moraites 2014]

Applying these criteria, along with a physical examination and thorough medical and medication history, can reliably establish a diagnosis of primary or secondary hyperhidrosis. [Walling 2011; Moraites 2014] According to Dr Kerdel, however, physicians who ignore the obvious signs of hyperhidrosis also fail to identify the most likely explanation for the problem and thus may pursue extensive and expensive testing in search of an underlying condition. “In the great majority of cases, the hyperhidrosis is idiopathic, or primary, and not attributable to some other disease.” [Kerdel 2018]

Beyond classifying hyperhidrosis as primary or secondary in nature, the condition can be further characterized as generalized, regional, or focal. The extent and location of excessive sweating has important implications for treatment. [Moraites 2014]

Determining the severity of hyperhidrosis and the degree to which it interferes with daily activities and affects quality of life is another important component of the diagnostic process. Established instruments, such as the Hyperhidrosis Disease Severity Scale (HDSS), and newer resources, such as the Axillary Sweating Daily Diary (ASDD), have been validated and can provide clinicians with an efficient, consistent means of assessing the impact of hyperhidrosis. [Kowalski 2004; Glaser (ASDD) 2017] Educational activities that promote physician use of these validated tools are important because, in the words of one hyperhidrosis researcher, “Despite morbidity equal to other well-known dermatologic conditions, hyperhidrosis has historically been underacknowledged and undertreated because of the lack of accessible, scientifically accurate information and dispersal of that information within patient and medical communities.” [Pieretti 2014]

**Gap: Physicians are not familiar with the range of approved and late-stage investigational first-line and secondary therapies for hyperhidrosis, or the candidacy criteria for each.**

*Learning objective: Review the evidence regarding the efficacy and safety profile of various first line and subsequent therapies for various types of hyperhidrosis, as well as patient candidacy for the different treatments.*

Hyperhidrosis is undertreated even though effective therapy is available. Topical, injectable, and oral medications, surgical management, and other interventions involving electrical or microwave techniques all can be employed in treating hyperhidrosis. [Stolman 2008; Grabell 2017] Given the high proportion of patients who have not yet sought medical attention for hyperhidrosis, and the importance of identifying and initiating treatment in those patients, [Moraites 2014] expanded options for first-line therapy may be particularly welcome and of interest not only to dermatologists but also to primary care clinicians. As Doolittle and colleagues note, “For individuals who seek treatment, their physicians will need more effective (first-line) treatment options at their disposal to have more confidence in identifying and diagnosing the condition.” [Doolittle 2016]

Several topical anticholinergic agents are being developed to meet that need for additional first-line therapies. Current research is focusing on glycopyrronium tosylate (formerly DRM04), oxybutynin, sofpironium bromide, and umeclidinium, among others. [Grabell 2017]

Glycopyrronium tosylate is under review by the Food and Drug Administration (FDA) for the treatment of primary axillary hyperhidrosis. [Dermira 2017] The safety and efficacy of the medication relative to vehicle was assessed in the phase 3 ATMOS-1 and ATMOS-2 pivotal trials, which involved more than 690 patients. [Pariser 2017; Dermira 2016] The co-primary endpoints in both trials were the proportion of patients who achieved ≥4-point improvement from baseline in sweating severity as measured by the ASDD and the average absolute change from baseline in gravimetrically-measured sweat production. Secondary endpoints were the proportion of patients who had ≥2 grade improvement from baseline as measured by HDSS and the proportion of patients with at least a 50% reduction from baseline in gravimetrically-measured sweat production. All endpoints were assessed at the end of the 4-week treatment period. In ATMOS-2, glycopyrronium tosylate demonstrated statistically significant improvements in all primary and secondary endpoints relative to vehicle. [Pariser 2017; Dermira 2016] In ATMOS-1, the agent met the co-primary endpoint of reduction in sweating severity and both secondary endpoints. It also showed statistically significant improvement in reduction in gravimetrically-measured sweat production following exclusion of one outlier data center in accord with a pre-specified statistical analysis plan submitted to the FDA. [Dermira 2016]

Meanwhile, therapies involving the use of medical devices under study for their utility in treating hyperhidrosis include radiofrequency thermotherapy, laser therapy, and ultrasound therapy, among others. [Grabell 2017]

The expansion of the treatment armamentarium, while welcome, provides an information challenge to clinicians comparable to the need to fully appreciate the physical and psychosocial burden hyperhidrosis imposes on patients. As one team of researchers notes, “Physicians should understand the impact of focal hyperhidrosis and the need to stay abreast of the available treatment options to provide the best care for patients.” [Glaser 2007] However, the critical prerequisite to enabling patients with hyperhidrosis to realize the benefits of those treatment options remains better identifying patients. “With a modest improvement in the recognition of hyperhidrosis, a provider has the opportunity to make a major impact on a patient’s life.” [Moraites 2014]

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**Moles, Melanoma, and Cutaneous Oncology**

**Gap: Increasing rates of advanced melanoma demonstrate the need for earlier suspicion and diagnosis of melanoma across all age groups and socioeconomic statuses.**

*Learning objective: Distinguish between benign nevi and suspicious neoplasms.*

Melanoma is a neoplasm of melanocytes or a neoplasm of the cells that develop from melanocytes. The incidence of new melanoma cases increases by 1.4% yearly, an annual increase second only to lung cancer in women. According to the American Cancer Society, in 2019, an estimated 96,480 new cases of melanoma will develop, causing 7230 deaths; about 60% of these cases will be in males. Melanoma is more than 20 times more common in whites compared to African Americans. Overall, the lifetime risk of getting melanoma is about 2.6% for whites, 0.1% for blacks, and 0.58% for Hispanics.[American Cancer Society 2019] Risk increases with age, with an average age of 63 at diagnosis, but melanoma is one of the most common skin cancers in patients, especially women, younger than 30.[American Cancer Society 2019] Although melanoma accounts for only 1% of skin cancers, it causes a large proportion of skin cancer deaths. However, there are no current formal guidelines from either the US Preventive Services Task Force (USPSTF) or the American Cancer Society regarding screening for melanoma.[ACS 2019; USPSTF 2016]

The incidence of melanoma is rising, according to a recent study of California populations. A new analysis in non-Hispanic whites suggests that rising melanoma rates are real, not attributable to increased levels of detection, and that the burden of the disease could rise significantly in the coming years.[Clarke 2017] Researchers tracked incidence and stage at diagnosis of melanoma across different socioeconomic status (SES) groups. Across all groups, the researchers found increases not only in incidence, but also in advanced disease. Overall, the incidence rose 25% in men from 1998-2002 to 2008-2012 (an average annual age-adjusted incidence of 34.7 to 43.5 per 100,000 person-years), and by 21% in women between those two time periods (from 21.7 to 26.2 per 100,000). Melanoma incidence rate ratios (IRR) increased across all SES classes: by 27% among men in the highest SES neighborhoods, and by 12% among men in the lowest SES neighborhoods. For women, the rates increased by 28% and 13% respectively. The highest increases in the incidence of regional and distant disease occurred in the lowest SES neighborhoods. Researchers noted the importance of not only prevention but developing methods to enhance early detection, particularly in areas where access to providers is limited.[Clarke 2017]

Melanoma is highly curable when detected early, but advanced melanoma spreads to the lymph nodes and internal organs, resulting in death. On average, one American dies from melanoma every hour.

Melanoma has no unique clinical presentation, as it varies depending upon the anatomic location and histopathological type: superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, and acral lentiginous melanoma.[Situm 2014] Differential diagnosis include a wide range of benign and malignant skin tumors. Initial observation includes the ABCDE rule (Asymmetry, irregular Border, multiple/unusual Color, large Diameter, evidence mole is Evolving). A dysplastic nevus (also called an atypical or Clark’s nevus) is an acquired mole with a unique clinical and histopathologic appearance which sets it apart from the common nevus. These moles appear atypical clinically, often with a “fried-egg” appearance, and are commonly biopsied by providers due to the concern for melanoma. A clinical diagnosis of atypical nevi is based upon the presence of at least 3 of the following features: diameter greater than 5 mm, ill-defined borders, irregular margins, and lesional color variation. Individuals with these nevi have an increased risk for melanoma.[Baigrie 2018]

Identifying new or changing melanocytic lesions, particularly in patients with numerous or atypical nevi, can be challenging.[Berk-Krauss 2017] Dermascopy can be a valuable aid in the detection (augmented by biopsy and histopathological analysis), but clinician experience and education are crucial in optimizing the use of dermoscopy.[Situm 2014] Total-body photography and sequential digital dermoscopy imaging, together known as digital follow-up, are 2 prominent forms of noninvasive imaging technology used in mole mapping that have been found to improve diagnostic accuracy, detect earlier-stage melanomas, and reduce costs.[Berk-Krauss 2017]

Melanoma incidence continues to increase across many populations globally and there is significant mortality associated with advanced disease. However, if melanoma is detected early, patients have a very promising prognosis. The methods that have been utilized for early detection include clinician and patient skin examinations, dermoscopy (static and sequential imaging), and total body photography via 2D imaging. Total body photography can create a 3D representation of the patient linked with dermoscopy images of individual lesions.[Rayner 2018] 3D total body photography is a particularly beneficial screening tool for patients at high risk due to their personal or family history or for those with multiple dysplastic nevi. Appropriate use of this technology can improve diagnostic accuracy, is time- and cost-efficient, may optimize crucial early detection. A recent study that highlighted the challenges in diagnosing repigmentation within or adjacent to lentigo maligna or lentigo maligna melanoma scars found reflectance confocal microscopy and dermoscopy aided in the comprehensive assessment.[Navarrete-Dechent 2019] Clinicians would benefit from education and training aimed at improving the detection and evaluation of suspicious melanocytic lesions.

Debate is ongoing about the value of melanoma screening. Screening imposes a significant burden on practitioners and on the overall health care system. One-fifth of individuals who undergo skin cancer screening are at low risk of skin cancer. Increased screening among these low-risk patients leads to increased numbers of biopsies of benign lesions and increased health care costs; furthermore, overscreening in the office may reduce access to care for those who need treatment for other conditions.[Stratman] Dermatologists lack consensus on skin cancer screening guidelines; a prospective screening trial is unlikely given the complication and the expense involved.[Stratman] Only 33% of dermatologists are aware that skin cancer screening guidelines exist from major health policy organizations.[Federman] Given the lack of a unified skin cancer screening guideline, it is difficult to measure whether dermatologists are screening appropriately, overscreening, or underscreening. [Stratman]

There is also reason to be concerned about the accuracy of melanoma diagnosis. One study found a wide range of diagnoses among pathologists in the US.[Elmore] The researchers concluded that “Diagnoses spanning moderately dysplastic nevi to early stage invasive melanoma were neither reproducible nor accurate.”

**Gap: Clinicians who treat skin diseases need more information about the various treatment approaches that are used for melanoma, including newer forms of immunotherapy and targeted therapy.**

*Learning objective: Discuss available treatment strategies for melanoma at various stages of its progression.*

Surgery is the definitive treatment for early-stage melanoma, with medical management generally reserved for adjuvant treatment of advanced melanoma. Until 2011, the FDA had only approved 2 therapies for metastatic melanoma: dacarbazine and high-dose interleukin-2. Adjunctive radiation therapy may be recommended in late stage disease. Since 2011, there have been 8 new approved chemotherapies for advanced melanoma in the US, including ipilumumab, peginterferon alfa-2b, vemurafenib, dabrafenib, trametinib, pembrolizumab, nivolumab, and talimogene laherparepvec (T-VEC), as well as combination dabrafenib with trametinib and nivolumab with ipilumumab. Ipilimumab at the high dose of 10 mg/kg produced a significant improvement in relapse-free survival and overall survival for stage III melanoma patients, but this approach poses a high risk for immune-related toxicities.[Napolitano 2018] New avenues include pathway targeted therapies and immunotherapies. Current immunotherapy approaches include immune checkpoint blockade, interferons, interleukins, combination immunotherapy, and T-VEC vaccine (oncolytic virus therapy).[AIM Foundation]

The discovery that up to 60% of all melanoma tumors have a genetic mutation that causes the amplification of BRAF – a signaling molecule that causes cellular proliferation by the tumor – has led to the approval of selective BRAF enzyme inhibitor that causes programmed cell death in tumors with this mutation. Ipilimumab – one of a new class of agents known as immune checkpoint inhibitors – is a human monoclonal antibody that blocks the activity of CTLA-4 as a down-regulator of T-cell activation. It is approved for the treatment of unresectable or metastatic melanoma based on results of two prospective, randomized, international trials, one each in previously untreated and in treated patients. Vemurafenib is an orally available, small molecule, selective BRAF inhibitor that is approved by the FDA for patients who have unresectable or metastatic melanoma and who test positive for the *BRAF* V600E mutation. Treatment with vemurafenib is discouraged in wild-type BRAF melanoma because data from preclinical models has demonstrated that BRAF inhibitors can enhance rather than downregulate the mitogen-activated protein kinase (MAPK) pathway in tumor cells with wild-type *BRAF* and upstream *RAS* mutations. In May of 2013, two more drugs that target mutations on the BRAF gene were approved: dabrafenib, a BRAF inhibitor and trametinib, a MEK inhibitor. These two inhibitors were then approved in January 2014 as the first approved combination of oral targeted therapies for unresectable or metastatic melanoma with *BRAF* V600E or V600K mutations.

In September 2014, pembrolizumab became the first anti-programmed death (PD-1) antibody to be approved in the United States. PD-1 protein, a T-cell co-inhibitory receptor, and one of its ligands, PD-L1, play a pivotal role in the ability of tumor cells to evade the host’s immune system. Blockade of interactions between PD-1 and PD-L1 enhances immune function in vitro and mediates antitumor activity in preclinical models. The anti-PD-1 and anti-PD-L1 antibodies potentiate immune responses by blocking the interaction between the PD-1 protein, a T-cell co-inhibitory receptor, and one of its ligands, PD-L1—critical players in the ability of tumor cells to evade the host’s immune system. In December 2014, the FDA granted accelerated approval for nivolumab, another PD-L1 inhibitor.

In October 2015 the two-pronged immunological strategy pairing the anti-PD-1 antibody nivolumab with ipilimumab was approved. Several other promising therapies are in various clinical trial stages, including another combination therapy of cobimetinib plus vemurafenib. Oncolytic virus immunotherapy is a new approach that uses native or attenuated live viruses to selectively kill melanoma cells and induce systemic tumor-specific immune responses. A new therapy in this class, talimogene laherparepvec (T-VEC), which is injected directly into melanoma tumors, is a genetically modified version of herpes simplex virus that replicates only in cancer cells, thus destroying tumors while sparing healthy tissues.

Experimental immunotherapy approaches include inhibitory checkpoint molecules (PD-L1, TIM-3, LAG3, and IDO), stimulatory checkpoint molecules (CD40, 4-1BB, KIR, GITR), as well as adoptive T cell therapy. Vaccines against melanoma, incorporating killed melanoma cells that trigger the body’s immune response, are also being evaluated in clinical trials; results to date have been mixed. Another emerging immunotherapy approach involves a combination of chemotherapy and radiation, followed by tumor-infiltrating lymphocytes; early evidence suggests this technique can shrink melanoma tumors and prolong life. An even more complex approach involves modifying certain genes within the lymphocytes before administering them to patients. Combinations of these immunotherapeutic strategies are also being investigated.

Certain melanomas – typically those involving the palm of the hand or sole of the foot – involve changes in the C-KIT gene. Clinical trials are underway using drugs such as imatinib, dasatinib, and nilotinib, which are known to target cells with changes in C-KIT. Other studies are investigating drugs that target still other abnormal genes or proteins, such as axitinib, pazopanib, and everolimus.

Given these fast-evolving new therapeutic approaches, and given that many other approaches to the treatment of melanoma are under investigation, clinicians need to stay current about clinical trial updates and emerging therapy options. As the results from clinical trials mature in the next years, a change in the landscape of adjuvant treatment for melanoma is expected, resulting in new challenges in treatment decisions such as optimizing patients’ selection through predictive and prognostic biomarkers, and management of treatment related adverse events, in particular immune-related toxicities.[Napolitano 2018]

**Gap: Clinicians may not be knowledgeable regarding the high-risk skin cancer indications for Mohs surgery**.

*Learning objectives: Identify high-risk tumor characteristics and indications for Mohs surgery and the impact of patient characteristics and expectations on the results of the procedure*.

A significant percentage of nonmelanoma skin cancers (NMSCs) have been shown to be of an aggressive histologic subtype not initially diagnosed on initial biopsy at the time of Mohs micrographic surgery (MMS).[Kyllo 2019] In one prospective study, more than 10% of tumors were upgraded at time of MMS, and were more surgically challenging than non-upgraded tumors. At the same time, there is controversy regarding whether NMSC in elderly individuals should undergo Mohs micrographic surgery.[Rogers 2018] A recent retrospective study of nearly 500 elderly patients (>85 years) with NMSC who underwent MMS had a median survival of 20 months longer than those who did not undergo MMS.[Rogers 2018] These findings suggest primary dermatologists would benefit from education regarding Mohs appropriate use criteria guidelines.[Bichakjian 2019; Kyllo 2019; Rogers 2018]

Noting that patients recall less than 50% of the information provided by their physicians, a new approach to increase patient comprehension is through informational videos.[Newsom 2018] A recent study found that watching an information video on Mohs surgery was beneficial and aided in their understanding of the Mohs surgery; further, patients appear to prefer a narrative video that includes patient testimonials and animations over a purely didactic format.[Newsom 2018]

**Gap: Clinicians may not be aware of the higher risk posed by immunosuppression for the development of cutaneous cancers.**

*Learning objective: Recognize the need for increased vigilance for the development of skin cancer in immunocompromised patients.*

The prevalence of skin cancer is higher among immunosuppressed patients, including those with lymphoproliferative disorders (non-Hodgkin lymphoma, chronic lymphocytic leukemia) or those with iatrogenic immunosuppression following organ transplantation.[Brin 2014] In addition, these patients experience greater morbidity and mortality associated with skin cancers. The most common skin cancer in immunosuppressed patients is squamous cell carcinoma, which often presents with more aggressive features and has a greater rate of metastasis.[Brin 2014] Surgical therapy is the cornerstone of treatment, but comprehensive management also involves pharmacologic treatment options, lifestyle modifications, and adjustment to the immunosuppressive regimen.[Brin 2014] Clinicians should be aware of the higher risk for skin cancer among immunocompromised patients and should be prepared to design appropriate strategies to prevent, monitor for, and treat skin cancer in this group.

**Gap: Clinicians may be challenged to distinguish between benign lesions, such as Spitz nevi, and melanoma in its early stage.**

*Learning objective: Describe available methods for assessing and monitoring Spitz nevi.*

In everyday dermatology practice, the identification of Spitz nevi can cause anxiety, confusion, and controversy.[Marghoob 2013] This is due in part to the overlap between the features of these lesions and those of melanoma. Clinicians and patients alike worry whether a spitzoid nevus is truly benign, whether it is actually a malignant tumor in disguise, and whether it can transform into melanoma. There is also risk that a melanoma can be misdiagnosed as a Spitz nevus. Clinicians would benefit from knowledge about when to biopsy the lesion, as well as how apply current techniques for assessing and monitor these lesions, including dermoscopy and digital monitoring to assess the evolution of the nevus.

**Gap: Clinicians may not be utilizing the full armamentarium of methods for managing basal cell carcinoma and squamous cell carcinoma.**

*Learning objective: Describe available nonsurgical options for managing superficial nonmelanoma lesions.*

Many skin cancers can be removed from the skin quickly and easily during a surgical procedure such as curettage and dessication, Mohs surgery, or wide excision. Often no other treatment is needed. In other cases, however, treatment is needed beyond surgery.[Cancer.net] Topical chemotherapy may be indicated for superficial lesions. Agents available for include diclofenac, fluorouracil, and ingenol mebutate are approved for the treatment of precancerous actinic keratosis. Photodynamic therapy may also be valuable for this condition. For small basal cell cancers not located on the face, topical imiquimod, an immune stimulator, can be considered. Topical fluorouracil is approved to treat superficial basal cell carcinomas. Cryotherapy and laser therapy also be appropriate for selected patients. Clinicians should be aware of current and emerging options to address nonmelanoma lesions.

**Gap: Merkel cell carcinoma, while uncommon, is aggressive, and clinicians may not be aware of its optimal management**.

*Learning objective: Define the underlying processes that lead to Merkel cell carcinoma, how recurrences can be diagnosed early, and resources for management.*

Merkel cell carcinoma (MCC) is a rare and aggressive form of skin cancer associated with aging and immunosuppression. Its incidence is therefore increasing, in large part owing to the aging of the US population.[Paulson 2018] Where the number of melanoma cases increased 57% from 2000 to 2013, the number of MCC cases increased by 95%, with the greatest increase among people aged ≥85 years. It is anticipated that there will be 3300 cases/year by 2025.[Paulson 2018] The past decade has seen substantial advances in the understanding of the biology of MCC, which has led to investigation and development of a highly effective immunotherapy via programmed death 1 (PD-1) blockade with pembrolizumab.[Bichakjian 2018; Harms 2018; Nghiem 2016; Nghiem 2019] However, not all patients have a durable response to this therapy.[Harms 2018] Clinicians should have a sufficient understanding regarding optimal patient selection and monitoring, as well as how to facilitate a multi-disciplinary treatment team approach.

**Gap: There is controversy regarding which imaging and blood tests are indicated to identify advanced melanoma early.**

*Learning objective: Discuss National Comprehensive Cancer Network guidelines on melanoma surveillance, diagnostic tests, and recurrence risk calculators.*

Advanced melanoma can now be treated with multiple approaches, and optimal outcomes are associated with early detection of recurrent disease. However, there is controversy as to which imaging and blood tests are indicated in this setting. Clinicians would benefit from a review of the existing data and guidelines from the National Comprehensive Cancer Network regarding the sensitivity, specificity and cost of leading approaches to detect melanoma recurrence using imaging and blood tests.[NCCN 2019]

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**Pediatric Dermatology**

**Gap: Clinicians may not always tailor their diagnosis and treatment approach to meet the needs of their pediatric and adolescent patients.**

*Learning objective: Apply current strategies for assessing and treating dermatologic conditions in pediatric patients, including acne, atopic dermatitis, birthmarks and scar management.*

The range of conditions seen by the pediatric dermatologist is diverse and includes bacterial, viral, and fungal infections, acne, atopic dermatitis, hemangiomas, and many other conditions. One area that is frequently overlooked in pediatric patients is the potential for conversion of benign moles to dysplastic nevi. Literature also indicates that clinicians are not differentiating moles that are dangerous from those that are harmless.

Timely diagnosis of melanoma in children requires that clinicians maintain a high index of suspicion.[Moreira 2014] A recent study identified clinically recognizable factors associated with a mole-prone phenotype that may facilitate the identification of individuals at risk for melanoma.[Xu 2017] A prospective observational cohort study was conducted from January 1, 2009, to December 31, 2014, with a 2- to 3-year follow-up. A total of 569 students enrolled in the 8th or 9th grade was included. The overall retention rate was 73.3%, and 417 students were reassessed in the 11th grade. Of the 417 students assessed at follow-up in the 11th grade (166 females and 251 males), 111 participants (26.6%) demonstrated a mole-prone phenotype: 69 students (62.2%) with 1 nevus greater than 5 mm in diameter, 23 students (20.7%) with total nevus count in the top decile, and 19 students (17.1%) with both characteristics. On multivariate analysis, baseline total nevus count and increased variability of nevus dermoscopic pattern were associated with a mole-prone phenotype.[Xu 2017]

A serious concern has been the use of indoor tanning booths among adolescents, but data show generally improving behaviors. The prevalence of indoor tanning decreased from 15.6% in 2009 to 7.3% in 2015, according to a new JAMA Dermatology report.[Guy] Analysis of the Youth Risk Behavior Survey data from 2009, 2011, 2013, and 2015, including 15,000 to 16,000 high school students nationwide, showed decreases in indoor tanning among male (from 6.7% in 2009 to 4.0% in 2015) and female (from 25.4 % in 2009 to 10.6 % in 2015) students overall, non-Hispanic white (from 21.1 % in 2009 to 9.4% in 2015) and Hispanic (from 8.2% in 2009 to 4.7% in 2015) students overall, and all age groups.[Guy 2017]

Pediatricians and dermatologists must also be able to assess treatment approaches for complex skin diseases such as atopic dermatitis (AD) and manage the disease across the severity spectrum. AD is a complex, multifactorial, chronic, pruritic, eczematous skin disease that is mediated through an immediate hypersensitivity reaction. AD typically manifests in infants aged 1 to 6 months; 60% of patients experience their first outbreak by 1 year and 90% have had their first outbreak by age 5 years. Emollients — moisturizing agents that inhibit water loss and provide a protective coating — are recommended in all patients with atopic dermatitis. Additionally, emollients may reduce the need to use topical corticosteroids. Analysis has identified an increased risk for AD and other skin diseases among infants of black or Asian race/ethnicity at 6 months of age.[Eichenfeld 2017]

In the realm of psoriasis treatment, the FDA in 2016 approved the use of etanercept for pediatric patients (aged 4 to 17) with chronic moderate-to-severe plaque psoriasis. The agent is administered by subcutaneous injection. For pediatric plaque psoriasis, the recommended dose and frequency is 0.8 mg/kg weekly, with a maximum of 50 mg per week.

Clinicians should keep current on the scientific understanding the disease pathophysiology as it manifests in younger vs older patients and should be aware of the rapidly evolving armamentarium of approved agents for with indications for younger age groups.

**Gap: Patch testing is underutilized in pediatric patients.**

*Learning objective: Identify when epicutaneous patch testing is appropriate in pediatric patients.*

Although both adults and children are equally likely to have allergic contact dermatitis (ACD), evidence indicates there is a substantially lower likelihood of patch testing performed on pediatric patients.[Jacob 2017; Yu 2018] However, ACD may complicate the clinical course of atopic dermatitis (AD), and patch testing remains the standard diagnostic tool for identifying ACD.[Ascha 2016; Chen 2016; Owen 2018; Yu 2018] Expert consensus opinion recommends patch testing in patients with AD who fail to improve with topical therapy, with atypical dermatitis or with patterns suggestive of ACD, and before initiating biologic therapy for the treatment of AD.[Chen 2016]

A survey of US dermatologists, including members of the Society for Pediatric Dermatology (SPD) and the American Contact Dermatitis Society (ACDS), responded to a survey regarding the use of patch testing in pediatric patients.[Jacob 2017] Members of SPD were the most likely to perform a commercially available patch test but had a significantly lower likelihood of performing North American Contact Dermatitis Group standard tests than nonmembers. The survey indicated pediatric patch testing is underutilized and under-reported.[Jacob 2017]

Clinicians would benefit from expert guidance regarding the clinical scenarios in which patch testing is indicated, the preferred patch-testing series, contraindications to patch testing, and the meaning of positive patch-test results in patients with atopic dermatitis.[Owen 2018]

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**Psoriasis**

**Gap: Many clinicians have a poor understanding of psoriasis as a systemic, immune-mediated disease with multiple comorbidities, psoriasis is often underdiagnosed and undertreated.**

*Learning objective: Describe recent scientific findings that explicate the inflammatory basis of psoriasis.*

Psoriasis is an inflammatory chronic, immune-mediated systemic disease affecting 3.2% of the adult US population (approximately 8 million people). Characterized by pruritic inflammatory plaques with a chronic remitting and relapsing disease course, psoriasis is associated with significant comorbidities including obesity, metabolic syndrome, cardiovascular disease, psoriatic arthritis, autoimmune disease, psychiatric illness, liver disease, smoking, malignancy, chronic obstructive pulmonary disease, sleep apnea, and alcohol abuse, resulting in a markedly decreased quality of life.[Menter A, AAD agenda, July 2017] Psoriatic arthritis develops in 10% to 30% of these patients approximately 10 years after the onset of skin disease.[ [MAPP 2016; Mease et al 2014; Young 2017] Insight into the overlapping pathogenesis of psoriasis comorbidities highlights the importance of immune-mediated mechanisms in these disease states.[Menter, AAD 2017; NPF Guidelines 2016; Eissing 2015]

Clinicians may lack a thorough understanding of psoriasis beyond its dermatologic manifestations. For example, in a recent survey, 75% of dermatologists and rheumatologists acknowledged that psoriatic arthritis may be underdiagnosed because of a failure to connect skin and joint symptoms. Fewer than half of primary care physicians reported screening psoriasis patients for cardiovascular risk factors, as recommended by National Psoriasis Foundation guidelines.[Parsi 2012] Thus, accurate diagnosis and effective management of psoriasis and its comorbidities requires a deeper understanding of its pathophysiology.

**Gap: Many clinicians fail to apply updated treat-to-target guidelines for diagnosis, treatment, and assessment of progress in patients with psoriasis, who often remain undertreated or unsatisfied with treatment.**

*Learning objective: Discuss current clinical guidelines for optimal diagnosis and treatment of psoriasis.*

In a survey of dermatologists, 92% acknowledged that the disease burden of psoriasis is frequently underestimated and that the condition is undertreated.[van de Kerkhof, MAPP 2015] Among patients with psoriasis, 24% to 35% of those with moderate psoriasis, and 9% to 30% with severe psoriasis were untreated.[Armstrong 2017] In a 2016 survey, only 1 in 3 patients reported being satisfied with their treatment plan, and more than 80% reported emotional impacts resulting, in part, from lack of knowledge about what to expect.[Gould 2016] Barriers to guideline adherence frequently cited by physicians include lack of knowledge and fear of side effects, suggesting the need for further educational strategies.[MAPP]

Clinicians also need expanded knowledge and improved clinical confidence in assessing disease severity, treatment results, and quality of life.[Gottlieb 2016] Clinicians should discuss treatment goals with patients, stressing that control of the disease is the primary aim and that remission may be achievable with appropriate use of therapies in appropriately chosen patients. Treatment goals for psoriasis include rapidly controlling the disease process; achieving and maintaining remission; minimizing adverse events; and enhancing quality of life. For mild-to-moderate disease, topical therapies may suffice. Choices include emollients, corticosteroids, vitamin D analogs such as calcipotriene and calcitriol, tar, and topical retinoids (tazarotene). Topical tacrolimus or pimecrolimus are alternatives for use in facial or intertriginous areas. Using different vehicles and combination topical therapies may also be effective. Severe psoriasis (affecting >5%-10% of body surface area) requires phototherapy or systemic therapies such as retinoids, [methotrexate](https://www.uptodate.com/contents/methotrexate-drug-information?source=see_link), [cyclosporine](https://www.uptodate.com/contents/cyclosporine-ciclosporin-drug-information?source=see_link), [apremilast](https://www.uptodate.com/contents/apremilast-drug-information?source=see_link), or biologic immune modifying agents.[Young 2017] Keeping the regimen simple and acceptable to the patient can maximize adherence.

Oral methotrexate has been a mainstay of immune-mediated inflammatory joint and skin diseases for decades. However, because each patient has a unique pharmacogenomic profile, and because the manifestation of diseases such as psoriasis can be different in different patients, there may be significant variability in an individual’s response to treatment with methotrexate.[Vena 2018] Awareness of the limitations of oral methotrexate has sparked interest in the use of parenteral (subcutaneous [SC]) methotrexate. SC administration may offer greater efficacy, due in part to higher drug exposure, but with no increased risk for adverse reactions and with a lower frequent of gastrointestinal complaints.[Vena 2018] At this time most of the research on SC methotrexate has focused on its role as a therapy for rheumatoid arthritis; very little data are available on its use in psoriasis. However, clinicians should be aware of ongoing research in this area, which could lead to even more effective therapeutic options for managing psoriatic disease.

The National Psoriasis Foundation (NPF) suggests that clinicians need to understand and use defined treatment targets, citing clinical assessment tools including changes in BSA (Body Surface Area), Psoriasis Area and Severity Index (PASI), Physician Global Assessment (PGA), and Dermatology Life Quality Index (DLQI).[Armstrong 2017] The treat-to-target strategy allows patients and their health care providers to take better control of psoriatic disease by setting specific targets and goals for improved health outcomes.[NPF Treat to Target, 2017]

Periodic assessments using treatment targets provide a clear evaluation of progress and a guide for adjusting treatments. A recent consensus of experts concluded that an initial goal should be to reduce psoriasis BSA to ≤1% within 3 months of starting treatment; if the goal is not met, an “acceptable response” is 75% improvement in BSA. During the maintenance period, the consensus on the target response was BSA ≤1% at every 6-month assessment interval.[Duffy 2016]

**Gap: Patients with psoriasis may not respond adequately to treatment or they may experience diminished benefit over time. New and emerging treatments show favorable efficacy and safety for psoriasis, but many clinicians fail to understand the role of biologics and may underutilize these therapies.**

*Learning objectives:*

* *Review safety and efficacy data on new and emerging therapies for psoriasis.*
* *Implement a strategy for stepwise management of psoriasis with topical and biologic agents, including the use of treat-to-target goals*

The advent of biologic agents has allowed treatment goals for psoriasis to be more aggressive. These agents also have made remission a potential and realistic goal.[Feldman 2017] Biologic immune- modifying agents act through targeted inhibition of specific cytokines associated with inflammatory immune responses and skin lesions.[Leonardi 2015, Young 2017]

Recent years have seen a flurry of activity in the realm of biologic therapies for psoriasis. Older biologics target TNF-alpha, while some of the more recently approved agents target interleukin (IL)-17. In 2017 the FDA approved guselkumab, the first monoclonal antibody that selectively blocks IL-23, for treatment of moderate-to-severe psoriasis in adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.[Tremfya PI] Two other IL-23 biosimilars, tildrakizumab-asmn and rizankzumab-rzaa, were approved in March and April 2019, respectively, for moderate-to-severe plaque psoriasis. Other biosimilars available for plaque psoriasis include adalimumab-adaz, adalimumab-adbm, adalimumab-atto, infliximab-abda, infliximab-dyyb, and infliximab-qbtx. A once-daily topical lotion for psoriasis combining halbetosol propionate and tazarotene was approved in April 2019.

An agent with a unique mechanism, piclidenoson, acts as an A3 adenosine receptor agonist and is in phase 3 trials. Various other drugs with various mechanisms are in phase 2. Namilumab, a granulocyte-macrophage colony-stimulating factor inhibitor, proved ineffective in a phase 2 trial.[Papp 2019] Neihulizumab (T cell apoptosis inducer), sotrastaurin (pan-protein kinase C [PKC) inhibitor), and tegralizumab (anti-CDV antibody) are on the horizon. Clinicians should be educated about the burgeoning armamentarium of treatment options for psoriasis at all levels of severity and in a range of patients.

Some expertssuggest that, based on results of studies with newer biologic agents, the current objective criterion of PASI 75 as a therapeutic endpoint in clinical trials should be raised to PASI 90 or 100.[Manolo 2015; Jancin 2018] Clinicians would benefit from education that presents the rationale for more aggressive therapeutic targets and provides information about how best to design therapy to achieve these goals in real-world practice.

Adherence may be significantly better in patients receiving biologic therapies, but costs can be a challenge.[Cheng 2014] Clinicians need to become familiar with patient eligibility for biologics as well as strategies for assisting patients with access and payment.[Gottlieb 2016] Primary care clinicians would benefit from guidance regarding when to refer patients with psoriasis to specialists.[Gottlieb 2016]

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**Rosacea**

**Gap: Many clinicians have a poor grasp of the typology, risk factors, and triggers of rosacea.**

*Learning objective: Discuss safety and efficacy data on current and emerging therapies for rosacea.*

Rosacea is a common chronic skin condition of the face that affects approximately 16 million American adults; according to the National Rosacea Society (NRS), only a small fraction of these patients are being treated.[NRS] More than 90% of rosacea patients have reported reduced self-confidence and self-esteem, and 41% reported avoiding public contact, and 88% of those with severe symptoms said the disorder had adversely affected their professional interactions; half of these patients reported missing work because of their condition.[Moustafa 2014; NRS] Nearly half of respondents to another NRS survey had never heard of rosacea prior to receiving their diagnosis, and 95% had known little or nothing about the signs and symptoms of rosacea prior to their diagnosis.

Rosacea is a chronic disorder with intermittent periods of exacerbation. The underlying pathogenesis is unknown. However, major pathogenic components appear to be inflammatory, vascular, and neural in origin.[Wilkin] Histology identifies blood vessel dilation, infiltration of T-helper cells, macrophages, and mast cells. Keratinocyte Toll-like receptors may play a role in the pathogenic process of immune system activation.[Weinkle 2015] A genetic component has been identified in about half the cases.[Aldrich 2015]

Triggers and risk factors may not be clear to patients and often are not clear to clinicians. In a recent survey of clinicians’ rosacea knowledge, 90% of respondents were not aware that rosacea is associated with past but not current smoking.[Frontline Medical Communications 2016; Li 2017] Many need education about diagnostic signs. For example, 60% failed to identify conjunctival hyperemia as the most commonly reported sign of ocular rosacea.

Physician education and physician/patient communication need to become an important part of the treatment plan for patients with rosacea as well.

**Gap: Many clinicians lack current, clinically relevant information on traditional, novel, and emerging therapies for rosacea, their mechanisms of action, and their efficacy and safety as monotherapy and in combination treatment regimens.**

*Learning objective: Define appropriate goals and strategies for the optimal management of patients with rosacea.*

No cure exists for rosacea, but clinicians have several options to treat the symptoms. In this regard, many clinicians could benefit from education to improve their clinical practice. For example, 60% of survey respondents did not know that tetracyclines are the most common antibiotic that is effective in ocular rosacea.[Frontline Medical Communications 2016]

Many topical agents are available. Topical [azelaic acid](file:///F:\rizzom\topic\azelaic-acid) may be used to reduce inflammatory lesions, bumps, and papules. Metronidazole, a cornerstone of papulopustular rosacea treatment, seems to have antimicrobial, antioxidant, and anti-inflammatory properties.[Wick 2016] Brimonidine tartrate gel, FDA-approved in 2013 for facial flushing, acts as a vasoconstrictor. In 2014, the FDA approved a topical formulation of ivermectin cream for the treatment of inflammatory lesions related to papulopustular rosacea.[FDA 2014] Azelaic acid in a foam formulation that is effective against papulopustular rosacea, was FDA approved in 2015. Topical oxymetazoline hydrochloride cream, which significantly improves rosacea-associated erythema, was approved by the FDA in 2017. In phase III studies, efficacy of topical oxymetazoline increased over the course of 52 weeks.[McNamara 2017] Minocycline foam (FMX101), which inhibits numerous bacterial species and inflammation, has completed several phase 3 trials.[Jesitus 2017] In the most recent trial, researchers observed the percentage of inflammatory [acne lesions](https://www.cosmeticsandtoiletries.com/research/universitydata/A-New-Intersection--Could-Anti-pollution-Mean-Anti-acne-434560143.html) between treatment and vehicle groups to be significantly different; at week 12, the FMX101 treatment group experienced a reduction of 56%, while the vehicle group experienced a 43% reduction.[Raoof 2019] In February 2019, results of a 1-year open-label extension trial showed topical minocycline foam proved safe and effective for patients with moderate-to-severe papulopustular rosacea.[Foamix] A new drug application for minocycline foam was submitted in December 2018.

Oral [tetracycline antibiotics](file:///F:\rizzom\topic\tetracycline-antibiotics) and topical antibiotics are often the first line of therapy, prescribed to relieve papules, pustules, and inflammation. If papules and pustules persist, isotretinoin, which reduces sebum production and the size of sebaceous glands, may be considered.[Wick 2016] Doxycyline 40 mg (a sub-antimicrobial dose) may be as effective as monotherapy or used in combination with topical agents.[Wick 2016]

Omiganan pentahydrochloride, under study for papulopustular rosacea, is an aqueous-based topical cationic antimicrobial peptide with rapid bactericidal activity against microorganisms colonizing the skin.[Clinical Trials.gov 2017; Cong 2019]

Light therapy such as pulsed dye laser and intense pulsed light can be used for multiple types of rosacea.[Do 2016] In one survey, patients given a series of recurring pulse dye laser treatments reported decreasing symptoms and improved quality of life.[Do 2016]

Clinicians must be kept apprised of new data on traditional, novel, and emerging therapies for rosacea, their mechanisms of action, and their efficacy and safety as monotherapy and in combination treatment regimens.

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**Scars and Keloids**

**Gap: Clinicians may underestimate the burden of keloid disease on their patients and may not be treating keloids adequately, including use of strategies that avoid scarring.**

*Learning objective: Discuss techniques for managing keloids that offer the greatest benefit with minimal risk of scarring.*

Hypertrophic scars and keloids are aberrant variations of typical wound healing. Keloids, which result from an overgrowth of dense fibrous tissue that develops after healing of a skin injury, involve tissue that extends beyond the borders of the original wound, do not usually regress spontaneously, and tend to recur after excision. Hypertrophic scars are common after thermal injuries and other injuries that involve the deep dermis, and typically do not expand beyond the borders of the original wound. These scars are characterized by erythematous, pruritic, raised fibrous lesions.[Berman 2017]

Clinicians may underestimate the impact of keloids on their patients’ quality of life. In one study, keloid disease was associated with considerable impairment of emotional wellbeing, as assessed by emotional and mental health-related quality of life measures.[Bijlard 2017] Pain and itch were cited as the worst symptoms. The authors conclude that patients with keloids require access to effective treatment aimed at alleviating physical symptoms.

Standard treatment of hypertrophic scars and keloids includes occlusive dressings, compression therapy, and intralesional corticosteroid injections, alone or in combination.[Berman 2017] Compression treatments and devices include button compression, pressure earrings, ACE bandages, elastic adhesive bandages, compression wraps, spandex or elastane (Lycra) bandages, pressure-gradient garments made of lightweight porous Dacron, bobbinet fabric (usually worn 12-24 hours per day), and zinc oxide adhesive plaster. Overall, 60% of patients treated with these methods showed 75% to 100% improvement.[Berman 2017]

Intralesional injection of various agents including triamcinolone, interferon, 5-fluorouracil, doxorubicin, and bleomycin, alone or in combination, have resulted in modest degrees of keloid flattening. Therapies have also included cryosurgery, laser therapy, verapamil, retinoic acid, imiquimod 5% cream, tamoxifen, tacrolimus, botulinum toxin, hydrogel scaffold. Many of these therapies are not yet approved by the FDA.[Berman 2017]

One study reported molecular-based evidence of the clinical benefits of adding 5-fluorouracil to a steroid injection for improved scar regression and reduced recurrence of keloids.[Huang] 5-fluorouracil–induced G2 cell-cycle arrest and apoptosis may be associated with p53 activation and p21 up-regulation. The combination of 5-fluorouracil and triamcinolone significantly affected the treatment, leading to more significant cell proliferation inhibition, apoptosis, Col-1 suppression, and MMP-2 induction [Huang 2013]

In another study, surgical excision combined with intraoperative platelet-rich plasma (PRP) and adjuvant postoperative in-office superficial radiation therapy (SRT) achieved a 94% nonrecurrence rate on follow-up over a 2-year period. Researchers conducted a retrospective analysis of 49 patients treated with extralesional surgical excision of keloids localized to the ear followed by the application of autologous PRP to the wound site and postoperative in-office SRT. Fifty ear keloids were treated with this method in patients aged 15 to 66 years (mean=32, SD=16) of which 14 were male and 35 female.[Jones 2017]

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**Sunscreens**

**Gap: Clinicians do not always provide their patients with appropriate counseling about effective strategies for protecting against sun exposure to reduce the risk for skin cancers and to prevent premature skin aging.**

*Learning objective:* *Counsel patients about effective strategies for photoprotection.*

The greatest degree of sun exposure occurs through adolescence.[Andreola 2018] Proper and consistent photoprotection can minimize the risk of photocarcinogenesis. Effective techniques include shade seeking, the use of physical agents (clothing, sunglasses, hats) to protect against ultraviolet radiation (UVR) exposure, and the proper application and re-application of sunscreens on all exposed areas.[Cestari 2017] Avoiding use of tanning beds is an important consideration for adolescents.[Cestari 2017]

Parents are generally responsible for instituting appropriate sun protection in younger children, while adolescents become responsible for their own photoprotective behaviors. Evidence demonstrates that, although adolescents are aware of the risks of sun exposure, they do not consistently use effective sun protective measures.[Andreola 2018] Further, adolescents may be more likely to get their information about the importance and means of sun protection from their parents, and not from their pediatrician or primary care clinician.[Andreola 2018]

Use of adequate sun protection is a crucial for preventing photodermatoses or for managing them once they occur. However, many people do not know about effective steps for prevention or they do not apply preventive techniques adequately. In a recent study, free sunscreen was provided to attendees at a state fair.[Wood] Observers reported that two-thirds of these subjects failed to apply sunscreen appropriately to all areas of exposed skin. Nearly 40% did not take additional protective measures, such as wearing a hat, sunglasses, or long-sleeved apparel. Reflecting the common misbelief that cloud cover obviates the need for protection, sunscreen use decreased dramatically on overcast days.[Wood] Clinicians would benefit from training on how to counsel patients about effective protective strategies. Notably, only one-third of those observed properly applied sunscreen over all of their exposed skin; further, sunscreen use substantially dropped on cloudy days, even though up to 80% of UV rays can penetrate the clouds. Adults who are not aware of effective sun-protection strategies or who do not use them properly for themselves will likely not provide proper guidance for their children.

Emerging evidence suggests that that individuals who have had previous nonmelanoma skin cancer (NMSC) have higher rates of use of shade, long sleeves, hats, and sunscreen compared with individuals without a history of NMSC. However, both groups were shown to have comparable rates of recent sunburn, indicating the need for continued education, particularly among younger adults, for sunburn prevention and sun avoidance.[Fischer 2016]

Clinicians must impart appropriate education to patients of all skin colors. A study in the UK found that lighter-skinned adolescents had greater use of sunscreen than darker-skinned adolescents.[Gould 2015] In addition, adolescents are less likely to routinely use sunscreen; 44% of adolescents reported never wearing sunscreen while at home during the summer, compared with 1% who used sunscreen when on holiday. The study suggests adolescents with fairer skin are more likely to be aware of the need to protect their skin compared with those whose skin tone is darker. Adults with skin of color are less likely to be diagnosed with melanoma; however, when they do develop melanoma, it is often at a later stage of disease than in lighter-skinned adults.[Barsh 2003; Baumann 2016]

Vitamin D – predominantly obtained via sun exposure – plays an important role in skeletal health in both young and elderly persons. Persons who do receive sufficient vitamin D from sun exposure need supplemental oral intake to prevent rickets and to minimize risk of developing osteoporosis later in life.[Kannan 2014] This may affect children with photosensitivity disorders owing to underlying systemic diseases. Pediatricians may need to work with dermatologists to diagnose and manage a photodermatosis in pediatric patients.[Chantom 2012]

Clinicians should be prepared to counsel patients about the importance of sun protection to minimize risk for skin cancer while ensuring that their vitamin D intake is sufficient to promote skeletal health.

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**Vitiligo and Pigmentation Disorders**

**Gap: Clinicians lack guidance to diagnose and manage pigmentation disorders.**

*Learning objective: Diagnose, and develop treatment strategies for, pigmentation disorders*.

Pigmentation disorders – whether hypo- or hyperpigmentation – can be particularly challenging to diagnose and manage, especially in skin of color (SOC). Most conditions are generally benign, but may substantially affect quality of life.[Plensdorf 2017] Types, etiologies, clinical manifestations, and treatments of pigmentation disorders differ by skin type. In addition, aging affects skin differently according to Fitzpatrick skin type.[Vashi 2016] The most common cause of hyperpigmentation disorders is exposure to ultraviolet radiation (UVR); other causes include reactions to medications, hormonal changes (melasma), and response to inflammation. Hypopigmentation disorders are either congenital (albinism) or acquired (vitiligo). Dermoscopy is a growing means for diagnosing facial melanoses without the need for biopsy.[Chatterjee 2018]

A particular challenge in managing hyperpigmentation disorders is the risk of causing hypopigmentation, particularly in SOC. The optimal strategy involves protecting skin from damaging ultraviolet and infrared radiation through the use of sunscreens and possibly topical antioxidants.[Schalka 2017] Hyperpigmentation is often treated with topical agents, chemical peels, cryotherapy, laser or energy-based therapies, and surgical excision, alone or in combination.[Plensdorf 2017] Topical hydroquinone-based bleaching agents for hyperpigmented skin is the only FDA-approved topical approach, but it is associated with substantial risks, including systemic absorption and cytotoxicity of neighboring cells. Various treatment approaches for melasma include topical therapies (tretinoin, corticosteroids, and triple combination creams); chemical peels; microneedling; radiofrequency; and lasers, alone or in combinations.[Ogbechie-Godec 2017]

Treatment of vitiligo depends upon the location and extent of skin/hair involvement. There currently is no definitive treatment for vitiligo.[Arora 2019] Therapeutic options include topical corticosteroids, calcineurin inhibitors, UVA therapy (with or without psoralens), narrowband UVB therapy, and cosmetics.[Plensdorf 2017; Speeckaert 2017] As the pathophysiology of vitiligo becomes clearer, new treatments may emerge.[Speeckaert 2017] It is important that clinicians understand that vitiligo is not just a cosmetic disease; as such, treatments must aim to also halt disease progression and stabilize depigmented lesions.[Rodrigues 2017] A recent meta-analysis observed that long-duration phototherapy optimizes treatment response for vitiligo, which is most apparent on the face and neck.[Bae 2017] An emerging option is afamelanotide, the first alpha-melanocyte-stimulating hormone (MSH) analogue, which has been approved in Europe for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP).[Minder 2017] A systematic review found that treatment with topical tacrolimus, as monotherapy or in combination with steroids, phototherapy, or lasers can induce repigmentation in more than 75% of patients.[Arora 2019] Clinicians should stay abreast of emerging options for managing pigmentation disorders to optimize outcomes for their patients.

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