

PedsCases Podcast Scripts

This is a text version of a podcast from PedsCases.com on “Acne.” These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at www.pedsCases.com/podcasts.

Approach to Acne – Part II

Developed by Laura Soong and Dr. Chris Keeling for PedsCases.com.
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Introduction

Welcome back to the second part of our series on Acne in children! My name is Laura Soong, and I am a third year medical student at the University of Alberta. I hope you had the chance to listen to Acne Part I prior to this podcast! In this episode we will be talking about treatment of acne in adolescent patients. Before we get started, I wanted to take a moment to recognize the contributions of Dr. Chris Keeling, Assistant Clinical Professor at the University of Alberta and Community Dermatologist who made sure this Podcast contained accurate and up to date clinical information.

After listening to this podcast, the learner should be able to:

1. Manage acne in adolescent patients based on acne severity.
2. Understand the mechanism of action, side effects, and appropriate use of topical and systemic acne treatments.
3. Demonstrate comfort in monitoring acne treatment and compliance, and recognize when to refer.

Before we begin, let's review a few things...

Remember in Acne Part I, we discussed the four processes that contribute to acne. Can you recall them? The four factors were: abnormal keratinization, increased hormonal stimulation of sebum production, inflammation, and bacteria. Keep those in mind today as we discuss treatment.

We also discussed in Part I the classification of acne severity. If you need to take a moment to review that classification, please do so! Remember that acne can be classified as mild, moderate, or severe and can present with non-inflammatory or inflammatory lesions.

We also, left you with the case of Joshua, a 14-year-old male with severe nodulo-cystic acne. We will return to this case at the end of the podcast.

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Now that we have quickly reviewed that, let's start talking about the real meat and potatoes of today's podcast – how to treat acne!

There are many over the counter and prescription products available for treatment of acne. The key to a successful regimen is to understand the mechanism of action of each product or medication you prescribe as well as their advantages and disadvantages. It is important to know the side effects and contraindications of each treatment so that you can tailor the regimen to your patient, especially if they have other comorbidities, drug allergies, or are taking concurrent medication and are at risk of drug interactions or toxicities.

You can think of acne treatment as a pyramid, with the base being general skin care and topical products, the middle being oral antibiotics and oral contraceptives, and the top of the pyramid being isotretinoin.

Let's start with some basic skin care counseling that is helpful to share with your patients.

Basic Skin Care

It is a long-standing myth that acne is caused by poor hygiene. In fact, too harsh of a cleansing routine can break down the skin barrier, dry out the skin, increase bacterial colonization, cause stinging and burning, and ultimately lead to the formation of more comedones. The goal of washing the face is to gently remove dirt, excess oil that builds up over the day, and makeup, not to scrub the acne away!

It is recommended that patients wash affected areas once to twice daily with a gentle, soap-free, pH neutral cleanser. Cleansers like *Dove*, *Aveeno*, or *Neutrogena* are less irritating than harsher soaps like *Irish Spring* or *Zest*. Alternatively, you can suggest a soap substitute like *Spectro Jel*, *La-Roche*, *Avene*, or *Cetaphil* face washes. It is recommended to avoid cream based cleansers. Counsel patients to avoid granular or abrasive cleansers, antiseptic solutions, and cleansing pads that contain alcohol or acetone, and focus on choosing milder cleansing agents.

If patients prefer to have a medicated face wash, a formulation that contains benzoyl peroxide is preferable, as other antibacterials have not been shown to be helpful and are often irritating to the skin. Salicylic acid can also be a helpful adjunct for mild comedonal acne and is a common ingredient in many over-the-counter formulations.

Toner can be helpful to remove residual oil, dirt, and makeup after using a cleanser. It is not a necessary component of daily skin care, but some patients like to use it. Just make sure it is not causing any excess irritation or dryness, especially if they are using other prescription acne medications.

Moisturizer is a helpful component of daily skin care. If they are using a moisturizer, encourage use of an oil free brand that contains SPF 15 or higher – consider it an opportunity to promote sun protection! Some acne medications can cause photosensitivity, so a moisturizer with SPF protection is especially useful.

Patients will often have questions about foundation or concealer to minimize the appearance of their acne. While some cosmetics can worsen acne, it is important to counsel patient that they can still use concealer. Encourage them to use a product that is noncomedogenic and oil free, as this can improve their quality of life and will not exacerbate their acne.

The Canadian Dermatology Association has a list of recognized products that may be helpful for patients to refer to. I have provided a link to their website in this podcast script. <http://www.dermatology.ca/programs-resources/programs/recognized-products/#/>

Topical Medications

Now let's discuss topical medications.

In general, when choosing the vehicle for topical therapies, solutions or gels are generally better for oily skin, while creams or lotions are better for dry skin.

Benzoyl peroxide is a first line option for mild to moderate Acne vulgaris. Some brands that you might recognize are *Benzagel*, *Clearasil BP*, *Panoxyl* gel, and *Proactiv*. The majority of benzoyl peroxide products can be purchased over the counter without a prescription.

Benzoyl peroxide works as a keratolytic, comedolytic, and anti-inflammatory agent. It is also bactericidal against *P. Acnes*. It therefore is helpful in the treatment of both comedonal and inflammatory acne lesions.

It is available over the counter in concentrations of 2.5 to 10%. It is recommended to start with the lowest concentration to minimize skin irritation, and to increase as tolerated. Some resources suggest that concentrations of 2.5-5% are as effective as 10% and cause less irritation. Instruct patients to apply it to the face at night. At first, they should wash it off after 1-2 hours, however if this is well tolerated then they can gradually increase the contact time to then leaving the gel on overnight. If this is tolerated, patients can increase to applying it in the morning as well. It should be applied to clean and dry skin 15-20 minutes after washing. An adequate trial is generally considered 8-10 weeks of consistent, appropriate use. It is important to warn patients that their skin may worsen over the first 2 weeks of use before it gets better.

Side effects include irritation in the form of erythema, peeling, and dryness and are proportional to the concentration used and length of contact time, though irritation tends

to decrease over time. Benzoyl peroxide is also photosensitizing to the skin, so remind your patients to wear their sunscreen during the day! In 2.5% of cases, patients can develop allergic contact dermatitis to benzoyl peroxide. If this occurs, it should be discontinued. It is important to let patients know that it can bleach clothing, bedding, towels, and hair – so make sure they use old sheets and pyjamas! They may also avoid using it in the morning to prevent staining of clothing throughout the day.

Another option is to prescribe a combination product of benzoyl peroxide + antibiotic, particularly if the patient has inflammatory lesions. Clindamycin and erythromycin are typically used in the form of topical antibiotics. They are not recommended to be used as monotherapy due to the slow onset of action and risk of bacterial resistance. Although acne is not an infectious process, the use of antibiotics helps to decrease colonization by *P. acnes* and thus reduce inflammation. *Benzamycin* is a combination of 5% BP and 3% erythromycin. *BenzaClin* or *Clindoxyl* gel are a combination of BP 5% and clindamycin 1%. These products can be applied once to twice daily and the combination of antibiotic and benzoyl peroxide prevents the development of bacterial resistance. Again, they should be used for 8-10 weeks for maximum effect.

The next class of topical medications we will discuss are topical retinoids. Most retinoids are labelled for use in children above the age of 12. Topical retinoids as a class of medication work to decrease abnormal keratinization and the pathological retention keratosis that occurs in the hair follicle. It therefore mitigates the formation of new comedones and inflammatory lesions, and helps to break down microcomedones that have already formed. In addition, they have anti-inflammatory properties and have a synergistic effect with other agents, allowing deeper penetration of topical adjuncts (i.e. Benzoyl peroxide, antibiotics).

Examples of topical retinoids include tretinoin, adapalene and tazarotene.

Topical retinoids are an excellent first choice for comedonal or inflammatory mild to moderate acne. They can be used as monotherapy or in combination with benzoyl peroxide or topical/systemic antibiotics. For mild comedonal acne, a topical retinoid may be the only medication needed. For mild to moderate inflammatory acne, patients may use a topical retinoid at night and benzoyl peroxide + antibiotic in the morning, or a combination product of BP + retinoid each night. Regimens can be tailored for each patient.

The main side effects of topical retinoids are irritation, erythema, and dryness, all of which improve after 2 weeks of use. Tretinoin and adapalene are both Pregnancy Category C (not enough research to confirm whether they are safe), while tazarotene is Category X (contraindicated in pregnancy). Two ways to mitigate skin irritation are to start with a lower concentration and increase the strength of the product as tolerated, or to titrate applications, starting with one application every 2-3 days increasing to once each night over the first 2 weeks. As with benzoyl peroxide, it is important to warn patients their skin may worsen before improvement is seen and to continue using the product if this happens. The product should be applied 30-45 minutes after washing the

face, and they should use only a pea sized amount and spread it evenly over their entire face. Topical retinoids should be used for a minimum of 12 weeks for maximal effect, and should be continued until no new lesions appear.

The final topical medication we will discuss is Azelaic Acid. Azelaic Acid has dual activity in that it prevents abnormal keratinization and is anti-bacterial against *P. Acnes*. It can be used in patients who do not tolerate topical retinoids with mild to moderate acne. In patients with lighter skin, it may be helpful in improving the appearance of post-inflammatory hyperpigmentation caused by previous acne lesions.

Oral Antibiotics

When topical therapy is not sufficient to control the disease process, oral antibiotics are often the next step. Antibiotics work by decreasing the proliferation of *P. Acnes* and decreasing inflammation. First line antibiotics are Doxycycline at 100 mg daily and minocycline at 50-100 mg daily. It is important to note that tetracycline antibiotics are contraindicated in children <9 years of age and in pregnancy due to the risk of irreversible dental staining. For patients with drug allergies or other contraindications, other antibiotics can be used, such as clindamycin, TMP-SMX, cephalexin, or macrolides.

Oral antibiotics are often prescribed in combination with topical therapies to avoid development of resistant *P. Acnes*. One approach is to prescribe an oral antibiotic with benzoyl peroxide and a topical retinoid. Antibiotics should be taken daily for 8-12 weeks and can be discontinued once the acne has been reduced to a level that can be controlled by topical medications. If antibiotics do not work, it may be due to resistant *P. Acnes* or poor adherence.

Doxycycline and minocycline are generally well tolerated. Important side effects to discuss with your patient include gastrointestinal upset, esophagitis, and photosensitivity. To mitigate GI upset, patients can take the medication with food. To prevent pill esophagitis, counsel your patient to take the medication with a full glass of water and stay upright for 30-60 minutes after swallowing the medication. To avoid photosensitive reactions, patients should be counselled on appropriate sun safety and sun protection measures. In approximately 5% of patients, vaginitis or perianal itching secondary to *Candida* infection may occur. Benign intracranial hypertension has also been reported as a rare but concerning side effect.

Doxycycline is generally chosen before minocycline as the latter has been associated with other rare but serious side effects including blue discoloration of skin, teeth, nails, sclera, and mucosa, hypersensitivity reactions, Stevens-Johnson syndrome, lupus like syndrome, autoimmune hepatitis, and serum sickness-like reactions. Minocycline has also been reported to cause more vertigo, dizziness, and headaches.

Oral Contraceptive Pill

We have discussed therapy mainly from the perspective of tackling the therapeutic targets of abnormal keratinization, inflammation, and proliferation of *P. Acnes*, however one therapeutic target we have not yet discussed is excess sebum production. Oral contraceptives offer a therapeutic strategy for female patients to decrease androgen levels, and therefore decrease sebum production. Combined hormonal contraceptives that contain both ethinyl estradiol and a synthetic progestin can be used to decrease androgen levels. Testosterone and other androgens in plasma may be in their free form or bound to sex hormone binding globulin (SHBG). When bound to SHBG, the hormones are inactive. Estrogen essentially increases the level of SHBG, thereby decreasing the level of androgenic activity. Additionally, combined hormonal contraceptives also block ovarian production of androgens. Yasmin, Yaz, Alesse, Diane-35, or Tri-Cyclen would all be suitable options. Counsel patients that it may take 3-6 months to see results. Also, don't forget to review the contraindications and side effects of estrogen-containing oral contraceptives before prescribing them!

Isotretinoin

I think it's safe to say most people have heard of Accutane. The generic name for it is isotretinoin. Some parents may shiver when you say the word, but it's important to reassure them that it is not as awful or dangerous as it has been portrayed in the media. There have been anecdotal reports concerning an association between Accutane and suicide or major depressive disorder, however this claim has largely been disproven. The reports are confounded by isotretinoin generally being given to patients with severe acne who may already be struggling with their mental health prior to starting therapy. Population level studies have not demonstrated an association between isotretinoin and depressive symptoms, although have found that patients with severe acne were more likely to struggle with depression, suicidal ideation, and other mental health issues.

Isotretinoin is a vitamin A metabolite, similar to tretinoin as we talked about earlier, only this medication is taken orally instead. It is indicated for patients with severe acne that is predominantly pustular, cystic, or nodular. It can also be used for patients at risk of scarring from their acne, or who have tried other first line medications with limited success.

Isotretinoin is the only medication that targets all four pathogenic factors of acne. It is comedolytic, anti-inflammatory, decreases *P. Acnes* concentration, and decreases sebum production. It follows a weight based dosing regimen, and is generally prescribed at 0.5-1 mg/kg/day for 15-20 weeks. More importantly, a total cumulative dose of 120-150 mg/kg/course is recommended. Most patients have an excellent response to treatment, and many do not experience recurrence of their acne after a course of therapy, and those who do can usually manage their acne with topical agents. Remission rates may be as high as 70-89% after one course of treatment. Keep in

mind, similar to other acne therapies, it is important to warn patients their acne may get worse before it gets better.

The most common adverse effects are related to dryness, and it is important to warn patients that they may develop dry skin, lips, and eyes. Decreased night vision may also occur, if a severe reduction occurs the medication should be stopped. Contact lens wearers may notice more irritation and discomfort with their lenses. Artificial tears may help to alleviate this side effect. Some patients also experience epistaxis from dry nasal mucosa. These effects usually diminish after the course of therapy is completed (but can take up to 4 months). Some patients also experience myalgias during the first several weeks of treatment. Other concerns are elevated triglycerides and liver enzymes, and bone marrow suppression. For this reason, a baseline CBC, ALT, and lipid panel is often ordered before starting a course of treatment, and is checked again at 1 month to assess for toxicity.

One very important point to note is that isotretinoin is a teratogen. It has been associated with severe birth defects, low IQ scores, spontaneous abortion, and risk of premature birth. For this reason, all female patients with child-bearing potential should be tested with a serum b-HCG prior to initiating therapy. They must also use two reliable forms of contraception (e.g. Oral contraceptive, condoms, or an intrauterine device) while taking isotretinoin or the physician must be very confident that they are not sexually active and will not engage in sexual activity.

It is also important that patients avoid Vitamin A supplements and using topical agents while taking oral isotretinoin due to the risk of Vitamin A toxicity and excessive skin dryness. Some medications such as methotrexate are also not recommended to be taken with isotretinoin due to hepatotoxicity, so a full medication history is important before starting treatment.

There are case reports and low quality studies that have looked at the potential association of isotretinoin and the risk of osteopenia or osteoporosis, as well as the risk of ulcerative colitis. Both of these associations are unclear at this time and are confounded by many factors.

Well, that covers most of the acne therapies you may see used or prescribed on your clerkship rotations particularly in pediatrics and family medicine!

Conclusion

Let's review briefly a treatment algorithm to help pull all of this together.

First, let's review mild acne treatment:

For initial treatment for comedonal or mild inflammatory acne, consider starting with benzoyl peroxide or a topical retinoid. If there are inflammatory lesions, consider starting

with a dual combination product of topical benzoyl peroxide + antibiotic or topical benzoyl peroxide + retinoid, or triple combination regimen of topical retinoid + antibiotic + benzoyl peroxide. Follow up with your patient in 3 months. If there is inadequate response, add one of the above agents that you have not yet used or change the topical retinoid concentration, type or formulation. Review expectations of acne treatment with your patient and assess compliance.

For moderate acne, you can start off with dual or triple combination topical therapy or an oral antibiotic + dual or triple topical therapy. If the patient has an inadequate response, change the topical regimen or consider hormonal therapy for females. Some clinicians may also consider isotretinoin as well.

For severe acne, start off with combination therapy with an oral antibiotic, topical retinoid, benzoyl peroxide, with or without a topical antibiotic. If the patient has an inadequate response, consider changing to a different oral antibiotic or consider oral isotretinoin.

For severe or refractory acne, a dermatology referral would be an important part of your management plan.

In summary, acne treatment can be seen as a pyramid with the foundation being general skin care and topical products, the middle being oral antibiotics and oral contraceptives, and the top of the pyramid being isotretinoin.

Now let's return to our case:

You diagnose Joshua with severe acne and after a discussion with him and his mom, you prescribe oral isotretinoin. You explain to him how to take the medication and give him enough for 3 months. You give him a lab requisition to have baseline liver function testing and CBC done, as well as another requisition to repeat blood work in one month. You also ask him to book another appointment in 1 month to see how things are going. You educate him that his hockey gear and sweating can contribute to his acne due to an occlusive effect. You suggest he shower immediately after hockey practice and games, and rinse his face with gentle soap and water. You also explain to him that acne is largely due to genetic factors and puberty, and that there are ways to manage it. You talk to him about how acne can affect self-esteem and that you're always available to him to talk if he is struggling with bullying or depression.

Now, let's summarize some important points from today based on our learning objectives:

1. When initiating acne treatment, use the least aggressive yet effective regimen.
2. Tailor the regimen to minimize the risk of bacterial resistance and target more than one pathogenic factor.

3. Educate the parents and adolescent about what to expect from treatment, and reasonable expectations for treatment outcome.
4. Educate about side effects of the treatment and how to manage them in order to promote compliance. Assess for adverse effects at follow up visits.
5. Reassess every 1 to 3 months until acne has improved and change the regimen to optimize compliance, efficacy, and tolerability.
6. When initiating oral isotretinoin therapy in a female who is of reproductive age, take an appropriate sexual history, order a serum b-HCG test, and ensure appropriate contraception.
7. Always consider other causes for acne if it is not improving with your treatment choices and the patient is following the regimen appropriately.
8. Refer to a dermatologist in cases of severe or refractory acne, moderate acne not responding to your treatment approach, or if you are uncomfortable initiating isotretinoin therapy and feel it is the best treatment option for your patient.

References:

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