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Clinical Evidence. Practical Advice.

EDITOR: DR. STUART MADDIN

Dr. Stuart Maddin, MD, FRCPC

EDITOR-IN-CHIEF

Dr. Stuart Maddin, Chairman of SkinCareGuide, is one of North America's leading dermatologists, and is the author of numerous dermatologic journal articles, monographs and textbooks. In addition to providing consultative input to a number of pharmaceutical and biotech companies, he is the director of the clinical trials unit at the Division of Dermatology, University of British Columbia. Dr. Maddin has also acted in an advisory capacity to a number of drug regulatory agencies, such as the Health Protection Branch (Ottawa), the AAD-FDA Liaison Committee and WHO (Geneva). He is the founder of the Dermatology Update symposia, now in its 21st year. As well, he is Past President of the Canadian Dermatology Association and served as Secretary-General of the International Committee of Dermatology — International League of Dermatological Societies.

**Dr. Janet McKay, MD, CCFP, CCFP-EM**

FAMILY PHYSICIAN ADVISOR

Dr. Janet McKay graduated from medical school at the University of Western Ontario in 1988, after which she completed a residency in Family Medicine and Emergency Medicine. She received her CCFP in 1990 and CCFP-EM in 1991. She became a Fellow of the College of Family Physicians of Canada in 2004. She has been in private family practice for the past 15 years, and is presently in solo practice in London, Ontario.



Psoriasis of the Scalp

G.D. Schachter, MD

*Division of Dermatology, Sunnybrook & Women's College Health Science Centre,
Toronto, ON, Canada*

The Disease

Psoriasis is a chronic, unpredictable, T cell mediated, inflammatory, papulo-squamous condition that affects approximately 2%-3% of any population.

- The average age of onset is mid- to late-20s, although onset may occur at any age.
- Psoriasis is characterized by accelerated proliferation of epidermal cells (keratinocytes), vascular proliferation, and an influx of inflammatory cells (neutrophils, macrophages, and activated T cells).
- Involvement of the scalp may be minimal (few plaques) or more significant. The entire scalp can be involved.
- Hair loss may be seen with significant involvement of the scalp, and is non-scarring. Hair should regrow when the psoriasis clears.

Areas Affected

Psoriasis affects the skin, especially extensor surfaces and also the scalp, body folds, and nails. The scalp may be the most frequently involved area. Approximately 15%-30% of patients have an associated arthritis.

Cause

There is a genetic basis to psoriasis with an increasing risk of developing the disease if one or both parents have psoriasis. The activated T cell plays a pivotal role in the pathogenesis of the disease.

Symptoms

- Itch
- Psychosocial distress (markedly affects quality of life)
- Hair loss with severe involvement

Classic Lesion

The classic lesion is a well-demarcated, erythematous plaque with a silvery scale. When the scale is removed, bleeding points are seen (Auspitz sign). Psoriasis can develop after trauma and lesions worsen with rubbing or scratching (Koebner phenomenon).

Forms/Types of Lesions

- Chronic Plaque
- Erythrodermic
- Pustular – Localized or Generalized
- Guttate
- Inverse

Triggers

- Stress
- Hormones – Pregnancy
- Trauma
- Drugs – Beta-Blockers, Lithium, Anti-Malarials
- Systemic Steroid Withdrawal
- Infections – Viral and Streptococcal

Differential Diagnoses

- Seborrheic Dermatitis – common
- Lichen Planus – unlikely
- Fungal Infection – unlikely
- Lupus Erythematosus – unlikely

Scalp Psoriasis vs. Scalp Seborrheic Dermatitis

Scalp Psoriasis	Scalp Seborrheic Dermatitis
Silvery white, dry scales	Yellow, greasy scales
Well demarcated	Poorly defined
Can extend onto forehead (check nails, extensor surfaces)	Remains within scalp hairline (check eyebrows, sides of nose, ears)

Seborrhiasis

Seborrhiasis presents with features of both psoriasis and seborrheic dermatitis. Psoriasis of the scalp is primarily treated locally with topical treatments. Systemic therapies are usually reserved for more widespread or severe forms of psoriasis.

Recalcitrant Psoriasis

Resistant or recalcitrant psoriasis of the scalp may require intralesional injections of corticosteroids, and less frequently a systemic treatment.

Treatments for Psoriasis

Topicals

- Tar
 - Coal Tar
 - Shampoo
 - Compounded with corticosteroids
 - Wood Tar
 - Anthralin (Infrequently used in North America; still popular in Europe)
- Corticosteroids
 - Lotion (e.g., betamethasone valerate)
 - Gel (e.g., fluocinonide)
 - Foam (Not available in Canada)
 - Shampoo (e.g., clobetasol propionate (Clobex[®]))
 - Oil and Corticosteroid (Dermasmoothe[®] FS oil)
- Vitamin D3 Analogues
 - Calcipotriol (Dovonex[®] Scalp Solution)
 - Calcipotriol + betamethasone dipropionate (Dovobet[®])
- Salicylic Acid 5%-15% in mineral oil

Treatments for Psoriasis (continued)

- Shampoos
 - Tar (T-Gel[®] or Sebcure T[®])
 - Salicylic Acid (Sebcure[®])
 - Zinc Pyrithione (Dangard[®] or Head & Shoulders[®])
 - Ketoconazole (Nizoral[®]) or Ciclopirox (Stieprox[®])
 - Potent Corticosteroid (Clobex[®]/Clobetasol[®])

Ultraviolet Light

- UVB
- Narrow Band
- PUVA – oral, bath, soaks
- Phototherapy (Rarely used for scalp) - Innovative “comb” to deliver ultraviolet light

Systemic Treatments

- Acitretin (Neotigason[®])
- Methotrexate
- Cyclosporin – A
- Biologics
 - Alefacept (Amevive[®])
 - Etanercept (Enbrel[®])
 - Efalizumab (Raptiva[®])

Intralesional Corticosteroid Injections (Triamcinolone / Kenalog Injections)

Combination or Rotational Treatments

Key Points

Mild-to-moderate cases of scalp psoriasis

- Gently shampoo scalp every morning (use palms NOT fingertips)
- Apply a corticosteroid gel or lotion once or twice per day
- Apply calcipotriol (Dovonex[®]) solution once or twice per day
- Antihistamines (hydroxyzine or doxepin) at night for itching

Moderate-to-severe cases of scalp psoriasis

- Apply oil and salicylic acid or Dermasmooth FS[®] oil at bedtime and wear a shower cap
- Resistant plaques can be injected with Triamcinolone 2.5-4 mg/u every 3 or 4 weeks as necessary
- Antihistamines (hydroxyzine or doxepin) at night for itching

It should be noted that rarely scalp psoriasis is severe enough to require systemic agents such as methotrexate or acitretin.

Warnings

- Do not rub, scratch, pick, or brush/comb roughly.
- Treat gently.
- Do not pick off scale.
- Moisturize.
- Trauma or surgery will cause the plaques to flare (thicker, scaly plaques, larger areas).

Conclusion

Psoriasis remains a therapeutic challenge. Involvement of the scalp can be minimal (“dandruff”) or more significant and difficult to manage. Gentle treatment, reducing trauma, and treating the inflammation and pruritus will improve therapeutic results.

New Classification of Rosacea and Present Therapy for Family Practitioners

B. Wang, MDCM, FRCPC

Department of Dermatology, McGill University, Montréal, Québec, Canada

Definition

Rosacea is a common condition that is prevalent worldwide. Its incidence is higher in fairer skin types, however it is also seen in Asians, and African-Americans. Rosacea occurs in males and females, often after the age of 30 years. There are currently no laboratory tests to diagnose rosacea; it remains a clinical diagnosis. The actual pathophysiology and etiology of rosacea also remain unclear; however, quite recently the spectrum of rosacea has been classified and standardized.[Wilkin JK, et al. *J Am Acad Dermatol* 46:584-7 (2002).]

The defining clinical finding is persistent erythema of the central face for at least 3 months. Other primary findings include flushing (transient erythema), papules and pustules, and telangectasias (dilated blood vessels). Secondary findings include stinging, burning, dryness, edema, plaques, ocular manifestations, and phymatous changes.

There are four recognized subtypes of rosacea, and it's important to distinguish among them, as they require different modes of therapy.

Subtypes of Rosacea

- **Erythematotelangectatic rosacea:** Flushing and persistent central facial erythema is seen, as well as telangectasias. Often, central facial edema, stinging and burning of the skin, and dryness occurs.
- **Papulopustular rosacea:** Papules and pustules are seen, often along with persistent facial erythema.
- **Phymatous rosacea:** Thickening of the skin, often presenting as rhinophyma. Irregular surface nodules, enlarged follicles, sebaceous appearance seen. The chin, forehead, cheeks, and ears may be involved.
- **Ocular rosacea:** Sensation of burning, grittiness, dryness, burning, "foreign body sensation", and telangectasia of the sclera. Often, blepharitis, conjunctivitis, chalazions, and styes present. Rarely corneal manifestations (keratitis, infiltrates, and ulcers) may occur.

These subtypes are then graded into mild, moderate, and severe. They may overlap; however, it is currently believed that patients do not progress from one subtype to the next.

Postulated Pathophysiology

- Vasomotor lability
- Exposure to UV radiation, heat
- Degeneration of dermal matrix
- Perifollicular inflammatory process.

The role of *Demodex* and *Helicobacter pylori* are not at present considered to be pathogenic in the development of rosacea.

Aggravating Factors

- UV exposure
- Extremes of temperature
- Consumption of hot beverages, spicy foods, alcohol
- Topical irritating products containing glycolic acid, alcohol, acetone, exfoliants, astringents, perfumes
- Medications that can cause flushing such as vasodilatation agents, nicotinic acid, amyl nitrate, calcium channel blockers, and opiates.

Differential Diagnosis

These diseases must be excluded before making the diagnosis of rosacea:

- Systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease, and other connective tissue diseases
- Polycythemia vera
- Carcinoid
- Mastocytosis

Other situations to be considered include photosensitivity and allergic contact dermatitis. Perioral dermatitis is no longer considered to be a variant of rosacea; it presents with erythematous papules around the mouth or periorbitally. Seborrheic dermatitis can co-exist with rosacea; it presents with orange-red scaling in the T-zone of the face, scalp, and chest.

Treatment Options for Rosacea

- **Erythematotelangiectatic rosacea:** Topical metronidazole, sodium sulfacetamide with sulfur, and azelaic acid help decrease erythema. Telangiectasias are best treated with laser and light therapies.
- **Papulopustular rosacea:** Topical metronidazole, sodium sulfacetamide with sulfur, azelaic acid, benzoyl peroxide, erythromycin, clindamycin, and tretinoin decrease inflammatory papules and pustules. For a more rapid response, oral antibiotics are used. Low dose oral isotretinoin (to avoid excessive dryness) can also be used.
- **Phymatous rosacea:** In early stages, topical therapies can decrease the papules and pustules often present centrally. Isotretinoin can also be used to control the nodules and cysts, as well as temporarily decreasing excessive sebum production. However, rhinophyma itself is treated surgically, including dermabrasion, electrosurgery, cryosurgery and laser surgery.
- **Ocular rosacea:** General lid care, tear supplements are essential. Often, oral tetracycline is used to treat the inflammatory lesions. If corneal involvement is suspected, consultation with ophthalmology is advised.

Basic Nonprescription Guidelines to Give Patients Include

- Daily use of broad spectrum sunscreens that include titanium dioxide and zinc oxide as UV blockers.
- Use of non-fragranced moisturizers that contain silicone (as dimethicone or cyclomethicone) to protect the skin barrier.
- Soap-free cleansing of the skin.
- Green-tinted foundations in powder, liquid, or cream form to help camouflage erythema.
- Avoidance of aggravating factors (listed above).

Patient Communication

It is important to inform patients that rosacea is a chronic disease, that there is no cure for rosacea, but there exist effective therapies to maintain control. Remission of the disease can be obtained using maintenance treatment to which the patient may have to adhere for life and avoiding aggravating factors. Patients should be counseled that progression of disease can occur when therapy and avoidance behaviors are not maintained.

Dosage and Course of Prescription Treatment for Rosacea

Topical

- Metronidazole 0.75% cream, gel, lotion; also a 1% cream q.d.
- Sodium sulfacetamide 10% with 5% sulfur cream or lotion b.i.d.
- Erythromycin 2% lotion, solution b.i.d.
- Azelaic acid 15% gel b.i.d.
- Tretinoin 0.025% cream q.h.s.

Systemic

- Tetracycline 250-500mg, PO, q.d. or b.i.d. for 6-12 weeks
- Minocycline 50-100mg, PO, q.d. or b.i.d. for 6-12 weeks
- Doxycycline 50-100mg, PO, q.d. or b.i.d. for 6-12 weeks
- Erythromycin 250mg, PO, q.d. or b.i.d. for 6-12 weeks.

Hormonal Agents Approved for Treatment of Acne

J.K.L. Tan, MD, FRCPC

Department of Medicine, University of Western Ontario, Windsor, Ontario, Canada

What is Acne?

Acne is an occlusional and inflammatory disorder of pilosebaceous follicles (oil pores) resulting from the combined effects of:

- androgenic hormones (testosterone, dihydrotestosterone, hydroxyprogesterone)
- follicular bacteria (*Propionobacterium acnes*),
- abnormal desquamation of the pore orifice,
- excessive sebum excretion.

Hormonal therapy

Hormonal agents have long been recognized as being effective for treating acne in women. This paper focuses on agents officially indicated for treatment of acne in Canada:

- Ethinyl estradiol 0.020mg and levonorgestrel 0.100mg (Alesse[®])
- Ethinyl estradiol 0.035mg and cyproterone acetate 2mg (Diane-35[®])
- Ethinyl estradiol 0.035mg and norgestimate in increasing doses (0.180mg, 0.215mg and 0.250mg each for 7 days (Ortho Tri-Cyclen[®]).

These agents may be used in women with:

- moderate acne as adjunctive therapy to topicals in women desiring contraception.
- severe acne in women unresponsive to topical agents and oral antibiotics (Diane[®]-35).
- severe acne requiring oral isotretinoin as one of two preferred forms of contraception.

Spironolactone is a synthetic steroid antiandrogen that competitively binds androgen receptors, inhibits 5-alpha-reductase activity, and reduces androgen biosynthesis. It has been used for treatment of acne in doses ranging from 50-200mg/day. Due to the limited number of trials and small sample sizes, the efficacy of spironolactone for treatment of acne has been deemed indeterminate by a recent Cochrane review.[Farquhar C, et al. The Cochrane Library (Oxford) 2; CD000194 (2003).]

Treatment Duration

While improvement in acne is generally noted by the second cycle with these agents, longer treatment durations of 6 cycles or more provide for greater effectiveness.

Consider long-term maintenance treatment while acne is active to avoid the potential for rebound of symptoms on discontinuation. A statement issued by the Society of Obstetricians and Gynaecologists of Canada (SOGC) stated that "Repeated 'stop-start' regimens are not an optimal strategy for treating androgen-dependent disorders."

Summary of Evidence

Product	Evidence	Results
Ethinyl estradiol 0.020mg and levonorgestrel 0.100mg (Alesse®)	2 placebo-controlled randomized trials involving 721 women with moderate facial acne over 6 cycles [Leyden J, et al. <i>J Am Acad Dermatol</i> 47:399-409 (2002); Thiboutot D, et al. <i>Fertil Steril</i> 76: 461-8 (2001).]	Significant improvement in lesion counts and global assessments. Overall 40% reduction in inflammatory lesions and 20% in noninflammatory lesions.
Ethinyl estradiol 0.035mg and cyproterone acetate 2mg (Diane®-35)	1 randomized trial with active comparator – ethinyl estradiol 0.030 mg and levonorgestrel 0.15 mg in 85 patients over 6 cycles [Carlborg L. <i>Acta Obstet Gynecol Scand Suppl</i> 134:29-32 (1986).]	Significant improvement in inflammatory lesion counts with 72% reduction (vs. 35% in comparator group).
Ethinyl estradiol 0.035mg and norgestimate in increasing doses (0.180mg, 0.215mg and 0.250mg each for 7 days (Ortho Tri-Cyclen®)	2 placebo-controlled randomized trials involving 324 women with moderate facial acne over 6 cycles [Lucky AW, et al. <i>J Am Acad Dermatol</i> 37:746-54 (1997); Redmond GP, et al. <i>Obstet Gynecol</i> 89:615-22 (1997).]	Significant improvement in lesion counts and global assessments. Overall, 56% reduction in inflammatory lesions and 41% in noninflammatory lesions.

Table 1: A literature review of the effectiveness of these contraceptives for treating acne identified numerous controlled clinical trials. It should be noted that in both the Alesse® and Ortho Tri-Cyclen® studies, the placebo effect is high.

Comparing Hormonal Treatments

While there are no controlled clinical trials on the relative efficacy of these 3 agents in treating acne, a survey of Canadian acne patients previously treated with these agents indicated that

- Ethinyl estradiol 0.035mg and cyproterone acetate 2mg (Diane®-35) was ranked to be the most effective of the 3 agents.
- Effectiveness ratings of moderate-extremely were highest for Diane®-35 (42%) compared to Ethinyl estradiol 0.035mg and norgestimate in increasing doses (0.180mg, 0.215mg and 0.250mg each for 7 days Ortho Tri-Cyclen® (22%) and Ethinyl estradiol 0.020mg and levonorgestrel 0.100mg (Alesse®) (19%).
- The 3 treatments have different mechanisms of action because Diane®-35 has progesterone with antiandrogenic properties in addition to the estrogen components.

[Tan J. Effectiveness of Hormonal Treatment in Acne – The Canadian Acne Epidemiological Survey. Presented at: Dermatology Update 2005, Montreal, Canada.]

Safety

The use of these agents may be associated with minor adverse events such as nausea, breast tenderness, headaches, mood changes, and weight gain. Serious potential complications include venous thromboembolism (VTE), myocardial infarction, and stroke. While the risk of low-dose combined hormonal treatments for venous thromboembolism (VTE) is increased 3-4 fold, the magnitude of this risk is of minimal clinical significance in women without additional risk factors [Contraception Guidelines Committee of SOGC. Canadian Clinical Practice Guidelines: Combined Hormonal Contraception. *J Obstet Gynaecol Can* 26(3):219-54 (2004).] A recent comprehensive epidemiological review did not demonstrate an increase in VTE risk for Diane®-35 [Spitzer WO. *J Obstet Gynaecol Can* 25:1011-8 (2003)]. Hypertension and smoking are independent risk factors for myocardial infarction and stroke in patients taking oral contraceptive pills. Accordingly, conditions contraindicating the use of hormonal treatments include VTE, cerebrovascular or coronary artery disease, headaches with focal neurologic symptoms, diabetes with complications, cigarette smoking >35 years, hypertension >160/100mmHg or with concomitant vascular disease, and conditions associated with prolonged immobilization.

Conclusion

Hormonal agents are important, effective therapeutic options for women across the spectrum of acne severity. The three preparations approved in Canada for this indication have safety profiles similar to conventional oral contraceptives.

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Family Practice Edition

EDITOR: DR. STUART MADDIN

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