

Ted Rosen, MD
EDITOR

Dr. Rosen graduated from the University of Michigan Medical School, then trained in internal medicine at the University of Alabama, and in dermatology at Baylor College of Medicine. He currently serves as Professor of Dermatology at Baylor and Chief of Dermatology at the Houston Veterans Affairs Medical Center. He is active in the American Academy of Dermatology, having served on the Board of Directors for the Sulzberger Institute for Dermatological Education and numerous committees and task forces. He is the current Chair of the AAD Poster Exhibit Task Force. Dr. Rosen has written more than 170 peer-reviewed journal articles and authored three medical textbooks.



Complete this CME program
online at no charge. Simply go to:
www.SkinTherapyLetter.com/CME



Sponsored by Boston University
School of Medicine

Thomas Ruenger, MD

COURSE DIRECTOR
Professor of Dermatology
Boston University School of Medicine

The Forgotten HPV: External Genital Warts

Alejandra Varela^{1,2} and Daniel A. Carrasco, MD²

¹University of Texas Health Science Center, San Antonio, TX, USA

²Dermatological Association of Texas, Houston, TX, USA

Background

Human Papilloma Virus (HPV) infection of the anogenital tract is extraordinarily prevalent with studies demonstrating that >50% of sexually active women have been infected with the 40-plus HPV types that affect this region of the body.^{1,2} Age matched males demonstrate similar infection rates, and data on first-time treatment seekers for genital warts show an increase in presentation of >500% in the past 3 decades.³⁻⁵ In 2005, the Centers for Disease Control estimated that 20 million people in the US had HPV.

Risk Factors

The single most established risk factor for genital HPV infection is an increased number of lifetime sexual partners. There is evidence that the number of partners a woman reports her current partner to have had is associated with her own risk.⁶⁻¹² While some studies have suggested a correlation between HPV infection and the use of oral contraceptives or smoking, the literature does not support a consistent association between these. Currently, the peak point prevalence of genital HPV infection is in the 15-25 year-old age group with the number of lifetime partners determining the greatest risk.^{13,14}

Pathogenesis

Infection with HPV occurs by direct inoculation of the virus into the epidermal layers of the skin through epithelial defects. Skin maceration is an important factor in transmission.¹⁵ Genital infections are predominantly obtained through sexual contact, which can then be transmitted vertically to newborns by passage through the infected birth canal.¹⁶⁻¹⁹ The rate of infectivity between sexual partners is estimated to be 60%.²⁰

Condyloma Acuminatum

Condyloma acuminatum (anogenital warts) is the most common presentation of genital HPV infection. The vast majority of these lesions are clinically benign and due to infection with HPV 6 or 11. The warts can present as small, verrucous papules; discrete, sessile, smooth topped papules or nodules; and even as large exophytic masses. The color of the lesions can range from flesh colored to pink to reddish brown, and often they are multifocal. Most often genital warts are asymptomatic but may cause pruritus, bleeding, or mild burning.²¹

The distribution of the lesions corresponds with the areas of highest friction during sexual activity: the perineum, external genitalia, intertriginous folds, anus, rectum, and urethra. In women the lesions may extend to the vagina and cervix. In uncircumcised men, the subpreputial region is especially affected.²²

Diagnosis

Diagnosis is primarily clinical, but for hard-to-detect lesions, especially those on the cervix, a 5% acetic acid solution can be applied to the suspected region. Within minutes, condylomata should appear as whitish patches on the mucosa. If the practitioner finds the clinical diagnosis to be less than clear, a biopsy may provide the diagnosis.

Differential Diagnosis

- Syphilitic condyloma lata
- Molluscum contagiosum
- Benign penile pearly papules
- Hymenal remnants
- Bowenoid papulosis
- Seborrheic keratosis
- Skin tags
- Squamous cell carcinoma
- Verrucous carcinoma (Giant condyloma of Buschke-Lowenstein)
- Vulvar dysplasia
- Linear epidermal nevus
- Lichen nitidus
- Angiokeratomas
- Milium
- Fordyce spots

Treatment

According to the Centers for Disease Control (<http://www.cdc.gov/std/treatment/2006/genital-warts.htm>), treatment of genital warts should be guided by the preference of the patient, the available resources, and the healthcare provider's experience. There is no definitive evidence to suggest that any of the available monotherapy treatments are superior to any other and

no single treatment is ideal for all patients or all warts. However, combination therapies may be more successful at treating warts in particular when monotherapies have failed, because they debulk the tumor and take advantage of different mechanisms of action to treat the virus. The majority of genital warts respond within 3 months of therapy. The response to treatment and its side-effects should be evaluated throughout the course of therapy, and treatment should be changed if a patient has not improved substantially within that time frame.²³

While genital warts are benign, they are often cosmetically unacceptable and embarrassing to patients. If left untreated, they commonly enlarge and multiply. Treatment options can be broken down into 5 categories:

- Antiproliferative agents
- Destruction/excision therapies
- Immunomodulatory therapy
- Combination therapy
- Antiviral agents

It is essential to screen patients for other sexually transmitted diseases.

Anti-Proliferative Therapies

This class of agents includes podophyllin resin 10%-25%, which is provider-administered, and podophylox 0.5% solution or gel, which can be applied by the patient and is used as a first-line drug. It is free of the mutagenic substances that podophyllin resin contains.²⁴

Destruction/Excision Therapies

The destructive therapies for condyloma include: local cryotherapy (safe during pregnancy), application of topical trichloroacetic acid (TCA), electrocautery, ablative laser treatment, or excision by scissor, curette, or scalpel.

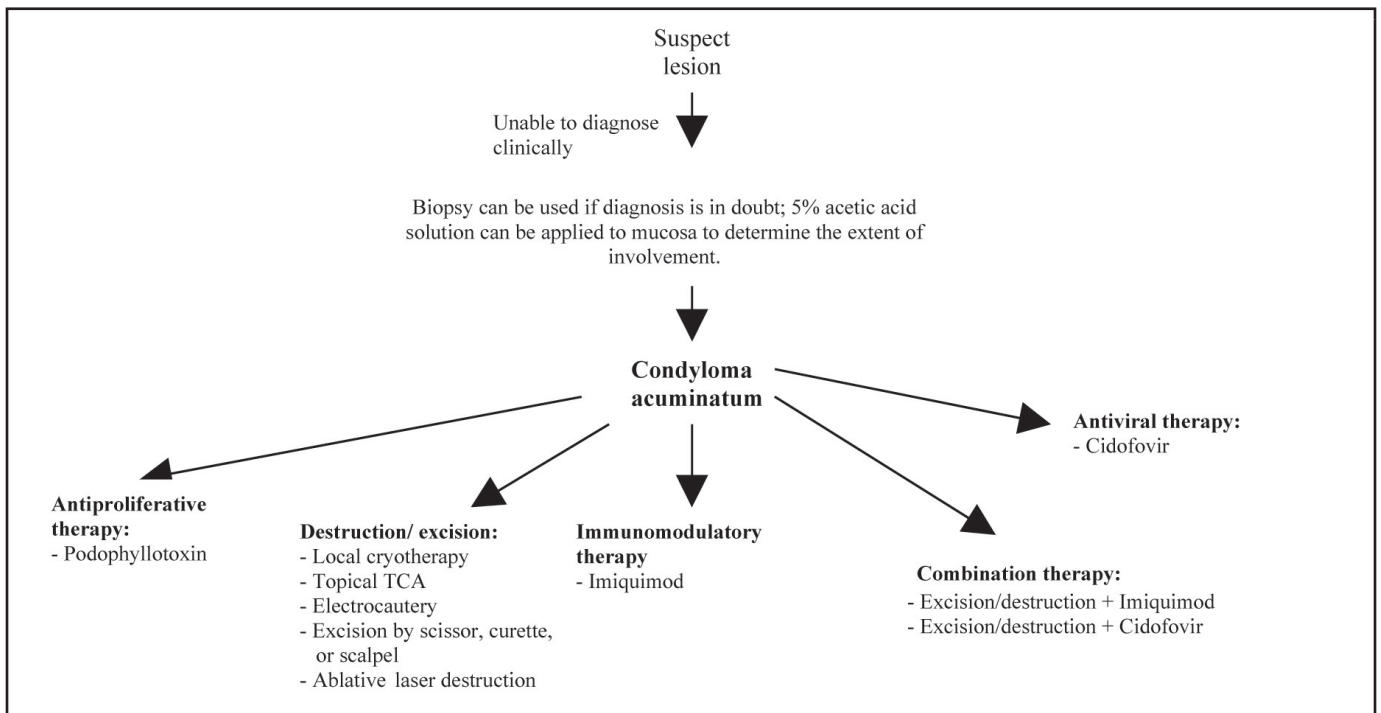


Figure 1: Algorithm for treatment of suspect lesions

Immunomodulatory Therapy

Imiquimod is a relatively new addition to the pharmacologic arsenal. Applied topically, imidazoquinoline enhances the cytotoxic immune response. Wart recurrence is significantly lower with this drug, compared with many other commonly used therapies. It is applied directly to the affected skin three times per week, and it has the added benefit of treating subclinical lesions.

Combination Therapy

Because anogenital warts frequently persist despite monotherapy, namely excision/destruction, and combination therapy with immunomodulators may provide better results. Carrasco, et al. revealed that treatment with imiquimod followed by excision of residual lesions may provide long-term clearance of anogenital warts in those patients for whom monotherapy was insufficient.²⁵

Antiviral Therapy

Cidofovir is an agent with antiviral activity that has been used in the treatment of genital warts refractory to other therapies. It is a nucleotide analogue with broad antiviral activity that has been used experimentally as a topical gel with fair success.²⁶ Cidofovir is not commercially available, but can be compounded at a local specialty pharmacy.

Prophylaxis

In the forefront of medicine, the advent of a quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine, is now being administered as HPV prophylaxis. It is indicated for girls and women aged 9–26 years for the prevention of the following diseases caused by HPV types 6, 11, 16, and 18:

- Genital warts
- Cervical cancer
- AIS (noninvasive cervical cancer)
- CIN grades 1, 2 and 3 (cervical intraepithelial neoplasia)
- VIN grade 2 and 3 (vulvar intraepithelial neoplasia)
- VaIN grade 2 and 3 (vaginal intraepithelial neoplasia)

It should be administered IM as three separate 0.5ml doses. Studies with this agent are now ongoing in males.

Conclusion

HPV is a very common sexually transmitted disease that is associated with a number of benign, premalignant, and frankly malignant lesions of the anogenital tract. The majority of HPV infections are asymptomatic and are spontaneously cleared by a predominantly cell-mediated immune response. Condyloma acuminatum, generally due to HPV types 6 and 11, is the most common benign clinical manifestation of HPV infection, and a number of antiproliferative, destructive, antiviral, immunomodulatory, and combination therapies are available for this condition. The majority of genital warts respond within 3 months of therapy. The response to treatment and its side-effects should be evaluated throughout the course of therapy and treatment should be changed if a patient has not improved substantially within that time frame. A quadrivalent HPV recombinant vaccine

is now available for HPV prophylaxis against types 6, 11, 16, 18 and is indicated in girls and women 9–26 years of age. Currently, studies with this agent are ongoing in males.

Editor's Commentary

The majority of clinicians will attempt to treat external genital warts (EGW) initially utilizing the various destructive techniques outlined by Dr. Carrasco. Healthcare provider-administered ablative methods are relatively simple, safe and expeditious. However, as noted repeatedly in the medical literature, both incomplete response and recurrence are common problems following the use of such modalities.^{1,2} While requiring prolonged and diligent application, the use of self-administered imiquimod is an effective and convenient treatment alternative. The efficacy is likely due to the establishment of adaptive immunological response and/or persistent immune memory against etiologic HPV.³ The FDA-approved imiquimod regimen for EGW calls for three times weekly application for 16 weeks. Recent clinical work from Australia suggests that far shorter courses (as little as 4 weeks) may be equally efficacious; this is particularly true in women who routinely demonstrate higher complete cure rates.⁴ Shorter courses of therapy are not only more convenient, but have been associated with considerably less treatment-related morbidity (e.g., erythema, erosion and pain).

Real-world use of imiquimod brings up the concern of safety in women of child-bearing potential who already may be, or may inadvertently become, pregnant during therapy. While documentation is limited, a recently published small case series is reassuring with regards to imiquimod safety during gestation.⁵

One unanticipated complication of imiquimod therapy has been the development of localized vitiligo-like depigmentation limited to the area of treated skin.^{6,7} This may be due to locally induced cytokines that are directly toxic to melanin producing cells or due to locally induced chemokines facilitating the ingress of melanocytotoxic immune effector cells. The Editor has observed this phenomenon, but also noted eventual spontaneous and complete remission in the affected patient.

The EGW therapeutic armamentarium will expand shortly due to FDA approval 15% Polyphenon® E Ointment. This is a standardized, polymolecular aqueous extract of green tea leaves, and it represents the first prescription botanical officially approved in the US. Application frequency and duration will closely resemble that of imiquimod 5% cream. Although the mechanism of action is uncertain, components of this formulation have been shown to inhibit epidermal cell proliferation, as an essential feature of HPV-induced lesions, including EGW.⁸

Future generations may be spared considerable EGW burden due to the development, approval, and release of HPV polyvalent vaccines. Not only will vaccination largely prevent incident EGW, but it will also protect against genital tract HPV-associated neoplasia.⁹

References

References are listed online at www.SkinTherapyLetter.com

Oral Therapy for the Treatment of Rosacea

Hilary Baldwin, MD

Department of Dermatology, State University of New York, Brooklyn, NY, USA

The Disease

Rosacea is a common condition that is prevalent worldwide. Its incidence is said to be higher in fair-skinned patients, however it is also seen in Asians and African-Americans. Rosacea occurs in both men and women most often after the age of 30 years. It is characterized by the presence of one or more of the following:

- Central facial erythema and telangiectasias
- Papules and pustules
- Granulomatous nodules
- Phyma formation
- Ocular changes.

Known triggers include UV exposure alcohol intake, spicy foods, and changes in temperature. However, sometimes flares and remissions occur with no rationale.

Classification

A National Rosacea Society¹ committee has classified rosacea into four types based on predominant lesion morphology:

Erythematotelangiectatic

- Flushing and persistent central facial erythema with telangiectasias. Central facial edema, stinging and burning of the skin, as well as dryness occurs.
- Most difficult subtype to treat
 - Topical and oral therapy largely ineffective
 - Laser and light therapy most effective

Papulopustular

- Papules and pustules often seen with persistent facial erythema.
- Easiest subtype to treat
 - May respond to topical therapy
 - Oral agents more effective. May be used as first-line therapy, when topicals are ineffective or when it is important to speed up the response time.

Phymatous

- Thickening of the skin, often presenting as rhinophyma
- Irregular surface nodules, enlarged follicles and sebaceous appearance.
- The chin, forehead, cheeks, and ears may be involved.
- Isotretinoin can halt progression and shrink volume, but will not eradicate completely.
- Surgical/laser ablation necessary to eradicate existing lesions.

Ocular

- Sensation of burning, grittiness, dryness, “foreign body sensation”, telangectasia of the sclera. Often, blepharitis, conjunctivitis, chalazions, styes present. Rarely, corneal manifestations (keratitis, infiltrates, and ulcers) may occur.
- May respond to topical agents and eyelid hygiene.
- Oral antibiotics readily resolve ocular rosacea.
- May remit after discontinuation.

This system allows therapy evaluation based on similar lesion types; there are few medications or therapies that are significantly effective in more than one category.²

Pathophysiology

Inflammation plays an important role in lesion formation, however the etiology of rosacea is not well understood. It is generally believed that there is no microorganism involved in the pathogenesis of rosacea.

Common denominators are believed to include inflammation and degradation of the dermal connective tissue; angiogenesis caused by the upregulation of proinflammatory cytokines; neutrophil chemotaxis; and the production of nitric oxide, reactive oxygen species, and matrix metalloproteinases.

In the face of an absence of a defined pathogenesis, treatment has traditionally been based on disease endpoints rather than targeting the underlying problems.:

- Inflammation is treated with anti-inflammatory agents.
- Flushing is treated with vasoconstrictors.
- Telangiectasias are treated with vascular lasers.
- Pustules are treated with antibiotics without a target organism.

Vasoconstricting Agents

A number of agents have been reported anecdotally to reduce flushing including beta blockers in low doses,³ naloxone,⁴ ondansetron,⁵ aspirin,⁶ and serotonin reuptake inhibitors.⁷ Clonidine, at 0.05mg b.i.d., has also been reported to be effective for reducing flushing.⁸ While this suboptimal dose does not reduce blood pressure, it does lower baseline malar temperature by peripheral vasoconstriction.

Antibiotics

Oral antibiotics have been used off-label since the 1950s, but until May of 2006 none had been approved for treating this condition. Antibiotics are highly effective in papulopustular rosacea. However, justification for their use must be based on the recognition that there is little or no evidence demonstrating that rosacea is the result of a bacterial infection, and that reports of antibiotic resistance have been increasing over the past 10 years.

Tetracyclines

Because tetracyclines act to reduce inflammation, they are very effective for papulopustular acne and rosacea with substantial improvement seen after 3–4 weeks. However, relapses often occur after discontinuation.⁹ Tetracycline 250–1000mg q.d., doxycycline 100–200mg q.d., and minocycline 100–200mg q.d. are most commonly used. Using oral tetracyclines until clinical improvement is seen, then tapering to topical antibiotics, offers a way to maintain control and minimize relapses. However, we should not ignore the lessons learned from the use of long-term oral antibiotics and the resultant potential for bacterial resistance that have developed while treating other skin diseases.

Anti-inflammatory Dose Doxycycline – A New Treatment Option

The reason why tetracyclines are so effective for treating rosacea is likely due to their anti-inflammatory properties, not their role as antibiotics. In May 2006, the FDA approved the first oral prescription therapy for the treatment of inflammatory lesions (papules and pustules) of rosacea in adult patients. This product, doxycycline (Oracea™), is a once daily 40mg capsule containing 30mg immediate-release and 10mg delayed-release beads. It allows for blood levels of doxycycline to stay within a narrow window: high enough to act as an anti-inflammatory medication, but well beneath the antimicrobial threshold. In two Phase III, double-blind, placebo-controlled clinical trials, patients receiving this drug experienced a 61% and 46% mean reduction in inflammatory lesions compared with 29% and 20%, respectively for placebo ($p < 0.001$ for each study).¹⁰ Side-effects were similar to placebo. Most notably, since the low dose exerts no selection pressure on bacteria, there were no yeast infections reported and continued use did not result in antibacterial resistance.

Erythromycin

Erythromycin is effective for treating papulopustular rosacea, but patients often complain of GI side-effects. Second generation macrolides have been shown to be more effective than erythromycin. However, resistance has been noted in patients in whom an infectious etiology cannot be demonstrated.

Metronidazole

Oral metronidazole, 200mg b.i.d., is often used for long-term treatment of rosacea in Europe.^{11,12} In a double-blind study, this drug was shown to be as effective as oxytetracycline 250mg, b.i.d.¹² Side-effects include rare neuropathy and seizures. Alcohol abstinence is required during use.²

Isotretinoin

Isotretinoin is less commonly used for the treatment of rosacea than it is for acne vulgaris. By reducing the size and number of sebaceous glands, treatment-resistant rosacea patients who were given this drug had fewer papules and pustules, a decrease in erythema, and a reduction in nasal volume in rhinophyma.^{13,14} Unlike acne therapy where isotretinoin is generally curative, improvement in rosacea is often not as long-lasting. Erdogan, et al. used a low dose of 10mg daily for 4 months with a significant reduction in inflammatory lesions, erythema and telangiectasia at 9 weeks.¹⁵ Long-term, low-dose therapy is highly effective in controlling papulopustular rosacea. Use of isotretinoin in adult females of child-bearing potential requires birth control monitoring and extensive counseling because of its teratogenic properties. Distribution of isotretinoin is restricted by a special computer-based risk management program approved by the FDA, designed to further the public health goal to eliminate fetal exposure to isotretinoin. (For more information see www.iplledgeprogram.com)

Conclusion

Novel uses of old medications and new formulations of systemic medications have broadened the therapeutic armamentarium for treating rosacea patients. It is of primary importance to

offer patients safe and effective therapies for this chronic and incurable condition, improving both the clinical and psychosocial consequences of rosacea.

Editor's Commentary

As Dr. Baldwin points out, there is increasing concern in the medical community about prolonged ingestion of oral antibiotics due to bacterial resistance patterns. This concern has been further validated by the recent elucidation of the complete genome of *P. acnes* and the finding that this organism possesses inherent mechanisms enabling it to transfer a variety of resistance genes to other microbial species.^{1,2} Thus, while oral antibiotics have long been the mainstay of rosacea therapy, apprehension about microbiological consequences has tempered enthusiasm for this type of treatment. Complete alcohol avoidance required of those receiving oral metronidazole, and the myriad of potential adverse events associated with isotretinoin have likewise made these alternate agents difficult to administer.

Prior investigation of very low-dose doxycycline suggested efficacy for rosacea.³ Thus, the recent FDA approval and commercial release of a subantimicrobial and purely anti-inflammatory dose of this drug in a convenient once-daily formulation might, indeed, have several advantages, i.e. no development of resistance and fewer or no problems with yeast infections. However, comparative clinical trials to demonstrate such advantages have not been done. The goal of such therapy is to administer an antibiotic moiety in a dosage formulation that preserves anti-inflammatory properties but eliminates anti-infective properties, thereby avoiding ecologic pressure on bacteria to become resistant. The exact mechanism(s) by which anti-inflammatory doxycycline improves rosacea is uncertain. Suppression of cytokine and chemokine elaboration, inhibition of matrix metalloproteinases, decreased vasodilatation and other properties have been described.⁴ This formulation is also notable for its lack of photosensitivity, and for the minimal risk of secondary candidiasis and troublesome side-effects traditionally associated with the tetracycline family.

Another promising oral therapy for rosacea involves the use of an oral blend of nicotinamide and zinc (Nic/Zn).⁵ The formulation tested contained nicotinamide 750mg and zinc 25mg as active ingredients, along with small amounts of copper and folic acid. Nearly 80% of subjects reported a patient global evaluation of “moderately” or “much” better when compared with baseline after 8 weeks. Similar to anti-inflammatory dose doxycycline, the precise mechanism of action is uncertain, but suppression of vascular permeability, reduced accumulation of inflammatory cells, depressed mast cell degranulation, and stabilization of lysosomes have all been implicated.⁶ If larger scale and longer duration studies verify the aforementioned data, then Nic/Zn may further expand our oral therapeutic options.

Rosacea patients often exhibit “irritable” skin, which may be hyper-reactive to a host of topical medications as well as to over-the-counter skin care products.⁷ Oral therapy may be mandatory for such individuals, and transitioning to topical maintenance should be deferred until significant improvement occurs.

References

References are listed online at www.SkinTherapyLetter.com

Seborrheic Dermatitis: New Formulations for Treatment

Janet G. Hickman, MD

Dermatology Consultants, Inc. and the Education & Research Foundation, Inc. Lynchburg, VA, USA

Seborrheic dermatitis is a common cutaneous disorder occurring in at least 3%–5% of the population.¹ Dandruff, the less inflammatory form of seborrheic dermatitis, occurs in 50%–80% of teenagers and adults.²

Diagnosis

Seborrheic dermatitis is diagnosed clinically by observing:

- Oily flaking
- Erythema
- Occurrence in characteristic locations
 - Scalp
 - Creases around the nose
 - Glabellar crease
 - Behind the ears
 - In eyebrows, beard, or moustache
 - Midsternum

There may be symptoms of:

- Itching
- Burning
- Stinging

There are no diagnostic or necessary laboratory tests and biopsy is seldom needed.

Clinical Course

In infancy, seborrheic dermatitis presents as “cradle cap”—thick yellow flaking at the vertex of the scalp. It may also cause diaper dermatitis in infants and intertriginous rash in infants and adults. Seborrheic dermatitis is absent in the preadolescent child but recurs after puberty. The course is usually chronic and intermittent with flares induced by:

- Stress
- Temperature and humidity changes
- Changes in general health
- Changes in skin care

Seborrheic Dermatitis in Systemic Disease

Worsening of seborrheic dermatitis is a common finding in Parkinson’s disease and related neurological conditions. Pronounced seborrheic dermatitis is one of the earliest and most common findings in HIV/AIDS, even in the era of highly active antiretroviral therapy (HAART).³

Differential Diagnosis

It is important to distinguish seborrheic dermatitis from dermatophyte infections. Scalp flaking with hair loss, or scalp flaking in preadolescent children, especially if accompanied by lymphadenopathy, should be evaluated with microscopic examination and culture to detect tinea capitis. Similarly, finding erythematous flaking areas on the face or body beyond the

typical distribution should raise the suspicion of tinea corporis. Lupus erythematosus and rare conditions such as Langerhans cell histiocytosis may mimic seborrheic dermatitis and might be considered if the clinical course and response to treatment are atypical.

Etiology

While the detailed pathophysiology of seborrheic dermatitis remains to be clarified, the following are involved:

- *Malassezia* (formerly called *Pityrosporum*) yeasts
- Sebum
- Hereditary propensity

Sebum is necessary to support the growth of *Malassezia*. Although *Malassezia* yeasts are common colonizers of most adult scalps, only some individuals develop the flaking and inflammatory response of seborrheic dermatitis. The frequency of positive family histories implies a genetic component to the propensity to develop seborrheic dermatitis. The exact mechanism by which *Malassezia* yeasts induce inflammation is not fully understood. Lipases created by the organism produce free fatty acids such as oleic acid from sebum. Experimentally, application of oleic acid to scalps of susceptible individuals can mimic the scaling and erythema of seborrheic dermatitis.¹ Other proposed mechanisms of inflammation initiation are alternative complement activation and Toll-like Receptor (TLR) stimulation by *Malassezia*.

Treatment

Treatment approaches include:

- Sebum removal
- Use of anti-*Malassezia* agents
- Use of anti-inflammatory agents

Sebum Removal

Many patients mistakenly believe the flaking of their face or scalp is “dry skin”; they need to be encouraged to shampoo regularly and use gentle but effective facial cleansers. Greasy and oily face and scalp products can aggravate the condition and should be avoided. It is especially important for African-American patients to find suitable scalp products; newer gel formulations of medications for seborrheic dermatitis may successfully replace greasy pomades.

Topical Agents

- **Anti-*Malassezia*:** Several of the anti-*Malassezia* agents are available by prescription for the treatment of seborrheic dermatitis.⁴ These include:
 - Ketoconazole 2% gel (Xolegel™) (FDA approved July 2006)
 - q.d. for 2 wks
 - anhydrous gel formulation with propylene glycol
 - Ketoconazole 2% cream (Nizoral®, generic)
 - b.i.d. for 4 weeks
 - Ciclopirox 0.77% cream, gel, suspension (Loprox®, generic)
 - b.i.d. for 4 weeks
 - Sulfacetamide 10% cream, foam, gel, wash (Ovace™)
 - b.i.d. for 8-10 days
 - Sulfacetamide/sulfur suspension, cream, emulsion, gel, wash (Plexion®, Rosac®, Rosanil®, Rosula®, generic)
 - 1-3 times daily

Vehicle choice is important as the poor barrier function of skin with active seborrheic dermatitis makes it prone to stinging or burning. Propylene glycol containing nonalcohol gels (or anhydrous gels) are well tolerated and have the advantage of being acceptable for hairy areas, e.g., the beard, as they do not leave a residue. Additionally, the use of the anhydrous gel formulation eliminates the potential for adverse effects associated with sodium sulfite-containing cream. Some cream formulas cake on the skin accentuating the flaking, whereas ointments may be too greasy.

- **Anti-inflammatory:** Topical low- and mid-potency corticosteroids may be helpful for brief intermittent use, but the chronic nature of seborrheic dermatitis makes dependence on steroids inadvisable because of the risks of developing skin atrophy, steroid rosacea, dyspigmentation, and absorption.

To avoid steroid side-effects, the topical calcineurin inhibitors tacrolimus⁵ (Protopic® ointment) and pimecrolimus⁶ (Elidel® cream) have been used off-label for seborrheic dermatitis.

Treatment Shampoos for Seborrheic Dermatitis and Dandruff

First-line treatment includes the use of an antiseborrheic (antidandruff) shampoo. The scalp is a reservoir for *Malassezia*; regular use of a treatment shampoo improves long-term control. Dandruff shampoos depend on the anti-*Malassezia* efficacy of the following active ingredients:^{7,8}

Non-prescription:

- Ketoconazole 1% (Nizoral A-D®)
- Pyrithione zinc (ZPT) 0.3%–2% (Head and Shoulders®, Zincon®, DHS® zinc)
- Selenium sulfide 0.6%–1% (Selsun Blue®, Head and Shoulders® Intensive Treatment)
- Coal tar 0.5%–5% (T-Gel®, Denorex®, Polytar®, XSebT®, DHS® tar, Ionil® T)
- Sulfur 2%–5% (Meted®)

Prescription:

- Ketoconazole 2% (Nizoral®, generic)
- Selenium sulfide 2.5% (Selsun®, generic)
- Ciclopirox 1% (Loprox®)

In general, the efficacy of these active ingredients parallels their anti-*Malassezia* potency. Note that formulation also makes a difference to efficacy, with micro-dispersed ZPT or selenium sulfide more effective than standard formulas. The incorporation of non-oily conditioners into some antidandruff products makes them more acceptable cosmetically. The addition of menthol can give some short-term itch relief. Salicylic acid, urea, or glycolic acid may assist scale removal. Among herbal products, tea tree oil has shown some efficacy against *Malassezia*.^{9,10}

Editor's Commentary

Seborrheic dermatitis is a common problem of variable severity which prominently affects the facial skin and scalp surface. Although Dr. Hickman rightly asserts that a biopsy is rarely needed to establish the diagnosis, some degree of medical investigation may be warranted. Ninety to ninety-five percent of those with HIV infection and some 35% of those afflicted with neurological disorders (such as, but not limited to, Parkinson's Disease) will develop seborrheic dermatitis.¹ Hereditary or acquired zinc deficiency may present as seborrheic dermatitis; psoriasis and rosacea may overlap clinically with it; and facial dermatophytosis may closely mimic it.² Drugs, including gold derivatives, anabolic steroids, cimetidine, psoralens, and some psychotropic agents may induce seborrheic dermatitis.³ Acute onset seborrheic dermatitis may be a sign of eating disorders, such as occult anorexia nervosa or bulimia.⁴

Because we do not really know the cause of seborrheic dermatitis, we treat a number of putative etiologic factors. This explains why such diverse drugs as anti-inflammatory agents (corticosteroids and topical calcineurin inhibitors), keratolytics (salicylic acid) and anti-fungal agents (ketoconazole and ciclopirox) may be of benefit. Tachyphylaxis is not rare, and therefore periodic rotation of therapeutic agents may be necessary.⁵ This is particularly evident when treating scalp disease with shampoo products.

As is true of many rosacea patients, those with seborrheic dermatitis are more susceptible to cutaneous irritation.⁶ This is especially true on the face. Therefore, it is wise to consider the formulation of potential treatment modalities. The newest ketoconazole product is supplied in a rapidly vanishing and well-tolerated anhydrous gel formulation which also has the advantage of once-daily use.

References

References are listed online at www.SkinTherapyLetter.com

Complete this CME program online at no charge. Simply go to www.SkinTherapyLetter.com/CME

Continuing Medical Education Accreditation

Boston University School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Boston University School of Medicine designates this educational activity for a maximum of .75 *AMA PRA Category 1 Credit*[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Physicians must complete the activity online at www.SkinTherapyLetter.com/CME.

Target Audience:

Family Physicians and Primary Care Physicians

Educational Objectives:

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

- 1) effectively diagnose external genital warts, rosacea and seborrheic dermatitis.
- 2) prescribe appropriate medications for the treatment of these conditions.
- 3) apply effective treatment for these conditions.

Supported through unrestricted educational grants from:

3M Pharmaceuticals

Barrier Therapeutics

CollaGenex Pharmaceuticals

Disclaimer

All programs, activities, and materials provided by the SkinCareGuide.com Ltd, Trustees of Boston University, or their associates, are provided on the condition they be used solely for educational purposes by qualified health care professionals. In no event shall SkinCareGuide.com Ltd. or Trustees of Boston University be liable for any decisions or actions taken in reliance on the information contained in the stated materials. In no event should the information in the materials be used as a substitute for professional care. No physician-patient relationship is being established.

Disclosure

Boston University School of Medicine asks all individuals involved in the development and presentation of Continuing Medical Education (CME) activities to disclose all relationships with commercial interests. This information is available at www.SkinTherapyLetter.com/CME. Boston University School of Medicine has procedures to resolve apparent conflicts of interest.

All of these activities include discussion of unapproved use of pharmaceuticals or devices.

Copyright 2006 by SkinCareGuide.com Ltd. Skin Therapy Letter[®] – US Family Practice Edition is published quarterly by SkinCareGuide.com Ltd, 1107-750 West Pender, Vancouver, British Columbia, Canada, V6C 2T8, skintherapyletter@skincareguide.com. All rights reserved. Reproduction in whole or in part by any process is strictly forbidden without prior consent of the publisher in writing. While every effort is made to see that no inaccurate or misleading data, opinion or statement appears in the Skin Therapy Letter[®] – US Family Practice Edition, the Publishers and Editorial Board wish to make it clear that the data and opinions appearing in the articles herein are the responsibility of the contributor. Accordingly, the Publishers, the Editorial Committee and their respective employees, officers and agents accept no liability whatsoever for the consequences of any such inaccurate or misleading data, opinion, or statement. While every effort is made to ensure that drug doses and other quantities are presented accurately, readers are advised that new methods and techniques involving drug usage, and described herein, should only be followed in conjunction with the drug manufacturer's own published literature.