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# Acne-vulgaris

A 17-year-old male presents with a four year history of inflammatory papules and nodules on his face. He has been treated with various topical and oral therapies, all of which provide some benefit and then seem to stop working. He is otherwise healthy, on no medications, and has no drug allergies. What is your diagnosis and what are the treatment options?

## Diagnosis: Acne vulgaris - moderate inflammatory type

Acne is a common skin disease affecting > 90% of people at some point in their lives. It is characterized by noninflammatory papules (comedones) and/or by inflammatory papules, pustules, and nodules in its more serious form. It affects skin that is dense with sebaceous follicles, including the face, upper chest, and back. While the face is most commonly affected, the chest, back and upper arms are also often affected and portend more management difficulties.

The four key etiopathogenic factors are: follicular epidermal hyperproliferation and hyperkeratinization, excess sebum, the bacteria *Propionibacterium acnes*, and inflammation. Follicular epidermal hyperproliferation with hyperkeratinization appears to be one of the primary events in the development of an acne lesion. The amount of sebum produced and the degree and severity of the acne are strongly correlated. Sebum excretion is under hormonal control. Androgens stimulate sebocyte differentiation and sebum production, whereas estrogens have an inhibitory effect. Of note is that most men and women with

acne have normal circulating levels of androgen hormones. The bacteria *P. acnes* appears to show up in later acne lesions, and stimulates inflammation by producing pro-inflammatory mediators. Acne is more common in males than in females during adolescence, although the opposite is true in adulthood.

Acne can have significant psychosocial impact on patients, regardless of the severity of the disease, resulting in depression, anxiety, relationship difficulties and other psychological sequelae. Individual lesions may be tender or painful, and can bleed with trauma (e.g., sports). Severe acne with associated systemic symptoms (e.g.; fever, arthritis) is termed acne fulminans.

Acne can be worsened by some cosmetic agents and hair pomades, as well as by such medications as: steroids, lithium, antiepileptics, and halogens (e.g., iodides). There are genetic influences to acne as well, and both congenital adrenal hyperplasia and polycystic ovarian syndrome (PCOS) can trigger acne.

The diagnosis of acne is made clinically. Female patients with dysmenorrhea/anovulation and/or hirsutism require a hormonal evaluation (total and

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free testosterone, DHEAS, serum lipids; LH, FSH, prolactin, and 17-hydroxyprogesterone are often ordered as well), and those with signs of Cushing disease require a 24-hour urine cortisol.

Patients should be advised to wash their face with a mild soap or soap substitute cleanser once or at most twice a day. Over-the-counter (OTC) salicylic acid preparations can be useful for mild or early cases of acne, although products that provide “scrubbing” can, in fact, worsen acne.

uuals. Note that topical therapy is or should be used for many years, while systemic therapy is usually for much shorter durations measured in months.

Systemic therapy often starts with oral antibiotics, particularly tetracycline, minocycline, or doxycycline. They are effective against *P. acnes*, but more importantly are its anti-inflammatory effects. Other antibiotics (e.g., erythromycin, trimethoprim +/- sulfamethoxazole, azithromycin) show some benefit. Unfortunately, bacterial

ethinyl estradiol), while others can worsen the condition. Spironolactone (Aldactone) can also be used with very good efficacy since it binds the androgen receptor and thus reduces androgen production; it can be used concurrently with OCs. It is preferred in older women (due to its adverse effects on the fetus in women of childbearing age) or those on oral contraceptives, and is prescribed at 50-200 mg/d.

Medically, the “big gun” is isotretinoin (Accutane), a systemic retinoid that is highly effective for severe, recalcitrant acne, but is also being used for more moderate cases as well (e.g., older female with stubborn acne, mild-moderate scarring acne). It is the only agent that works on the entire spectrum of etiopathogenesis by normalization of epidermal differentiation, reduced sebum excretion by 70%, anti-inflammatory effects, and even reduced numbers of *P. acnes*. Typical treatment lasts for 5-6 months at 1 mg/kg/day for a total cumulative dose of 120-150 mg/kg is reached. This is a potent medication, with a large assortment of potential and real side effects that should be discussed with patients. The main side effects to note are: xerosis and cheilitis (most common), joint pain, fatigue, alopecia, headaches (pseudotumor cerebri), photosensitivity, teratogenicity, mood changes and depression (rare), and elevated triglycerides (can cause pancreatitis). Baseline and regular blood work for pregnancy, cholesterol, triglycerides, and liver function should be assessed.

Some patients can benefit from manual extraction of comedones and occasional intralesional steroid injections or cryotherapy for large papules/nodules. There is also benefit from regular glycolic acid peels. Phototherapy using red or blue light and photodynamic therapy are showing mild-moderate benefits. Acne scarring should be managed by an experienced dermatologist or plastic surgeon. ■

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Treatment is geared towards the multiple pathogenic factors. Topical retinoids are predominantly comedolytic with mild anti-inflammatory activity. They are used nightly, and can be used in combination with other topical or oral agents. Patients should be advised as to the peeling and redness that can occur, and they can reduce the frequency of application until the skin adjusts to nightly therapy. Topical antibiotics (e.g., clindamycin, erythromycin) work mainly on *P. acnes*, and may have some anti-inflammatory effects as well; they are not comedolytic, and unfortunately there is increasing resistance to topical antibiotic monotherapy. They can be used once or twice a day, and the vehicle (gel, lotion, cream) should be based on the patient skin type. Benzoyl peroxide is available OTC and by prescription, and can be found in combination with topical antibiotics and retinoids. This agent also has irritant effects similar to retinoids and so should be used with graduating frequency, and should be carefully used in fair-skinned individ-

resistance is increasingly common, although adding benzoyl peroxide is not only more efficacious, but appears to significantly reduce resistance rates. Oral antibiotics are often prescribed for three months, and then patients reassessed for response for consideration of another 3-6 months of therapy. Patients should be advised that minimal benefit is expected in the first 4-6 weeks of therapy, and in fact, the acne may flare during this time. Multiple courses may be needed over time.

In female patients, hormonal therapies can be of significant benefit. Oral contraceptives (OC) increase sex hormone binding globulin, which results in reduced free testosterone in the circulation. Cyproterone acetate/ethinyl estradiol (Diane-35), levonorgestrel/ ethinyl estradiol (Alesse), and norgestimate/ ethinyl estradiol (Tri-cyclen) are approved for their role in moderate acne (Diane-35 is not approved in Canada as an OC, although it is in Europe). Other contraceptives can be beneficial for acne as well (especially Yasmin: drospirenone/