

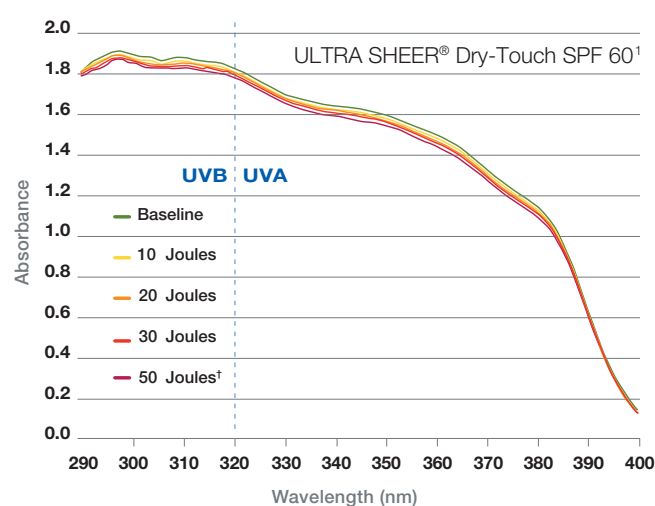
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1. Data on file. Johnson & Johnson Inc., Neutrogena.  
†Laboratory conditions representative of five hours of midday sun.

## Management of adult acne



*Treatment principles are similar to those in younger patients, but hormonal therapy plays a greater role*

**BY MEGAN SURKAN**  
faculty of medicine,  
University of  
Saskatchewan,  
Saskatoon

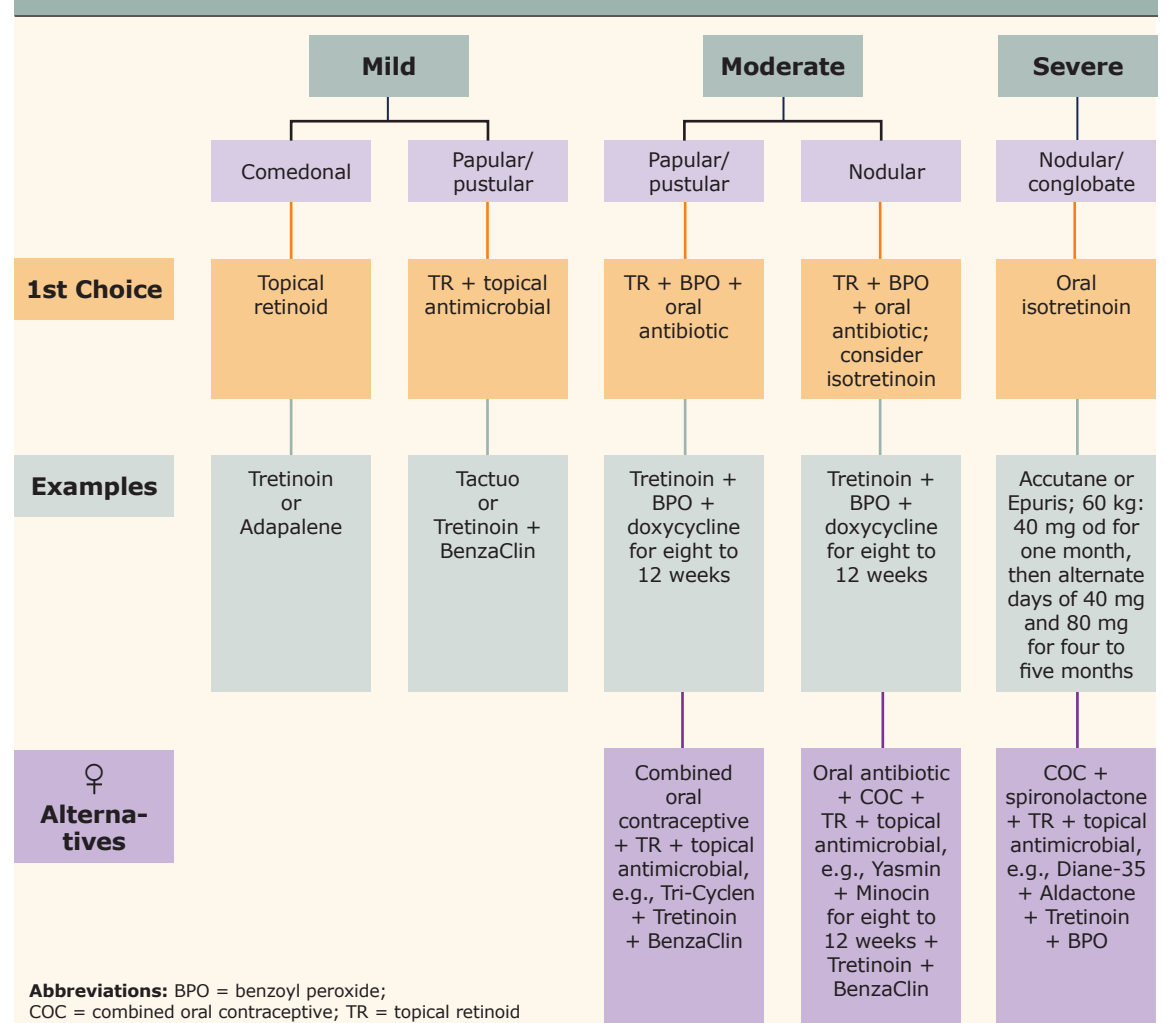
**DR. ANIL KURIAN**  
division of dermatology  
& cutaneous sciences,  
department of medicine,  
University of Alberta,  
Edmonton

**DR. BENJAMIN BARANKIN**  
Toronto  
Dermatology  
Centre

Acne vulgaris is not just a teenage condition. Acne can manifest as comedones (open and closed), inflammatory papules and pustules, and nodulocystic lesions on the face, chest and back. The pathogenesis of acne is based around the sebaceous gland. Androgenic changes increase sebum production and trigger the formation of comedonal acne. Comedones are open if the blockage is high in

the duct where keratin and sebum become oxidized, or closed if the blockage is deeper. If comedones become overgrown with bacteria, cytokines are released and it is transformed into an inflammatory papule, which can develop a central pustule. If this ruptures below the dermis, an inflammatory cyst develops, which can create scarring. Acne can be mild, moderate or severe and is classified by the type, number and distribution of lesions.<sup>1</sup> Two subtypes of

Figure 1: **Treatment algorithm for adult acne** <sup>5, 6</sup>



**Abbreviations:** BPO = benzoyl peroxide;  
COC = combined oral contraceptive; TR = topical retinoid



adult acne exist: persistent acne from youth and late-onset acne that first develops after the age of 25, accounting for about 75% and 25% of cases, respectively.<sup>2</sup>

Acne arising in adulthood more commonly affects females than males in all age groups older than 20 years. Adult acne tends to be slower to respond and more resistant to treatment. Those with a first-degree relative with severe acne or with an endocrinopathy may present with more severe acne requiring systemic treatment; those with persistent acne from adolescence often present with mild to moderate acne.<sup>3</sup>

Secondary acne is more common in adulthood. Medications or an underlying endocrinopathy are common culprits. Exogenous steroids, anti-epileptics, lithium, progesterone, testosterone, azathioprine, cyclosporine, bromides, gabapentin and tetracyclines have been implicated in exacerbating acne.<sup>4, 5</sup> Late onset of acne, oligomenorrhea, hirsutism, androgenic alopecia or infertility can point toward an underlying endocrine cause. The differential includes: polycystic ovarian syndrome, Cushing’s syndrome, congenital adrenal hyperplasia, androgen-secreting tumours and acromegaly.<sup>4</sup>

**Therapeutic choices**

The management of acne is primarily pharmacologic. Often control takes two to three months to achieve. Maintenance treatment should be attempted with topicals, including a retinoid with or without benzoyl peroxide, resuming systemic therapy if necessary.<sup>1</sup> Topical therapy is the standard of care for mild to moderate acne, while moderately severe and severe acne require systemic agents. The principles of acne treatment in adults do not differ significantly from those in younger patients, but hormonal therapy plays a greater role due to female predominance.<sup>2</sup>

**Topical agents**

Topical agents (see Table 1) should be selected based on the type of acne lesions: topical retin-

oids for comedonal acne, benzoyl peroxide with a topical antibiotic for inflammatory lesions, and a combination of all three agents if comedones and papules/pustules are present concurrently.

- **Topical retinoids** are the most effective comedolytic agents that also reduce inflammation and post-inflammatory hyperpigmentation. Tretinoin is the most cost-effective, but is photosensitizing. Adapalene is the least irritating, and tazarotene the most potent and most irritating. Local dryness, burning and erythema can be reduced by starting with a lower concentration, and initially using every two to three nights or as short contact therapy.<sup>1</sup>
- **Benzoyl peroxide** (BPO) is a bactericidal agent that targets Propionibacterium acnes. It causes mild skin irritation and bleaches fabric. Concentrations of 2.5% and 5% have been shown to have similar efficacy to a 10% formulation but with less irritation.<sup>4</sup> There is no resistance to BPO.
- **Clindamycin or erythromycin** applied topically in combination with BPO have been shown to reduce bacterial resistance. Once inflammatory lesions are controlled, maintenance therapy should include a topical retinoid, adding BPO if an antimicrobial effect is needed.<sup>1</sup>
- **Dapsone gel** is a synthetic sulfone with anti-inflammatory properties. It can achieve a 46% reduction in inflammatory lesion count after 12 weeks.<sup>5</sup> It is generally well-tolerated, and particularly effective in adult female acne.
- **Glycolic and salicylic acids** are mild comedolytics available over-the-counter that can be used when topical retinoids are not tolerated. Higher concentrations can be used in chemical peels to reduce comedones, but can cause irritation.<sup>1</sup>

**Light therapy**

At this time, there is insufficient evidence to support or refute light therapy’s efficacy as an acne treatment. Light-based therapies include ultraviolet A and B, **continued on • page 30**

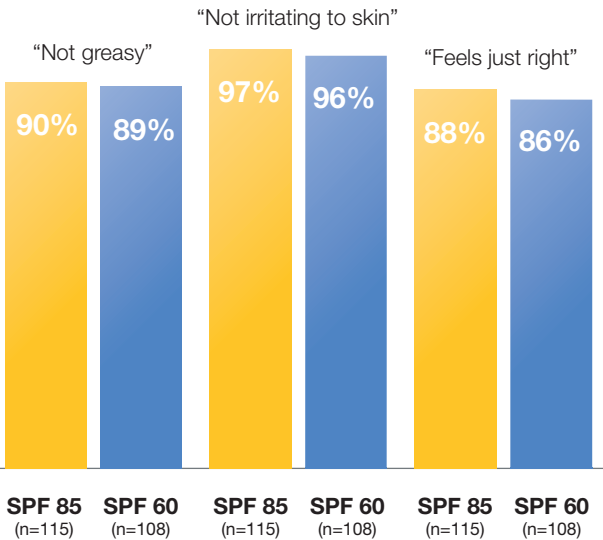
Table 1: Topical agents <sup>1, 5</sup>			
Class	Drug	Adverse effects	Indication
Retinoids	Tretinoin 0.01%, 0.025%, 0.05%, 0.1% Retin-A, Retin-A Micro	Photosensitivity. Irritation. 12 weeks for max response	First-line treatment for comedonal acne
	Tazarotene 0.05%, 0.1%. Tazorac cream or gel		Papulopustular acne in combination with anti-bacterial agents
	Adapalene 0.1%, 0.3% Differin, Differin XP cream or gel		Treatment of choice for maintenance after completing systemic therapy
Combination product	Tactuo (0.1% adapalene + 2.5% benzoyl peroxide gel)	Less irritating and photosensitizing. May be applied in morning	Reduces post-inflammatory hyperpigmentation
Peroxides	Benzoyl peroxide 2.5%, 5%, 10%	Dryness, contact dermatitis. Rarely allergenic	Papulopustular acne  Prescribe concurrently with both topical and oral antibiotics to minimize resistance
Antibiotics (with benzoyl peroxide)	Erythromycin 3% + benzoyl peroxide 5% (Benzamycin)	Dryness. Two to four weeks for improvement, eight weeks for optimal results	Papulopustular acne
	Clindamycin 1% + benzoyl peroxide 5% BenzaClin, Clindoxyl		More severe acne in combination with systemic agents
Sulfones	Dapsone 5% gel Aczone	Peeling, dryness, erythema.	Inflammatory acne
Alpha and beta hydroxy acids	Glycolic acid 2% to 15%. Neostrata, Reversa, others	Dryness, irritation	Can be used when topical retinoids are not tolerated
	Salicylic acid 0.5% to 2%. Oxy, Clearasil, Neutrogena, others		Available OTC



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**from • page 29**

blue light, blue-red light, and photodynamic therapy (PDT) with 5-aminolevulinic acid (ALA) or methyl-aminolevulinate. They may improve acne by reducing levels of Propionibacterium acnes, disrupting sebaceous gland function and decreasing inflammation.<sup>4</sup> The Global Alliance to Improve Outcomes in Acne concluded that current data are insufficient to define the role of light therapy in acne.<sup>6</sup> Narrow-band blue-light PTD with ALA as a photosensitizer has been shown to significantly improve global acne severity ratings and decrease inflammatory papules transiently. Adverse effects include erythema, pustular eruptions and crusting after treatment. PDT may be effective for acne, but studies are limited by variation in regimens and methodology.<sup>4</sup>

Currently, light therapies are rarely covered by insurance, have shown similar benefit to traditional acne treatments and have not clearly been shown to offer lasting benefit. Laser therapy (e.g., ablative fractionated lasers) plays a greater role in acne scar revision.<sup>4</sup>

**Systemic agents**

Use systemic agents (Table 2) when topicals have failed to achieve control after two to three months, or in nodulocystic acne where topicals have little chance of success.<sup>7</sup>

• **Oral antibiotics** are indicated for moderately severe inflammatory papules and pustules. By reducing Propionibacterium acnes within the follicles, bacteria-induced inflammatory cytokines are minimized. These agents also possess inherent anti-inflammatory properties. Tetracyclines are first-line therapy (and the most cost-effective), with a 50% to 60% reduction of inflammatory lesions after eight weeks. Tetracycline, doxycycline and minocycline are equally efficacious in reducing lesion count.<sup>5</sup>

Doxycycline is advantageous due to once-daily dosing without the cost or some of the potential side-effects of mino-

cycline. Doxycycline causes the most photosensitivity of the three, but this is minimal for doses of 100 mg per day.

Tetracycline must be taken on an empty stomach for optimal absorption and requires twice-daily dosing initially. It also causes the most gastrointestinal upset of the three, thus it has become less popular.

Minocycline is well-tolerated, has once-daily dosing and does not have cross-resistance with doxycycline. It causes the most dizziness. It can cause bluish hyperpigmentation of the skin if used for extended periods. Rare but serious side-effects include a lupus-like reaction, autoimmune hepatitis and a hypersensitivity reaction.<sup>5</sup>

Erythromycin has similar efficacy in reduction of lesion count over eight weeks to the tetracyclines. It is not a first-line antibiotic because of increased resistance and its gastrointestinal effects. Erythromycin is reserved for instances where tetracyclines are contraindicated, such as in patients younger than eight or in pregnancy.<sup>7</sup>

Trimethoprim with or without sulfamethoxazole is a third-line antibiotic that is useful when other antibiotics cannot be used, such as in patients who are resistant or intolerant to other antibiotics.<sup>7</sup>

Currently, there is no evidence guiding duration of use. Recommendations for eight to 12 weeks of treatment are based on expert opinion. When possible, therapy should be limited to three months, and benzoyl peroxide should be used concurrently to reduce antibiotic resistance. If relapse occurs despite adherence to a topical regimen, antibiotics may be used on a long-term suppressive basis, although alternative systemic therapies should be considered.<sup>1</sup>

• **Hormonal therapy** is an effective second-line treatment in all women with acne, regardless of whether an underlying hormonal imbalance is present. Tri-Cyclen, Alesse, Diane-35, Yaz and Yasmin are officially

Table 2: Systemic agents <sup>5, 7</sup>			
Class	Drug	Adverse effects	Indication
<b>Oral antibiotics</b>  First line: Tetracyclines	• Tetracycline 500 mg bid initial course (eight to 12 weeks); 250 mg to 500 mg od maintenance	GI upset, must be taken on empty stomach	Moderate to severe inflammatory acne
	• Doxycycline 100 mg to 200mg od	Photosensitivity greatest of the tetracyclines (dose-dependent)	
	• Minocycline 50 mg to 200 mg od initial; 50 mg od maintenance	Bluish skin pigmentation; Rare: lupus-like reaction, autoimmune hepatitis, hypersensitivity reaction; Consider liver function tests and anti-nuclear antibody q4m	
Second line: Macrolides	Erythromycin 500 mg bid initial; 250mg od maintenance	Nausea and vomiting, diarrhea	Moderate to severe acne  Overall greater than 50% improvement; three to six months for optimal response; relapse common with discontinuation
Third line: Diaminopyrimidines	Trimethoprim 200 mg to 300 mg bid	GI upset, rash (3%); Rare: agranulocytosis, toxic epidermal necrolysis (TEN)	
<b>Combined oral contraceptives</b>	• Tri-Cyclen  • Alesse  • Diane-35/Cyestra-35  • Yasmin  • Yaz	Contraindications: smoker older than 35 years, migraine with aura, known liver disease, past thrombosis, ischemic heart disease, hypertension, diabetes with microvascular disease	
<b>Androgen receptor antagonist</b>	Spironolactone (Aldactone) 25 mg to 200 mg daily	Hyperkalemia Potassium/electrolytes: baseline and monthly	Adjunctive treatment for women when other treatments have been ineffective or not tolerated
<b>Isotretinoin</b>	Accutane, Epuris 0.5 mg/kg/d for four weeks then 1 to 2 mg/kg/d for three to seven months. Total dose: 120 to 150 mg/kg.	Xerosis (cheilitis, nose bleeds, inability to wear contact lenses, itching), sun sensitivity, myalgias, headache  Increased cholesterol, LDL, triglycerides (>5.7 mmol/l in 25% of patients), pancreatitis  Initial flare in 6% of patients—decrease dose  Potent teratogen: reliable contraception, monthly B-hCG. No concern for males  Serious (discontinue): abrupt decreased night vision, depression, Stevens-Johnson syndrome/TEN	Severe nodulocystic acne; acne associated with scarring; failure to respond to other systemic therapies

indicated for acne. However, all combined oral contraceptives (COCs) are beneficial due to estrogen's ability to decrease levels of free testosterone by increasing sex hormone binding globulin. The evidence for superiority of one progestin over another is conflicting. All oral contraceptives have a small risk of thromboembolic events (3.4 per 10,000 women-years in the first year).<sup>5</sup> COCs

containing drospirenone have a higher risk of clots. Yasmin and Diane-35 reduced acne lesions by 63% and 59%, respectively, in a randomized trial involving 128 women.<sup>10</sup> Contraceptives containing only progesterone can worsen acne.<sup>7</sup>

Spironolactone is an anti-androgen therapy that can be used in women as an adjuvant to COCs when other treatments have failed. At doses

of 50 mg/day to 200 mg/day it acts as a 5-alpha-reductase inhibitor. Spironolactone alone may be effective, but only in less than half of women, and it requires two to three months for optimal response.<sup>7</sup>

• **Isotretinoin** is indicated for severe nodulocystic acne, or in less severe but treatment-resistant acne. Isotretinoin targets all four causative mechanisms of acne and is the only

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agent capable of long-term remission. It lessens abnormal follicular keratinization, reduces Propionibacterium acnes colonization, decreases sebum production by 70% and is anti-inflammatory. It is a well-known teratogen, with mucocutaneous, musculoskeletal, ophthalmic and dyslipidemic effects. Nearly 100% of patients experience xerosis and cheilitis. Serious adverse effects include an abrupt decrease in night vision, severe drug eruptions and depression. A cause-and-effect relationship between isotretinoin and



Topical treatment is based on lesion type: retinoids for comedonal acne, benzoyl peroxide with a topical antibiotic for inflammatory lesions, or a combination of all three agents if needed.

depression or inflammatory bowel disease has never been proven, but nonetheless it is imperative to monitor closely for mood changes. Baseline and subsequent labs include a CBC, lipid profile, ALT and beta-hCG.<sup>7</sup> Isotretinoin should preferably be

consumed with a fatty meal for optimal absorption, although this is less important with the newest formulation, Epuris. The recommended dose is 0.5 mg/day to 2.0 mg/day for 16 to 20 weeks. A lower starting dose reduces the chance of an initial acne flare. Total cumulative dose should be 120 mg/kg to 150 mg/kg.<sup>5</sup> A cohort study of 17,351 patients ages 17 to 35 years with acne and first-line treatment with isotretinoin between 1984 and 2003 showed that 41% experience acne relapse.<sup>8</sup> There is ongoing research that

shows success with a low-dose, long-term approach to using isotretinoin at 5 mg/day to 10 mg/day as an option for adults,<sup>9</sup> but this is not currently the standard of care. Patients who receive a cumulative dose below 120 mg/kg have higher rates of recurrence.<sup>7</sup>

**Therapy in pregnancy** Topical antibacterials and oral erythromycin are considered safe in pregnancy. Topical and oral retinoids, hormonal therapy and oral tetracyclines must be avoided.<sup>7</sup> **MP**

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