# Acne

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## INTRODUCTION

The management of acne presents numerous challenges for the primary care practitioner. Many products are available, yet evidence-based product information may be lacking. Treatment approaches differ depending on the severity of acne. Specific populations, such as adult women, pregnant women, patients with skin of colour, and adolescents require specifically tailored treatment plans. Because full response may take months, patient adherence issues may arise, and patient education is of prime importance in managing this disorder.

## OBJECTIVES

This module will enable clinicians to:

- Assess acne grade and prescribe treatment appropriately, including when and for how long to prescribe oral medications.
- Effectively treat specific populations, including adult women and patients with skin of colour.
- Employ patient education techniques and a stepwise approach to management to improve patient adherence to acne treatment.
- Assess the psychological impact of acne on the individual.

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## CASES

### Case 1: Hannah, female, age 16

Hannah presents to your office about her acne, which has been a problem for the past year. Her previous doctor prescribed daily 5% alcohol-based benzoyl peroxide gel and 0.05% tretinoin cream about six months ago, but Hannah stopped using them because her skin became very red and dry, and her acne worsened. She has also spent a substantial amount of money on estheticians, but this has not helped either. She is visibly upset as she tells you about her skin issues.

***Although typical adolescent acne is the most likely diagnosis for Hannah, what else would you like to know?***

### Part Two

The history reveals no symptoms of hyperandrogenism; Hannah is taking no medications and is not sexually active. She cleanses her skin with soap and applies foundation to conceal the acne lesions. On examination, she has scattered papules, pustules, and comedones on her face, but no nodules, back or chest lesions, or any evidence of scarring or hyperpigmentation. There are no signs of secondary causes of acne. You have Hannah complete the Cardiff Acne Disability Index (CADI) questionnaire (Appendix 1), and her score is 10 out of 15 (moderate).

***How would you approach management/treatment?***

### Part Three

After providing Hannah with information about acne and its treatment and answering her questions, you prescribe adapalene, 0.1%, a low-dose topical retinoid, for two weeks with instructions to add 2.5% benzoyl peroxide after two weeks if the retinoid is tolerated. At one month follow-up, Hannah's skin looks slightly worse but she is tolerating treatment and adhering to therapy. At three months, her skin has improved, she has continued on the regimen, and she is feeling much happier about her skin.

However, a year later, Hannah returns as her acne has worsened. On examination, she now has many more papules and pustules, a few nodular lesions, and some evidence of mild scarring. She is again distressed about her skin, as her high school graduation is approaching, and she wants to look good for the event.

***What treatment options would you now consider?***

### Case 2: Melissa, female, age 48

Melissa comes to your office today to ask about treatment for her acne. As a teenager and young adult, she had acne, but with age her skin improved. She hasn't been on any prescription treatment for her acne for the last 20 years. During the past six months, however, Melissa has noticed a substantial increase in acne lesions on her lower face, along her jaw line, and on her neck and back. Some lesions are painful. Melissa works as a bank teller and finds facing the public every day embarrassing.

***What else would you want to know before beginning treatment?***

### Part Two

Melissa has experienced intermittent hot flashes and a reduced menstrual frequency for the past several months. She has no other signs or symptoms of hormonal imbalance and no history of easy flushing or blushing or perioral distribution of her lesions. She is currently using Proactiv® (2.5% benzoyl peroxide) and a moisturizer. In the past, she has used both topical treatments and oral antibiotics. On examination, she has multiple papular, pustular, and nodular lesions on her lower face, neck, and back, and evidence of old acne scars.

***What treatment would you recommend?***

***What would be your follow-up plan for Melissa?***

### Case 3: Marcus, male, age 16

Marcus, an African Canadian, makes an appointment to find out if there are any treatments for his acne that might be better than the over-the-counter preparations he has been using for the past 18 months. He has never received prescription acne therapy and is taking no medications or over-the-counter supplements. He is moderately bothered by his acne but denies any significant depressive symptoms. Examination demonstrates papular and pustular lesions on his face, chest, and back, darkly pigmented macules on his face and back, and several small keloid scars on his upper chest and back.

***What treatment approach would you take?***

### Part Two

Marcus returns eight weeks later, and his skin shows minimal improvement. On examination, you note new nodular lesions and an increase in darkly pigmented macules. He read the information you gave him about isotretinoin and would like to try it.

***How would you initiate and monitor Marcus' use of isotretinoin?***

**Part Three**

You follow Marcus monthly until he finishes his course of isotretinoin, which significantly improves his acne. Marcus now wonders what he can do about his postinflammatory hyperpigmentation (PIH) and keloid scarring.

***What would you recommend to Marcus?***

## INFORMATION SECTION

1. *Definition:* Acne is a chronic inflammatory disease of the pilosebaceous unit. Open comedones (blackheads) and closed comedones (whiteheads) are noninflammatory lesions, whereas papules, pustules, and nodules are inflammatory lesions.[1]

### EPIDEMIOLOGY

2. *Prevalence:* The prevalence of acne is estimated to be 85% among individuals aged 12 to 24 years. Acne may persist into adulthood; the reasons for this persistence are unclear.[2] Population studies have found substantial rates of visible acne among adults in different age ranges:
   a) 20 to 29 years: 64%[3]
   b) 30 to 39 years: 43%[3]
   c) 40 to 49 years: 3% (males) and 5% (females)[4]
   d) 50 to 59 years: 6% (males) and 8% (females)[4]

3. *Genetic links:* The genes linked to acne have not been elucidated, but acne appears to have a high heritability, based on prevalence in first-degree relatives and on twin studies. No data on relative incidence and prevalence by ethnicity exist, but PIH and keloid scarring are more common among individuals with darker skin.[1]

### PATHOPHYSIOLOGY

4. Desquamation of keratinocytes lining hair follicles initiates acne lesions with formation of a microcomedone. Sebum production, which increases with puberty due to increased androgen production, creates a lipid-rich, anaerobic environment favouring colonization by *Proprionibacterium acnes.* Proliferation of *P. acnes* is accompanied by production of inflammatory and chemotactic factors, resulting in an influx of inflammatory cells. The role of *P. acnes* in the development and persistence of acne lesions has not yet been elucidated. Bacterial numbers are similar in patients with and without acne.[1]

### DIAGNOSIS

5. The differential diagnosis of acne includes the following conditions:[5]
   a) *Bacterial folliculitis:* Abrupt onset with variable distribution that spreads with shaving or scratching.
   b) *Hidradenitis suppurativa:* Onset as painful boils, double-ended comedones (similar to blackheads, with two heads separated by a varying distance), and sinus tracts.
   c) *Milaria:* Heat rash with nonfollicular papules, pustules, and vesicles.
   d) *Perioral dermatitis:* Papules and pustules on chin and nasolabial folds with a clear area around lips may occur spontaneously or may be associated with topical steroid use.
   e) *Pseudofolliculitis barbae:* Ingrown hairs in the beard area of individuals with curly hair who shave closely.
   f) *Acne rosacea:* Telangiectasis and erythema, if chronic, may have papular lesions but no comedones.

6. Key elements of the history are the following:[6,7]
   a) Duration of acne.
   b) Family history of acne.
   c) Over-the-counter and prescription therapies previously tried for acne: use, duration, reasons for discontinuation.
   d) Cosmetics and hair products used.
   e) Occupational or recreational factors that could affect acne: occlusion or pressure from sporting gear, tight clothing, or greases.



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f) Medical history.
g) Medications and over-the-counter supplements that may cause acne: danazol, testosterone, progesterone-only contraceptives, systemic glucocorticoids (e.g., prednisone), topical corticosteroids, lithium, dilantin, carbamazepine, isoniazid, B vitamins, and others.[8]
h) Impact of acne: psychological, quality of life.
i) Picking, which can worsen inflammation.
j) Symptoms of hormonal imbalance, including hyperandrogenism in female patients.

7. Key elements of physical examination are the following: [6,7,9]
   a) Signs of potential secondary causes of acne: hirsutism, androgenic alopecia, clitoromegaly, hypertension, and obesity.
   b) Distribution of acne, with a focus on the face, chest, and back.
   c) Type of lesions present.

   This information helps determine the severity of the acne, which in turn guides appropriate treatment, and also rules out acne mimics, such as rosacea and perioral dermatitis.

8. *Possible hormonal etiology:* Symptoms suggestive of a hormonal etiology include irregular menses; perimenopausal symptoms; perimenstrual acne flares; infertility; a deepened voice; abnormal hair growth on the face, chin, chest, or perineal area; and hair loss on the scalp. Signs on physical examination include hirsutism, clitoromegaly, and male-pattern balding. Laboratory investigation is appropriate in patients with signs or symptoms of hormonal imbalance or androgen excess to rule out an underlying disease such as polycystic ovary syndrome (PCOS), congenital adrenal hyperplasia, androgen-secreting neoplasms, or Cushing's disease. Blood work ordered depends on the particular concern but could include a complete blood count (CBC), dihydroepiandrosterone sulfate, serum testosterone (bioavailable), 17-OH progesterone, HbA1c, lipids, dexamethasone suppression test, luteinizing hormone, and follicle stimulating hormone.[6,7,9]

## PSYCHOLOGICAL IMPACT

9. *Psychological impact of acne:* The impact of acne can be significant and does not depend on the severity of the condition. Acne can produce a negative body image; decrease self-esteem and self-confidence; and cause anxiety, depression, suicidal ideation, psychosomatic symptoms, shame, embarrassment, social inhibition, and unemployment.[9,10] The impact may be greater in women than in men.[9] It is important to question patients about the psychological impact of acne, as they may not spontaneously mention symptoms.[10]

10. Numerous acne-specific measures of the psychological and social impact of acne exist, but several are long and may be difficult to use routinely in a primary care setting.[11] The CADI contains five items and was designed for use in teenagers and young adults (Appendix 1). The maximum score is 15, with higher scores linked to greater impact of acne.[12] Additional information about the CADI is available at http://sites.cardiff.ac.uk/dermatology/quality-of-life/cardiff-acne-disability-index-cadi/. Practitioners may choose to assess the psychological impact of acne in their patients less formally, by acknowleging that acne can be socially and psychologically difficult and asking some simple questions about the impact of acne on the patient.

> ***Practice Tip:***
> Occasionally an adolescent with significant acne involvement may present for a reason unrelated to acne. A nonjudgemental question may help your adolescent patients open up about their concerns. Some potential questions are:
> - Would you like some help with your skin care?
> - Could we talk about your skin care for acne?
> - Would you like to book a follow-up appointment to discuss treatment to help you with your skin?

## ADHERENCE AND EDUCATION

11. *Adherence:* A systematic review of randomized controlled trials focusing on adherence to acne medication found an oral therapy adherence rate of 76.3% and a topical treatment adherence rate of 75.8%.[13] A systematic review of studies of adherence to acne therapy found that the top reasons for lack of adherence were the occurrence of side effects and young patient age. The next most important reason was forgetfulness.[13] Other factors that can negatively influence adherence include need for daily treatment for a prolonged time,[14] male sex, smoking, use of alcohol, lack



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of family or social support, poor quality of life, and psychiatric morbidity.[14] It is important to evaluate patients for depression, as depression is a modifiable factor affecting adherence.[15]

12. A general strategy to encourage adherence recommends the following approach:[15]
    a) *Assess the patient's readiness to commit to a long-term treatment course:* Ensure the patient understands the time and commitment to medication use required for improvement.
    b) *Provide patient counselling:* Educate about the importance of adherence, proper medication use, potential side effects, and other possible issues.
    c) *Promote a therapeutic alliance:* Patient involvement in topical formulation choice can improve adherence.
    d) *Use adherence tools:* Patient diaries and integration of medication application into daily routines, such as toothbrushing, can reinforce adherence.
    e) *Prescribe a simple, effective, well-tolerated regimen.*
    f) *Use combination acne products for once-daily application.*

13. Specific strategies to improve adherence in acne treatment are the following:
    a) *Patient education:* Patients often have misconceptions about acne and unrealistic treatment expectations.[14] It is important for patients to understand that therapies may take weeks to months for full effect and that acne may worsen before it improves, especially with some topical treatments.[10] A sample patient handout is included in this module. Unbiased, accurate patient information is available from the following sources:
        - Evans Health Lab at www.evanshealthlab.com: Easy-to-understand patient education whiteboard video on acne and stepwise treatment.
        - Canadian Dermatology Association at http://www.dermatology.ca/wp-content/uploads/2012/01/Adult-Acne2009EN.pdf (adult acne) and http://www.dermatology.ca/wp-content/uploads/2012/01/Teen-Acne2009EN.pdf (teen acne).
        - American Academy of Family Physicians at http://familydoctor.org/familydoctor/en/diseases-conditions/acne.printerview.all.html.
        - Mayo Clinic at http://www.mayoclinic.org/diseases-conditions/acne/basics/definition/con-20020580.
    b) *Patient support:* Patient counselling and support are essential elements of an acne management strategy and may improve adherence.[10] Improvement in acne can promote adherence, but physician support, for example with close follow-up, may be needed until such improvement occurs.[14]
    c) *Tailored treatment regimens:* Simple-to-follow treatment regimens individualized to the patient's skin type and sensitivity can minimize side effects, therefore increasing likelihood of sustained treatment (Table 1).

> ***Practice Tip*:** Assessment of response can be facilitated by having the patient take a photo ("selfie") initially and then at regular intervals. Evaluating progress this way can also encourage the patient to persist with therapy until a full response is seen.

## MANAGEMENT

14. *Hygiene:* Mild acne may benefit from the use of antibacterial cleansers, but excessive washing stimulates oil production.[10] Generally, non-soap cleansers are better tolerated,especially when using topical acne treatment.

15. *Approach to management:* Few guidelines for the management of acne are evidence based, due to the paucity of evidence. Basic skin care recommendations (Patient Handout) may help with acne management and reduce skin irritation associated with topical treatments. Assessing the severity of the acne and whether it is inflammatory or noninflammatory (Appendix 2) is a critical first step, as it enables the clinician to choose the appropriate initial treatment plan.[10] Available treatment options are summarized in Appendix 3 (topicals) and Appendix 4 (orals).

**Table 1. Practice Tips for Prescribing Topical Therapy[16]**

| Prescribing Point | Practice Tip |
|---|---|
| Tailor topical vehicle to patient's skin type | Oily skin: solution or gel.<br><br>Dry or sensitive skin: cream, lotion, or aqueous gel. |
| Minimize irritation with topical retinoids and benzoyl peroxide | Choose the least irritating product available: adapalene is better tolerated than other available retinoids.[17]<br><br>Use non-soap cleansers.<br><br>Start with lowest concentration.<br><br>Use alternate-day dosing initially and increase to nightly use as tolerated.<br><br>After 4 to 6 weeks, introduce higher concentration if tolerated.<br><br>Add a noncomedogenic emollient to reduce irritation.<br><br>Avoid benzoyl peroxide concentrations > 5%, as they are more irritating without increasing efficacy. |
| Avoid antibiotic resistance | Prescribe topical antibiotics for a short time (8–12 weeks) and in combination with benzoyl peroxide. |
| Remind patients | Apply medication to all affected areas, not just the lesions.<br><br>Use sunscreen daily, as many acne medications are associated with photosensitivity (to be applied at least 15 minutes after the medicated topical treatment). |

16. *Maintenance therapy:* Once inflammatory lesions are controlled, discontinue topical and oral antibiotics. Continued treatment with a topical retinoid is recommended to prevent formation of new microcomedones. If antimicrobial therapy is still needed, a combination of benzoyl peroxide and a retinoid can be used.[18]

### Isotretinoin

17. *Isotretinoin (Accutane®, Clarus®, Epuris®) dosing:* The most effective acne medication for severe acne, oral isotretinoin, produces cure in about 85% of cases, especially at the high end of the total dose range (120–150 mg/kg over 5–6 months).[5,6,10] A starting dose ≤ 0.5 mg/kg/day can minimize flareups (see Appendix 4). Moderate acne may respond to 0.3 mg/kg/day with fewer adverse effects.

18. *Isotretinoin adverse effects:*[5,17,19]
    a) Common side effects include skin and mucous membrane dryness and irritation (cheilitis [96%], facial erythema/dermatitis [55%], dry nose [51%], desquamation [50%], pruritus [30%], dry skin [22%], conjunctivitis [19%], alopecia [13%], irritation of the eyes [11%], rash [< 10%]), gastrointestinal upset (5%), and headaches (5%).

    b) Serious but uncommon side effects are depression and suicidal ideation (causal relation not established), dyslipidemia (increased cholesterol [7%], decreased high-density lipoprotein cholesterol [15%], increased triglycerides [25%]), pancreatitis and hepatitis (several cases reported), blood dyscrasias, and hyperostosis (occasional reports, primarily high-dose, long-term therapy). Isotretinion is severely teratogenic (> 25% risk of serious birth defects).

    **Note:** Statistics are taken from the Accutane product monograph.

19. *Isotretinoin prescribing and monitoring:* Patient consent before treatment, use of two effective methods of contraception (for women), and monthly follow-up to monitor for the development of side effects and toxicities are required. Required monitoring for isotretinoin includes the following:
    a) *Pregnancy tests:* Two before therapy, monthly during treatment, and one month after completing treatment.
    b) *Fasting blood lipids:* Before treatment, monthly until lipid response is established, and at the end of treatment.
    c) *CBC and differential:* Before treatment, at one month, and then as clinically indicated.



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d) *Liver function:* Before treatment, at one month, and then at least every three months, unless more frequent monitoring is clinically indicated.
e) *Blood glucose levels:* Before treatment, at one month, and then as clinically indicated.

Details are found in the product monograph, which also contains comprehensive patient information about use of isotretinoin. Comprehensive checklists for monitoring and patient contracts for use of this medication are available in a kit which can be requested from the manufacturer of Accutane.

## Acne in Adult Women

20. *Acne in adult women:* Acne in women may persist after adolescence (80% of cases), or it may develop after 25 years of age (20% of cases), in which case it is considered late-onset acne. Women may have premenstrual acne flares or experience recurrent symptoms in the perimenopausal years.[20] Late-onset acne may require specific investigation, as it may be associated with hyperandrogenism, due to ovarian, adrenal, or androgenic metabolism alterations, especially PCOS.[7,9] PCOS or late-onset adrenal hyperplasia may be present in 10% of women with late-onset acne.[21]

21. *Management of acne in adult women:* Adult-onset acne may be treatment resistant, especially in women > 25 years of age.[8,9]
    a) Hormonal agents, including estrogen-containing oral contraceptives, are effective as second-line therapy in women, whether or not underlying hormonal abnormalities are present. A recent Cochrane review included a meta-analysis of the effectiveness of combined oral contraceptives in acne compared with placebo. Combined oral contraceptives reduced lesion counts, with inflammatory lesions demonstrating greater improvement than noninflammatory lesions; decreased the grade of acne severity; and improved patients' acne self-assessment. Limited clinical data demonstrated that products with chlormadinone acetate or cyproterone acetate (Diane-35) provided greater improvement than those containing levonorgestrel.[22] Diane-35 is indicated for the treatment of severe acne with accompanying symptoms of androgenization after topical therapy or systemic antibiotic treatments have failed; this treatment should be discontinued when signs of acne have cleared due to the risk of thrombus formation.
    b) Limited evidence supports the efficacy of spironolactone (50–200 mg/day). Topical combinations or oral antibiotics may be more effective than this anti-androgen agent.[19] Side effects of spironolactone include menorrhagia, lethargy, gastrointestinal upset, hyperkalemia, and teratogenicity, in particular feminization of a male fetus.[21] Electrolytes, blood urea nitrogen, and creatinine should be measured before therapy, after one week, and after dose increases.[20]

22. *Acne in pregnancy:*
    a) Some experts recommend that topical and systemic treatment be avoided during the first trimester if possible. Alternatively, therapy with the best evidence for safety during pregnancy should be used. Topical agents with adequate safety data in pregnancy include azelaic acid, metronidazole, erythromycin, clindamycin, and glycolic acid. First-line oral agents in pregnancy are penicllins and cephalosporins. Agents not to be used during pregnancy include topical retinoids, oral tetracyclines, isotretinoin, oral contraceptives, and spironolactone.[8]
    b) The Motherisk website (http://www.motherisk.org/prof/updatesDetail.jsp?content_id=946) indicates that topical therapies, with the exception of hydroquinone (high absorption) and tretinion (absorption controversial) act locally and are not expected to increase risk to the fetus.

## Acne in Skin of Colour

23. *Acne in skin of colour:* The most important consideration in selecting treatment is the risk of PIH in patients with skin of colour. Treatment should be aggressive but not irritating (See Table 1), and early follow-up is advised.[23]
    a) *Topical retinoids:* First-line choice for patients with skin of colour as they treat both acne and hyperpigmentation.[16,23]
    b) *Azelaic acid (Finacea®)*: This very well-tolerated topical choice for patients with skin of colour may also reduce PIH; it is beneficial in mild inflammatory and comedonal acne.[6] In Canada, azelaic acid is indicated for the treatment of acne rosacea.
    c) *Other topical therapies:* Benzoyl peroxide and antibiotics may also be useful.[16]
    d) *Oral agents:* It is important to have a lower threshold for using oral agents to minimize PIH.[16]
    e) *Procedural therapies:* Comedone extraction, intralesional corticosteroid injection, and superficial chemical peels may be useful adjunctive therapies in expert hands.[16,23]



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24. *Management of postinflammatory hyperpigmentation (PIH):* PIH prevention relies on early use of effective treatment, anti-inflammatory therapy, and regular use of sunscreen. Effective treatments for PIH include topical retinoids and azeleic acid at the same dosing as for acne. Another option is 2% or 4% hydroquinone cream (Lustra®), which is available over the counter and should be applied twice daily for up to six months.[16] The combination of hydroquinone with a daily retinoid and a mid-potency corticosteroid (twice daily for two weeks and then only on weekends) may be more effective than hydroquinone alone.[23] Chemical peels, microdermabrasion, and laser therapy are other possible treatments.[16] However, such treatments fall into the realm of specialist care, as they can sometimes lead to further pigmentary disturbances.

25. *Management of keloid scarring:* Early therapy produces the best outcomes, and combination therapy is often used. Intralesional triamcinolone (Kenalog®) every four to eight weeks is first-line therapy, with lower concentrations (10 mg/mL) used for the first injection and titrated based on response. It is important to assess for adverse effects, such as atrophy, hypopigmentation, striae, and telangiectasis before each injection. Other possible treatment options that could be offered under the care of a specialist include interferon, fluorouracil, bleomycin, surgical excision, laser therapy, radiation, and cryotherapy.[24]

**THE BOTTOM LINE**

- Little evidence is available to guide development of acne management strategies.
- Effective management of acne entails developing an individually tailored treatment plan based on an asssessment of acne severity and the presence or absence of inflammatory lesions.
- Patient education and counselling are essential to enhance adherence to long-term acne management.

## CASE COMMENTARIES

### Case 1: Hannah, female, age 16

***Although typical adolescent acne is the most likely diagnosis for Hannah, what else would you like to know?***

It is important to start with a thorough history and physical examination (appropriate to the history) to ensure there are no secondary causes of acne and to determine the acne severity and grade (Info points 6 and 7). Signs and symptoms of hyperandrogenism should lead you to consider hormonal etiologies and order appropriate blood work (Info point 8). Relevant symptoms include irregular menses; a deepened voice; abnormal hair growth on the face, chin, chest, or perineal area, or hair loss on the scalp; and signs on physical examination include hirsutism, clitoromegaly, and male-pattern balding. It is important to know if she is sexually active, as some acne medications are not considered safe in pregnancy (Info point 22). It is also useful to ask about any medications she might be taking that can cause acne, as well as to obtain a history of the products she has used previously or is currently using (Info point 6). Lastly, assessing her level of psychological distress, either using a questionnaire or more informally, is relevant (Info points 9, 10; Appendix 1).

Identification and documentation of the lesion types (comedones, papules, pustules, and nodules), distribution (face, chest, and back), and presence or absence of scarring and PIH determine the grade of her acne and allow you to establish the treatment approach (Info point 15).

### Part Two

***How would you approach management/treatment?***

As Hannah has mild papulopustular acne, it is reasonable to start with topical treatment only (Appendices 2, 3). The first step in treatment is to educate Hannah about acne, dispelling common misconceptions she may hold; discussing anticipated treatment response time, which for most medications is 8 to 12 weeks; and explaining the potential for worsening of her acne before improvement (Info points 12, 13). Taking the time for this step may help improve adherence to the medications you prescribe (Info point 12).

Topical treatment could start with a retinoid and a benzoyl peroxide, with the addition of a topical antibiotic, if she begins to develop additional inflammatory pustules (Appendix 3). As previous treatment significantly irritated her skin, it is important to minimize side effects using specific strategies to improve tolerability, such as initiating treatment with a lower-strength

product and a reduced application frequency (Table 1), as well as using a gentle non-soap cleanser. Based on her moderate score on the CADI and her previous adherence issues, you may want to arrange close follow-up (e.g., in four weeks) to ensure her adherence to treatment and assess her psychological state (Info point 13b).

### Part Three

***What treatment options would you now consider?***

The appearance of her skin indicates that Hannah now has moderate-to-severe acne (Appendix 2). Addition of an oral antibiotic, such as doxycycline, to topical therapy is an appropriate treatment approach (Appendix 4). To prevent resistance, it is recommended that oral antibiotic therapy be limited to a two- to four-month course and followed by maintenance topical treatment (Appendix 4). If she has become sexually active, it is important to review her contraceptive use, as some oral antibiotics are potentially teratogenic (Info point 22). An oral contraceptive for both acne treatment and birth control is another option (Appendix 4). Reassessment of the psychological impact of her acne is required to determine if she requires any treatment to help her deal with it (Info point 10).

## Case 2: Melissa, female, age 48

***What else would you want to know before beginning treatment?***

It is important for the history to identify signs and symptoms of hormonal imbalance and possible testosterone exposure, such as a partner using topical therapy, and ask about perimenopausal symptoms (Info point 6). If there are additional signs and symptoms suggestive of a hormonal etiology, then appropriate blood work should be ordered (Info point 8). It would also be useful to ask about past and current prescription and over-the-counter skin treatments and response to these agents (Info point 6). Other potential causes of acne-like lesions, such as rosacea and perioral dermatitis, should also be considered (Info point 5). A thorough physical examination is essential (Info point 7).

### Part Two

***What treatment would you recommend?***

Based on the distribution and types of lesions, Melissa's acne is moderate to severe (Appendix 2). The presence of significant psychological distress associated with the acne would also factor into a decision to start with oral therapy (Info point 9, Appendix 4). An antibiotic, such as doxycycline, would be appropriate, together with a topical regimen that included benzoyl peroxide and a retinoid (Appendix 2). An oral contraceptive is another option (Info point 21), if she has no contraindications (Appendix 4).

***What would be your follow-up plan for Melissa?***

It would be important to follow up after about two months to assess her treatment response (Appendix 4). Earlier follow-up is appropriate if you are concerned about her mental health (Info point 13). If a good response to the oral antibiotic is seen, then you may wish to consider stopping the oral antibiotic at about four months to help prevent development of antibiotic resistance, and continue with maintenance topical therapy (Appendix 4).

## Case 3: Marcus, male, age 16

***What treatment approach would you take?***

Although he has only moderate papulopustular acne, the presence of PIH and scarring dictates a more aggressive approach to treatment, starting with a first-line oral antibiotic combined with topical therapy to prevent further permanent skin damage (Info point 23). A topical retinoid and an oral antibiotic for four months is an appropriate choice in this situation (Appendix 4). Benzoyl peroxide or azelaic acid could also be added. As people with skin of colour are predisposed to scarring and PIH, it is particularly important to minimize any irritation associated with topical treatment (Table 1). As acne scarring is already present, you could also provide Marcus with information on isotretinoin as the next option if the oral antibiotic proves ineffective (Info point 17–19). Early follow-up is important to assess and adjust the treatment plan to minimize additional scarring (Info point 23).

## Part Two

***How would you initiate and monitor Marcus' use of isotretinoin?***

It is essential to educate Marcus about isotretinoin and potential side effects and toxicities, including gastrointestinal side effects, musculoskeletal problems, ocular problems, and depression (Info point 18). Specific blood work is required to monitor isotretinoin therapy (Info point 19). Marcus must also agree to monthly follow-up to monitor for the development of side effects and toxicities, including depression (Info point 19).

**Practice Tip:** Depending on the wait time for a dermatology consultation, you may wish to initiate a dermatologist referral for him to discuss management of his PIH and keloid scarring.

## Part Three

***What would you recommend to Marcus?***

You explain to Marcus that various treatments are available to manage these problems. For keloids, intralesional triamcinolone injection could be done in the office (Info point 24). Topical options demonstrated effective for PIH are retinoid creams; azelaic acid; 2% or 4% hydroquinone cream, which is available over the counter; and glycolic acid (Info point 24). The use of sunscreen is important to prevent further hyperpigmentation (Info point 24). More invasive approaches to scarring and PIH, including microdermabrasion, use of fillers, chemical peels, or laser resurfacing, should be discussed with a dermatologist as they have the potential to lead to further pigmentary disturbances. A consultation with a dermatologist can help determine the best way to manage PIH and keloid scarring.

*We always welcome your input. If you would like to provide feedback on this module, the following link will take you to an electronic survey:* **http://members.fmpe.org/modulefeedback**

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*Web-based resources cited within the module were active as of January 2016.*

**You can access this module and all its appendices online. Just go to: https://members.fmpe.org/**

**LEVELS OF EVIDENCE**

| Evidence Level | Type of Evidence Included |
|---|---|
| **High** | • Systematic reviews/meta-analyses that include a wide range of well-designed studies (few limitations/risk of bias, directly applicable to target population); summary estimate has a narrow confidence interval.<br>• Large, well designed RCTs.<br>Study conclusions are unlikely to be strongly affected by information from future studies. |
| **Moderate** | • Systematic reviews/meta-analyses of studies with more limitations/risk of bias (less well designed RCTs, cohort, case-control studies), or when the summary estimate has a wide confidence interval.<br>• Single, moderate-sized, well-designed RCTs.<br>• Well-designed, consistent, controlled but not randomized trials.<br>• Large cohort studies.<br>Study conclusions could change with additional information from future studies. |
| **Low** | • Small RCTs with a high risk of bias.<br>• Controlled or cohort studies with significant limitations/risk of bias or significant variation between study results.<br>Evidence from well-designed studies in representative populations is lacking or insufficient. |
| **Very Low** | • Expert opinion<br>• Individual case reports or series |

**Sources:**

**1)** Scottish Intercollegiate Guidelines Network-(SIGN) http://www.sign.ac.uk/guidelines/fulltext/50/annexoldb.html

**2)** U.S. Preventive Services Task Force Grade Definitions. May 2008. http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm

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**APPENDIX 1. The Cardiff Acne Disability Index**

| | | |
|---|---|---|
| 1. As a result of having acne, during the last month have you been aggressive, frustrated or embarrassed? | ☐<br>☐<br>☐<br>☐ | a) Very much indeed<br>b) A lot<br>c) A little<br>d) Not at all |
| 2. Do you think that having acne during the last month interfered with your daily social life, social events or relationships with members of the opposite sex? | ☐<br>☐<br>☐<br>☐ | a) Severely, affecting all activities<br>b) Moderately, in most activities<br>c) Occasionally or in only some activities<br>d) Not at all |
| 3. During the last month have you avoided public changing facilities or wearing swimming costumes because of your acne? | ☐<br>☐<br>☐<br>☐ | (a) All of the time<br>(b) Most of the time<br>(c) Occasionally<br>(d) Not at all |
| 4. How would you describe your feelings about the appearance of your skin over the last month? | ☐<br>☐<br>☐<br>☐ | (a) Very depressed and miserable<br>(b) Usually concerned<br>(c) Occasionally concerned<br>(d) Not bothered |
| 5. Please indicate how bad you think your acne is now: | ☐<br>☐<br>☐<br>☐ | (a) The worst it could possibly be<br>(b) A major problem<br>(c) A minor problem<br>(d) Not a problem |



The scoring of each answer is as follows:
(a) 3
(b) 2
(c) 1
(d) 0

The CADI score is calculated by summing the score of each question resulting in a possible maximum of 15 and a minimum of 0. The higher the score, the more the quality of life is impaired.

**APPENDIX 2. Initial Management of Acne**

| Acne Severity | Distribution and Scarring | Treatment Options | |
|---|---|---|---|
| | | First Line | Second Line |
| **Mild**<br>***Comedonal***: Few to several comedones | Acne with no scarring, less than one-quarter of the face involved | Topical retinoid | Alternative topical retinoid<br>Salicylic acid wash |
| ***Papular/pustular***: Few scattered papules | | Topical retinoid<br>Topical antimicrobial: benzoyl peroxide, clindamycin, erythromycin<br>Combination products | Alternative topical retinoid + alternative topical antimicrobial |
| **Moderate**<br><br>***Papular/pustular***: Many papules and pustules with variable comedones | Acne across about half of the face with little scarring and involvement of the chest and back | Oral antibiotics: tetracyclines, erythromycin (increased likelihood of resistance)<br>Topical retinoid ± benzoyl peroxide<br>Oral contraceptives | Alternative oral antibiotic<br>Alternative topical retinoid<br>Benzoyl peroxide |
| ***Nodular***: Few nodules | | Oral antibiotic<br>Topical retinoid ± benzoyl peroxide | Oral isotretinoin<br>Alternative oral antibiotic<br>Alternative topical retinoid<br>Benzoyl peroxide |
| **Severe**<br>Numerous papules, pustules, and nodules with variable comedones, sinus tracts and/or cysts | Acne across face, back, and/or chest with moderate-to-severe scarring, hypertrophic and/or deep, possibly with drainage, pain, and hemorrhage of lesions | Oral isotretinoin | High-dose oral antibiotic<br>Topical retinoid (also maintenance)<br>Benzoyl peroxide |

*In adult women, oral contraceptives or androgen receptor blockers may also be used.

**Sources:** Basak SA, Zaenglein AL. Acne and its management. *Pediatrics in review / American Academy of Pediatrics.* 2013;34:479-97; Laubscher T, Regier L, Jin M, Jensen B. Taking the stress out of acne management. *Canadian family physician Medecin de famille canadien.* 2009;55:266-9

## APPENDIX 3. Summary of Topical Acne Therapies

| Agent | Acne Severity | Response | Commentary | Dosing | Cost (package) |
|---|---|---|---|---|---|
| ***Benzoyl peroxide*** aqueous 2.5%, 4%, 5% (all OTC), 8%, 10% (Rx)* | Monotherapy: Mild-moderate acne<br>Combination: moderate-severe acne | 2–4 weeks: possible worsening<br>8–12 weeks for large improvement | Bactericidal, keratolytic<br>Avoid concentrations > 5% (more irritating but not more effective)<br>Help prevent antibiotic resistance<br>May bleach hair and clothes | Can be irritating (see Info point 16)<br>Start with 2.5%, go to 5% if ineffective<br>Optimal dosage: applied to affected area qhs or bid | OTC: $10–$15<br>Rx: $15–$25 |
| ***Retinoids***<br>Tretinoin: 0.01%, 0.025%, 0.04% 0.05%<br>Adapalene: 0.1% cream or gel, 0.3% gel<br>Tazarotene: 0.05% 0.1% cream, gel | Mild-moderate comedonal acne | 2–4 weeks: possible worsening<br>~12 weeks for maximum response | Inhibits comedone formation & promotes comedonal drainage, decreases inflammation & hyperkeratinization (helpful for PIH)<br>Adapalene least irritating<br>Concomitant sunscreen needed<br>Preferred agent for maintenance & PIH | Irritating and drying, peaks at two weeks (see Info point 16)<br>Optimal treatment dosage: thin layer applied qhs after washing<br>Use less frequently for maintenance | Tretinoin: $19, $24<br>Adapalene: $87<br>Tazarotene: $55 |
| ***Azelaic acid,*** 20% cream | Mild inflammatory & comedonal acne | Four weeks | Reverses abnormal keratinization, inhibits bacterial growth, lightens PIH | Once or twice daily, very well tolerated | $100 (50 g) |
| ***Dapsone 5% gel*** | Mild-moderate inflammatory & inflammatory acne | Evaluate at 12 weeks | May be more effective for women<br>Option for patients with sensitive skin who cannot tolerate other topicals | Apply bid<br>May cause erythema and dryness<br>May cause yellow-orange skin discoloration if combined with benzoyl peroxide (small number of patients) | $257 (30 g) |
| ***Antibiotics***<br>Clindamycin 1% solution | Mild-moderate inflammatory acne | 8–12 weeks for large improvement | Bactericidal<br>Use with benzoyl peroxide to prevent resistance<br>Most effective combined with benzoyl peroxide or retinoid | Use clindamycin bid<br>Discontinue when inflammation subsides | Clindamycin: $26, $58 |
| ***Combinations***<br>Benzamycin (BPO 5% + ERY)[1], BenzaClin (BPO 5% + CLI 1% gel)[2], Clindoxyl (BPO 5% + CLI 1% gel)[2], Stievamycin (TRE+ER)[3], Biacna (CLI + TRE)[4]<br>Tactupump, Clindoxyl ADV | Mild-moderate inflammatory acne for more intensive therapy | 2–4 weeks for noted improvement<br>8–10 weeks for maximal result | Convenience of combination product | Step down to retinoid or benzoyl peroxide when inflammation subsides<br>Stievamycin, Biacna: qhs<br>Benzamycin, BenzaClin, Clindoxyl: qhs or bid | Benzamycin $67<br>BenzaClin $60<br>Clindoxyl $55<br>Stievamycin $37<br>Biacna $84 |

PIH: Postinflammatory hyperpigmentation *Other formulations and products are available, including soaps and washes

[1]Benzoyl peroxide 5%, erythromycin 3% gel; [2]Benzoyl peroxide 5%, clindamycin 1% gel; [3]Tretinoin (0.01% in mild, 0.025% in regular, and 0.05% in forte), erythromycin 4% gel; [4]Tretinoin 0.025%, clindamycin 1%

**Source:** Acne pharmacotherapy: Comparison chart. RxFiles. Available at http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-acne.pdf. Accessed January 29, 2016. Laubscher T, Regier L, Jin M, Jensen B. Taking the stress out of acne management. *Canadian family physician Medecin de famille canadien.* 2009;55:266-9. Basak SA, Zaenglein AL. Acne and its management. *Pediatrics in review / American Academy of Pediatrics.* 2013;34:479-97. Radley K, Tucker R. Dapsone in the Management of Acne Vulgaris J Derm Nurs Assoc. 2013;5(6):316–9. Tanghetti E, Dhawan S, Green L, et al. Clinical evidence for the role of a topical anti-inflammatory agent in comedonal acne: findings from a randomized study of dapsone gel 5% in combination with tazarotene cream 0.1% in patients with acne vulgaris. J Drugs Dermatol. 2011;10(7):783-92.

**APPENDIX 4. Summary of Oral Acne Therapies**

| Agent | Acne Severity | Response | Commentary | Dosing | Cost (90 days) |
|---|---|---|---|---|---|
| ***Antibiotics***<br>Tetracycline 250 mg caps<br>Doxycycline 100 mg caps/tab<br>Minocycline 50, 100 mg caps<br>Erythromycin 250, 333, 500 mg | Moderate-severe acne if topicals fail<br>Moderate acne if tendency to scarring or PIH | 8–12 weeks for maximal response<br>Pulse 2–4 months | Combine with benzoyl peroxide to decrease resistance<br>Follow up with topical retinoid+ benzoyl peroxide<br>Doxycycline well tolerated<br>Serious potential side effects with minocycline* | Tetracycline: 500 mg bid then 250–500 mg daily if maintenance<br>Doxycycline: 100 mg daily<br>Minocycline: 100 mg daily, then 50 mg daily if maintenance<br>Erythromycin: 500 mg bid then 250–500 mg daily if maintenance | Tetracycline $18–$36<br>Doxycycline $68<br>Minocycline $40–$69<br>Erythromycin $28–$82 |
| ***Combination oral contraceptives***<br>Tri-Cyclen, Alesse, Aviane, Yasmin<br>Diane-35/ Cyestra-35: acne indication only | First line if also for contraception<br>Moderate-severe acne + seborrhea ± hirsutism ± androgenic alopecia ± late-onset acne | 3–6 months for optimal response | Antiandrogen effect<br>Caution if thrombosis risk, smoking, migraine with aura<br>Relapse common if discontinued<br>Progestin-only contraceptives may worsen acne | Use daily for 21 days then seven days off per cycle | Tri-Cyclen $71<br>Alesse, Aviane $59, $42<br>Yasmin $50<br>Diane-35 $109<br>Cyestra-35 $92 |
| Spironolactone 25, 100 mg tabs | Late-onset acne when other treatments fail | 2–3 months for maximum response | Monitoring: electrolytes (potassium) and renal function | 50 or 100 mg daily | $31–$34 |
| Isotretinoin 10, 40 mg caps | Severe nodulocystic acne, scarring, failure of oral antibiotics and/or oral contraceptives | Flare first two months (6%)<br>2–3 months for optimal response<br>3–4 months for complete suppression | Most effective for moderate-to-severe inflammatory acne<br>See Info points 18 and 19 for adverse events, monitoring, and contraceptive requirements<br>Teratogenic | Limit one month supply + monthly monitoring<br>Optimal cumulative dose 120–150 mg/kg<br>0.5 mg/kg divided daily; bid x 4 weeks; then 1 mg/kg/day x 3–7 months | $469/5 months (40 mg caps)<br>$890/5 months (10 mg caps) |

PIH: Postinflammatory hyperpigmentation
*Photosensitivity and rare reports of autoimmune hepatitis, lupus-like syndrome, and grey discolouration of sclera and mucous membranes

**Source:** Acne pharmacotherapy: Comparison chart. RxFiles. Available at http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-acne.pdf. Accessed January 29, 2016.
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**PATIENT HANDOUT: Please feel free to copy this page.**

# ACNE

### What causes acne?

Acne is a skin disease that is very common in both teenagers and adults. When oil production of tiny glands (found mostly on the face and scalp) increases due to hormonal changes, the glands can become plugged, inflamed, or infected. This can result in blackheads, whiteheads, pimples, or cysts.

### What doesn't cause acne?

Acne is **not** caused by diet, poor hygiene, or infection from contact with someone who has acne. Even though bacteria can infect plugged oil glands, bacteria do not cause acne, and acne is not contagious.

### What can worsen acne?

- Hair or skin products, such as moisturizers or foundation, that clog pores.
- Sweating can worsen acne in some people.
- Pressure from tight clothing, such as bra straps or chin straps, and frequent hand contact, such as resting your face in your hands, can worsen acne at the point of contact.
- Overwashing skin (more than twice daily) or using scrubs, harsh cleansers, or toners with alcohol.
- Some medications, including oral corticosteroids, oral contraceptives containing only progesterone, and anticonvulsants. Ask your healthcare provider about any medications you may be using.
- Menstrual cycles: some women and girls find acne worsens before their period.
- Picking, squeezing, or popping pimples can worsen acne, spread infection, and cause scarring.
- Exposure to sun or tanning beds.
- Stress can affect hormones and indirectly worsen acne.

### What can I do to help my acne?

- Wash your face once or (at the most) twice daily with a gentle or soapless cleanser.
- Wash makeup brushes with antimicrobial soap to eliminate bacteria on them.
- Wash pillowcases and sheets often to remove oil that has been absorbed from your skin.
- Give your skin a break from makeup at least once a week.
- Use only noncomedogenic skin products and oil-free makeup. These products do not promote clogging of pores and are usually labelled "noncomedogenic."
- Shave lightly (once only) in the direction of hair growth.

### What do I need to know about my acne treatment?

- Learn about acne so you can be a partner with your doctor in your treatment.
- There are many options for treating acne.
- Treatment takes a stepwise approach that usually starts with topical treatments (creams, gels or lotions).
- Your skin may temporarily get worse before it gets better; it can take six to eight weeks to see the full benefit from some acne treatments.
- Follow the prescription instructions to minimize potential skin irritation from topical treatments.
- For topical treatments, apply a *thin* layer of medication to the entire area, not just individual pimples.
- If you wear makeup, apply your acne medication and let it dry before applying makeup. Use sunscreen, as acne medications can increase sun sensitivity.
- Continue your treatment even after acne has improved to prevent new breakouts.
- If the acne medication is drying your skin, use a prescribed or recommended noncomedogenic moisturizer.

**Sources:** Basak SA, Zaenglein AL. Acne and its management. *Pediatrics in review / American Academy of Pediatrics.* 2013;34:479-97. Teen Acne. Canadian Dermatology Association. Available at http://www.dermatology.ca/wp-content/uploads/2012/01/Teen-Acne2009EN.pdf.