NEEDS ASSESSMENT AND RESULTING GAPS

Acne

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

Learning objective: Design a comprehensive treatment plan for acne patients based on clinical guidelines, incorporating pharmacologic and nonpharmacologic strategies.

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, 1/25/2016-8/03/2016]

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: Discuss and apply in clinical practice the most recent research on the etiologies and therapy of 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, anti-inflammatory, and allow for maintenance of 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 Gold, Semin Cutan Med Surg. 2016]

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 Gold 2016] 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 non-inflammatory elements of mild to moderate acne in adult women.[Bagherani 2014] Oral contraceptives have also shown efficacy in treating acne in adult women.[Harper J, 2015]

Several new agents are emerging that may reduce sebum production: SB204, a topical agent, releases nitric oxide, which has antimicrobial and anti-inflammatory activities and may also reduce sebum production. A second drug, DRM01, targets acetyl coenzyme-A carboxylase (ACC), which is a key regulator of sebum production. A third topical agent is a potent antiandrogen, CB-03-01 (cortexolone 17α-propionate 1%), which has shown at least comparable efficacy to tretinoin.[Stein Gold 2016]

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.

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Procedural and Aesthetic 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:

- *Summarize the efficacy and safety of fillers, toxins, devices, and techniques currently available in aesthetic and procedural dermatology*
- *Identify the considerations in the selection of appropriate filler agents for treating different areas of the face.*
- *Compare and contrast the efficacy and safety of agents, devices, and techniques currently available in aesthetic and procedural dermatology.*
- *Determine the appropriate nonsurgical techniques for facial rejuvenation.*
- *Describe the appropriate use of neuromodulators in the treatment of the aging face.*

According to the American Society of Plastic Surgeons, 17.1 million cosmetic procedures were done in 2016, an increase of 3% from 2015. The majority of these (15.4 million, a 3% increase over 2015) were minimally invasive procedures.[American Society of Plastic Surgeons https://www.plasticsurgery.org/news/press-releases/new-plastic-surgery-statistics-reveal-focus-on-face-and-fat] The top 5 procedures, total numbers, and change from 2016 were:

Procedure	**Number of procedures**	**Change from 2015**
Botulinum toxin type A	7.0 million	↑4%
Soft tissue fillers	2.6 million	↑2%
Chemical peel	1.3 million	↑4%
Laser hair removal	1.1 million	↓1%
Microdermabrasion	775 thousand	↓3%

The aesthetic field continues to grow and adapt as dermatologists are now seeing more patients who, unwilling to undergo surgery, are looking for less invasive treatments. Investigators offer several explanations for this trend, with cost being a contributing factor as well as the desire of many patients for less invasive treatments that offer long-lasting results with less downtime.[Cray 2010]

The nonsurgical procedures currently used in the United States by plastic surgeons and dermatologists include injectable shaping agents, skin rejuvenation/resurfacing procedures, and other nonsurgical procedures such as laser hair removal and treatment of superficial leg veins with lasers or sclerotherapy.

Research has demonstrated that 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, may negatively affect the contours, shape, balance, and proportions of the face. The goal of treating the aging face is to restore facial balance and modify shadows. The facial evaluation should focus on areas of volume loss and opportunities to use fillers and neuromodulators (eg, botulinum toxin A). These materials make it possible for clinicians to offer nonsurgical options as

alternatives and/or adjuncts to surgical techniques. Before initiating any cosmetic procedure, clinicians need to have a comprehensive understanding of underlying changes in facial anatomy that are part of intrinsic and extrinsic factors, and the effects and potential adverse events associated with the various fillers.[Funt; Gilbert]

Dermal filler injection is the second most frequent nonsurgical cosmetic procedure performed in the U.S. (Injection of botulinum toxin is the first).[Ballin 2015] Most fillers are composed of hyaluronic acid, which is processed in different ways to produce different clinical characteristics. A number of fillers approved earlier are formulated with lidocaine to control pain.[FDA] Although not a new concept, the use of blunt cannulas to deliver fillers allows the filler to be injected with great precision with minimal bruising and bleeding as well as minimizing downtime and discomfort.[Cray] Among the many currently available options, several products have received FDA approval within the past 6 years.

Non-animal stabilized HA (NASHA) products demonstrate greater resistance to deformation than other HA products. One such product approved in 2015 (Restylane Silk) is indicated for lip enhancement and the treatment of wrinkles and lines around the mouth in people over the age of 21. It improves lip definition and affords hydration but little volume.[Solish]

Neuromodulators can improve cosmesis of the forehead by relaxing muscles that contribute to folds and wrinkles.[Solish 2016] Recent additions to the roster of botulinum toxin agents approved for cosmetic use are abobotulinum toxin A and incobotulinum toxin A.[Schlessinger]

In 2015, the FDA issued a warning to healthcare providers and the public about serious complications that can occur if dermal fillers are inadvertently injected into blood vessels in the face.[US FDA 2015] The complications could include vision impairment, blindness, stroke, and damage and/or necrosis of the skin and underlying facial structures.

Clinicians should use caution to ensure proper placement of the filler material, and patients should be informed about the potential adverse effects and how to recognize symptoms of impending serious complications.[Beleznay 2017] In order to avoid unrealistic expectations, clinicians need to understand each patient's desires and expectations and need to learn how best to counsel each patient regarding results that can be realistically achieved. Regardless of the type of injectable shaping agent chosen, injection of the upper face requires a high level of skill to avoid problems such as tissue necrosis or the formation of emboli; therefore, clinicians need to be well trained and skilled in injection techniques.[Goh] Adequate pain control is important to prevent patient movement, bruising and/or improper placement of filler.

Skin Rejuvenation/Resurfacing Procedures: Improvements of many superficial flaws may be accomplished nonsurgically with topical medications (ie, retinoids and hydroquinone) and/or resurfacing procedures (such as acid peels, dermabrasion, or laser resurfacing). Laser skin resurfacing remains a major therapeutic tool for facial rejuvenation and the treatment of acne scars and other skin damage. The technologies work by altering the epidermis and dermis, either by full field treatment or fractionated delivery of coagulative or ablative injury, thereby inducing regrowth of new epidermis and growth of new collagen and elastin in the dermis.

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]

Device Type	Clinical Use	Effects/Outcome
Fractionated ablative and nonablative lasers	Aging, tightness, acne scarring	Low-density injuries to skin; target area responds uniformly
Hybrid laser systems	Pigmented lesions (epidermal and dermal), dermal elastosis, fine lines, texture, pore size	Combined ablative/nonablative effects; adjustable for length of penetration. Less pain; area may look worse initially
Picosecond lasers	Tattoo removal, pigmented lesions, nevi, melasma	Uses pulse durations in nanosecond range
Non-laser, non-intense pulsed light technology TRASER *	Telangiectasias, hair removal	Tunable pulse-dye device, could replace pulsed-dye or ruby hair removal lasers
Daylight PDT	Photoaged skin, acticinc keratoses, acne	Complex procedure similar and with comparable results to photodynamic therapy

*Total reflection amplification of spontaneous emission of radiation
Sources: Friedman et al. 2017; Solish 2016

Some patients require correction of more severe defects — particularly scarring from surgical or accidental wounds or burns, or sequelae of skin disorders (especially severe acne). Recently-issued 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] 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]

Body Shaping/Contouring: Dermatologists are also seeing the expansion of aesthetic medicine beyond the face to other parts of the body. Clinicians must stay abreast of the latest body shaping/contouring techniques as new options continue to become available.

Non-surgical fat reduction methods have been developed and are gaining popularity.[Kilmer SL 2015] Cryolipolysis destroys subcutaneous fat cells by freezing them, causing cell death of subcutaneous fat tissue without apparent damage to the overlying skin.[Kilmer] Using controlled cooling to non-invasively damage subcutaneous adipocytes, cryolipolysis is based upon the greater susceptibility of lipid-rich adipocytes to cold injury compared to surrounding water-rich cells [Kilmer]. 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] Another noninvasive technique, 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.[American Society for Dermatologic Surgery] Clinicians need education and training on the optimal use of these new and emerging techniques.

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Psoriasis

Gap: Because 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 the pathophysiology of psoriasis and the associated comorbidities of the disease.

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%-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]. 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: Diagnose and treat patients with psoriasis appropriately, based on current clinical guidelines.

In a recent 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%-35% of those with moderate psoriasis, and 9%-30% with severe psoriasis were untreated.[Armstrong, Dermatol Ther 2017] In a 2016 survey, only 1 in 3 patients were 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, cyclosporine, apremilast, or biologic immune modifying agents.[Young 2017] Keeping the regimen simple and acceptable to the patient can maximize adherence.

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 objective: Design treatment strategies that incorporate of biologic therapies in the management of appropriately selected patients with psoriasis.

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]

Several biologic agents have been approved for the treatment of psoriasis. Older biologics target TNF-α, while 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. Guselkumab received FDA approval for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.[Janssen press release] A number of other IL-23 antagonists are in late-stage development. A biosimilar was introduced to the US market within the last year, and alternative maintenance regimens have been studied.

Biologics and small molecules approved for psoriasis

Biologic	Target	Year Approved for Psoriasis
Adalimumab	TNF-α	2008
Apremilast	PDE-4	2014
Brodalumab	IL-17A	2017
Etanercept	TNF-α	2004
Golimumab	TNF-α	2009
Guselkumab	IL-23	2017
Infliximab	TNF-α	2006
Ixekizumab	IL-17	2016
Secukinumab	IL-17A	2015
Ustekinumab	IL-12/IL-23 p40	2009

Source: Blauvelt JAAD 2016; Blauvelt Br J Derm 2017; Reich 2017

Table 2: Agents Under Investigation

Biologic	Status	Target/Mechanism

BI 655066	Phase 3	IL-23
CF101	Phase 3	A3 adenosine receptor agonist
IMO 8400	Phase 2	Antagonist of Toll-like receptors (TLRs) 7, 8 and 9
Namilumab	Phase 2	Human monoclonal antibody; inhibits granulocyte-macrophage colony-stimulating factor (GM-CSF) signaling by binding the soluble cytokine
Neihulizumab	Phase 2	Preferentially induces apoptosis of late-stage activated T cells, effectively eliminating chronic pathogenic T cells while fully maintaining host defense
Risankizumab	Phase 3	IL-23
Sotrastaurin	Phase 2	Pan-protein kinase C (PKC) inhibitor; preserves regulatory T cells and prevents IL-17 production.
Tildrakizumab	Phase 3	IL-23
Tregalizumab	Phase 2	Humanized anti-CD4 monoclonal antibody; induces selective activation of regulatory T-cells

Source: Hilton L 2016; Leonardi 2017

A recent publication suggests that, based on results of studies with newer biologic agents, the current objective criterion of PASI 75 for therapeutic endpoints in clinical trials should be raised to PASI 90 or 100.[Manolo 2015] 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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Small Molecules and Biosimilars

Small molecules are emerging as potential options for several dermatological conditions. Several oral and topical small molecules, spanning different therapeutic classes, are undergoing study and analysis for efficacy and safety.[Gooderham] Apremilast and tofacitinib are 2 that have shown significant efficacy in psoriasis and psoriatic arthritis.[Bachelez; Crowley]

The phosphodiesterase-4 inhibitor apremilast is safe and well tolerated for 3 years and longer in patients with psoriasis.[Crowley] In the phase 3 ESTEEM clinical program, apremilast significantly reduced the signs and symptoms of psoriasis and had an acceptable safety profile through week 52. Adverse event rates, particularly those for diarrhea and nausea, decreased over time. The long-term laboratory results revealed no significant impact on hepatic, renal, or hematologic parameters.[Crowley]

A biosimilar product is a biological product that is approved based on a showing that it is highly similar to an FDA-approved biological product, known as a reference product, and has no clinically meaningful differences in terms of safety and effectiveness from the reference product. Only minor differences in

clinically inactive components are allowable in biosimilar products. An *interchangeable* biological product is biosimilar to an FDA-approved reference product and meets additional standards for interchangeability. An interchangeable biological product may be substituted for the reference product by a pharmacist without the intervention of the healthcare provider who prescribed the reference product. FDA requires licensed biosimilar and interchangeable biological products to meet theaAgency's rigorous standards of safety and efficacy. That means patients and health care professionals will be able to rely upon the safety and effectiveness of the biosimilar or interchangeable product, just as they would the reference product.[FDA] Biosimilars approved include etanercept and adalimumab, both indicated for plaque psoriasis and psoriatic arthritis.

As more biosimilars enter the market and are approved, the need for education becomes evident. The results of a recent survey highlight a significant need for evidence-based education about biosimilars for physicians across specialties. Five major knowledge gaps were identified: defining biologics, biosimilars, and biosimilarity; understanding the approval process and the use of "totality of evidence" to evaluate biosimilars; understanding that the safety and immunogenicity of a biosimilar are comparable to the originator biologic; understanding the rationale for extrapolation of indications; and defining interchangeability and the related rules regarding pharmacy-level substitution.[Cohen] The FDA announced their release of a continuing education course, FDA Overview of Biosimilar Products, to help guide healthcare professionals to make informed decisions when prescribing biosimilar products to their patients.[FDA] Clinicians should be familiar with this document.

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Rosacea

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

Learning objective: As part of rosacea treatment plans, design and implement self-education and patient education programs.

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 percent of rosacea patients have reported reduced self-confidence and self-esteem, and 41 percent reported avoiding public contact, and 88 percent 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]

Rosacea Typology

Classification of rosacea	Description
Erythematotelangiectatic	Central facial erythema (flushing) that can be persistent or transient
Papulopustular	Inflamed pustules or papules
Phymatous	Skin thickening and nodules on the nose, cheeks, or chin
Ocular	Red, itchy, burning, and watery eyes that often co-occur in 20% of patients with other types of rosacea

Source: Wick JY, 2016

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. MD-IQ quiz. 4/18/2016-8/03/2016] [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: Apply treatment strategies, based on knowledge of the indications, efficacy, and risks of available rosacea therapies, to achieve therapeutic goals in rosacea treatment.

No cure exists for rosacea, but healthcare professionals 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 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 papulopapular 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, which inhibits numerous bacterial species and inflammation, is currently in phase III trials.[Jesitus 2017]

Oral 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]

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]

Light therapy such as pulsed dye laser and intense pulsed light can be used for multiple types of rosacea.[Do 2016] In a recent 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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