Dermatologic and Eyes, Ears, Nose, and Throat, and Immunologic Disorders

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Learning Objectives

1. Evaluate antioxidant and multivitamin supplements for components and doses consistent with the AREDS (Age-Related Eye Disease Study) formulation for preventing the progression of macular degeneration.
2. Formulate an ophthalmologic drug therapy regimen for a patient that will decrease the patient's elevated intraocular pressures using agents that work synergistically (increased aqueous outflow and decreased production).
3. Create criteria to evaluate dry eye symptom treatment beyond traditional artificial tears.
4. Evaluate a medication profile to determine whether the signs and symptoms of vertigo are medication induced or a component of organic disease.
5. Construct an individualized pharmacy care plan for a patient with allergic rhinitis who has received no relief from intranasal corticosteroids.
6. Discuss the risks and benefits of agents used in addition to nonsedating histamine-1 blockers/antagonists for the treatment of urticaria.
7. Recommend immunizations for patients receiving injectable medications for the treatment and/or prevention of angioedema.
8. Determine how patients with acne should initiate, switch, or modify topical or oral therapeutic agents using a treatment algorithm.
9. Educate a patient using isotretinoin about therapy and the various monitoring variables that will ensure drug safety and efficacy.
10. Recommend single or multiple topical agents for treating plaque psoriasis given a patient's disease presentation, severity, and (if applicable) prior therapies.
11. Effectively educate a patient on an infestation and the purpose, proper use, and potential adverse reactions of the first-line treatment options for scabies and/or lice.
12. Create a pain management strategy for a patient with first-degree or superficial second-degree burns.
13. Create a monitoring plan for a patient using becaplermin for the treatment and healing of a decubitus ulcer.

Self-Assessment Questions

Answers and explanations to these questions may be found at the end of the chapter.

1. J.R. is a 68-year-old man with a medical history significant for type 2 diabetes. He presents to his ophthalmologist for his annual eye examination and is told he has signs of moderate (intermediate) macular degeneration. His ophthalmologist wishes to prescribe supplements. Which combination best resembles the formulation proven to decrease the progression of macular degeneration?

   A. Vitamin C, vitamin E, beta-carotene, and zinc.
   B. Vitamin C, beta-carotene, and zinc.
   C. Vitamin C, vitamin E, and beta-carotene.
   D. Vitamin C, vitamin E, and zinc.

2. A.A. is a 54-year-old man with a medical history significant for open-angle glaucoma, diabetes, and obesity, all of which are appropriately treated. At his most recent visit to the ophthalmologist (6 months earlier), he had increased intraocular pressures (IOPs) without changes in visual field or acuity. He was initiated on latanoprost therapy at that visit; now, he is returning for a follow-up. Today, his IOP is significantly decreased, but it still is not within an acceptable range to prevent progressive vision changes. Which medication is most appropriate to add to his therapy?

   A. Travoprost; one drop in each eye in the evening.
   B. Betaxolol; one drop in each eye twice daily.
   C. Dorzolamide; one drop in each eye three times daily.
   D. Brimonidine; one drop in each eye three times daily.

3. F.T. is a 52-year-old woman who works in a retail shop. She presents to an ophthalmologist with "scratching" in her eyes, constant irritation, and difficulty making it through the workday, leaving early once per week because of eye irritation and headaches. She has tried to use artificial teardrops, but they soothe her symptoms only temporarily. The ophthalmologist considers that F.T. has mild to moderate dry eyes and wants to adjust her therapy to better address the symptoms. Which is the best next step to recommend for therapy?

A. Artificial tear ointment.
B. Topical cyclosporine 0.05%.
C. Topical cyclosporine 0.1%.
D. Systemic cholinergic agents.

4. P.W. is a 45-year-old man who presents to the pharmacy and states that he has been having episodes of "dizziness" for the past several months. His medical history is significant for hypertension, seizures, type 2 diabetes, and headaches. He has discussed the matter with his physician and has undergone many tests, only to find that there is no readily identifiable cause for his symptoms. All radiographic study results of his head are normal, all of his laboratory values are within normal limits, and his blood pressure readings are "at target." He believes his dizziness may be caused by one of the medications he takes. In the past several months, he has started using hydrochlorothiazide, naproxen, fluoxetine, and metformin. Which medication is most likely associated with his dizziness?

A. Hydrochlorothiazide.
B. Acetaminophen.
C. Carbamazepine.
D. Metformin.

5. A.T. is a 9-year-old girl presenting to her pediatrician's office with her mother. The mother believes that A.T. has allergies because she has had a "runny nose and puffy and watery eyes" for the past few weeks. The child's nose has continuous, clear, thin discharge, and she is constantly sniffling. Her mother reports "waves" of sneezes two or three times daily. During the interview, the pediatrician observes several instances of the patient sniffling, rubbing her eyes, and making the "allergic salute" and wishes to prescribe an intranasal corticosteroid. The patient's mother refuses this medication because her daughter has frequent bloody noses, so instead, she requests an oral agent. Which would be the best oral agent for the child?

A. Clemastine 1.34 mg once daily.
B. Fexofenadine 30 mg twice daily.
C. Montelukast 5 mg once daily.
D. Pseudoephedrine 30 mg every 6 hours as needed.

6. Y.A. is a 26-year-old woman with a medical history significant only for dysmenorrhea, for which she takes naproxen 500 mg as needed, and low-dose oral contraceptive therapy. She is a schoolteacher at the local middle school and regularly contracts respiratory viral illnesses from her students. She is returning to work after being out with the influenza virus infection. She currently takes fexofenadine 60 mg twice daily for residual nasal symptoms and an urticarial rash she developed with the influenza virus. However, even though she may return to work, the rash has not completely resolved, and it is causing her moderate discomfort (noticeable, but not interfering with daily activities). She requests something to help further alleviate the symptoms of the urticaria. Which is the best agent for her (in addition to fexofenadine)?

A. Montelukast 10 mg once daily.
B. Diphenhydramine 25 mg every 6 hours as needed.
C. Famotidine 20 mg once daily.
D. Doxepin 25 mg once daily.

7. A.R. is a 24-year-old woman with a history of hereditary angioedema (HAE). She is treated with a plasma-derived C1 inhibitor (C1 INH) (Cinryze) every 3–4 days to prevent symptom onset. Given her medical condition and treatment regimen, which immunization is most important for her to receive?

A. Influenza annually.
B. Pneumonia (pneumococcal vaccine polyvalent) now and after age 55.
C. Herpes zoster now.
D. Hepatitis B series now.

8. F.D. is a 17-year-old female adolescent with a 5-year history of inflammatory acne conglobata on her face, neck, and upper torso. Since her initial diagnosis, she has been treated with a variety of topical and systemic agents such as benzoyl peroxide (with and without antibacterials), topical retinoids, and oral minocycline. Although these agents have partly controlled her symptoms, they have not offered sufficient relief. After much consideration, she and her family have agreed to try isotretinoin therapy. They have been counseled on the adverse events associated with its use and are ready to begin therapy.

Which additional measure best represents the next step before the clinician prescribes therapy?

A. Enroll the patient in the iPledge program to help avoid teratogenicity in the event of an unplanned or planned pregnancy.
B. Have the patient obtain clearance from a mental health provider to begin using the agent because it has been associated with suicidal ideations.
C. Remain diligent to testing hepatic transaminase concentrations every other week until therapy is discontinued; discontinue the medication if the patient does not adhere to testing.
D. Have the patient agree to avoid driving after sunset for 6 months secondary to vision changes associated with the drug.

9. J.F. is a 22-year-old man with moderate psoriasis of his back and legs. He has been treated with topical corticosteroids intermittently for the past 9 years. Each treatment course has been successful at alleviating his symptoms of itching and burning. However, his most recent symptom flare is the worst to date, and it is not responding to topical corticosteroids as it did previously. Which agent is best to add to his topical corticosteroid?

A. Prednisone 20 mg daily for 14 days.
B. Topical calcipotriene twice daily.
C. Methotrexate 20 mg once weekly.
D. Adalimumab 40 mg once every other week.

10. D.T. is a 46-year-old woman with severe and sometimes debilitating psoriasis with arthritis symptoms. She has had painful psoriatic arthritis complications in her hands, wrists, hips, and knees for the past 6 months and has gained only limited relief from nonsteroidal anti-inflammatory drugs (NSAIDs) and oral corticosteroids. She underwent a hysterectomy with a bilateral salpingo-oophorectomy 4 years ago and has poorly controlled hypertension, despite being treated with fosinopril, hydrochlorothiazide, and amlodipine. She is employed and has medical and prescription insurance. Which is the first choice to help lessen this patient's symptoms?

A. Methotrexate 20 mg once weekly.
B. Cyclosporine (equaling 1.25 mg/kg) twice daily.
C. Acitretin 50 mg once daily.
D. Etanercept 50 mg twice weekly.

Questions 11 and 12 pertain to the following case.

L.L. is a 14-year-old male adolescent visiting his aunt and uncle for a few weeks in the summer. He is up to date with his immunizations and has had a relatively unremarkable childhood. He attends a sleep-away camp every summer for 2 weeks and then visits his cousins the following week. On the second day of his visit with his relatives, L.L. begins to experience itching between his fingers, under his arms, and on the underside of his buttocks. The itching is unrelieved with bathing, loratadine, or hydrocortisone cream. His aunt takes him to her children's pediatrician for evaluation and is surprised to hear that he has contracted scabies. He has not had an infestation such as this before; most likely, he contracted it during the first few days of camp.

11. Which is the best first choice to eradicate this infestation?

A. Permethrin 1%.
B. Permethrin 5%.
C. Malathion 0.5%.
D. Lindane 1%.

12. L.L.'s aunt is concerned that her family may have also contracted scabies and wants everyone in the house to be treated. Which is the most appropriate response to this request?

A. All individuals in the house should be empirically treated, regardless of the presence of symptoms.
B. Household prophylaxis is unnecessary in scabies infestations, and patients should seek treatment on an individual basis.
C. Only those in the house who have had close contact with the patient's clothing or bedding need prophylactic therapy.
D. The family should have an "on-call" prescription for a scabicide and use it at the first sign of itching and discomfort.

13. T.S. is a 38-year-old man with no significant medical history. After a long weekend of working outside and not wearing sunscreen, he has developed sunburn on his upper arms, neck, face, and back. He is relatively uncomfortable and cannot wear a shirt or sleep on his back without discomfort. The sunburned areas are not blistering or weeping. They are erythematous and warm to the touch, and they

blanch with pressure. Which would be the best way to relieve his pain and make him more comfortable?

A. Topical silver-based cream applied once or twice daily.
B. Topical aloe vera and an occlusive dressing over the back, arms, and neck.
C. Ibuprofen 400 mg every 6 hours as needed for pain.
D. Hydrocolloid dressings (DuoDERM) for 5–10 days.

14. E.C. is a 73-year-old man with an extensive medical history. Most notably, the patient has poorly controlled type 2 diabetes, severe peripheral arterial disease, and a below-the-knee amputation on his left leg 6 months prior. Since the amputation, the patient has chosen to spend most of his time in bed and to use a wheelchair for activities outside the house. He has developed a 1 in. x 2 in. decubitus ulcer on his right hip that requires surgical debridement and medical management. He is prescribed becaplermin to promote wound healing. Ten weeks after starting the medication, he returns to the wound management group and is reported to have a 35% reduction in ulcer size. Which is the best way to continue with the patient's treatment?

A. Continue the current regimen for another 10 weeks.
B. Increase the becaplermin dose to 1.5 times his original dose (length of gel ribbon).
C. Decrease his becaplermin dose to 0.75 times his original dose (length of gel ribbon).
D. Discontinue this therapy because he has not had sufficient wound healing in the first 10 weeks.

I. MACULAR DEGENERATION

A. Professional Treatment Guidelines *(Domain 3)*
   1. 2015 American Academy of Ophthalmology (AAO) Age-Related Macular Degeneration Preferred Practice Pattern guidelines
   2. 2004 update of the American Optometric Association clinical practice guideline; care of the patient with AMD

B. Types *(Domain 1)*
   1. Dry (atrophic or non-neovascular); most common type
   2. Wet (exudative or neovascular); more damaging
   3. Best disease (rare genetic disease in children and adolescents)

C. Factors Associated with Developing Macular Degeneration *(Domains 1 and 2)*
   1. Age
   2. Family history of macular degeneration
   3. Women have a higher incidence and earlier onset than do men
   4. White race
   5. Cigarette smoking
   6. Cumulative light exposure
   7. Hypertension
   8. Higher summer sun exposure
   9. Excessive alcohol intake
   10. Genetic/familial predisposition
      a. Complement factor H (CFH) gene variant Y402H
      b. LOC387715 polymorphism
      c. Complement C3 variant (Arg80Gly)
      d. *SERPING1* gene
   11. After diagnosis
      a. Obesity associated with an increased risk of disease progression
      b. Physical activity associated with a decreased risk of disease progression

Table 1. Presentation and Diagnosis

Patient Presentation	Funduscopic Changes	Diagnostic Tests
Loss of visual acuity Poor color vision Central scotoma (blind/blurry spot in field of view) Metamorphopsia (wavy lines)	Retinal atrophy Retinal pigment abnormalities Soft drusen Choroidal neovascularization Retinal detachment (wet) Subretinal hemorrhage (wet) Exudates (wet)	Color fundus photography Fluorescein angiographic imaging Optical coherence tomography

Patient Case

1. M.C. is a 76-year-old man with a medical history of hypertension, type 2 diabetes, cerebrovascular accident with residual left-sided hemiparesis, peripheral neuropathy, and renal insufficiency. He has smoked 1 pack/day for the past 50 years and is not ready or willing to quit. He is treated for neovascular (wet) AMD with intravitreal bevacizumab. His ophthalmologist recommends that he begin an antioxidant vitamin regimen, but the patient is unsure what he is supposed to take. Which combination of products is best to recommend for this patient?

   A. Vitamin C, vitamin E, beta-carotene, and zinc.
   B. Vitamin C, beta-carotene, and zinc.
   C. Vitamin C, vitamin E, and beta-carotene.
   D. Vitamin C, vitamin E, and zinc.

D. Treatment *(Domains 1 and 3)*
   1. AREDS formula (vitamin C 500 mg, vitamin E 400 international units, beta-carotene 15 mg or 25,000 international units of vitamin A, and zinc 80 mg)

Table 2. Antioxidant STEPS

Safety	Increased risk of cardiovascular event in patients taking higher doses (> 400 international units) of vitamin E daily Increased risk of lung cancer in patients who smoke and use high doses of beta-carotene Potential increase in genitourinary disease with high-dose zinc supplementation
Tolerability	Excessive vitamin C will increase urinary oxalate (risk of nephrolithiasis) Carotenodermia reported in > 10% of patients using beta-carotene
Efficacy	No benefit for disease prevention or progression in patients with mild AMD Antioxidant plus zinc is effective for preventing patients with intermediate disease from progressing to advanced macular degeneration or visual acuity loss
Preference (Pearls)	Least invasive intervention for macular degeneration Antioxidants with or without zinc do not treat macular degeneration, but only prevent disease progression Patients who smoke should use the AREDS formulation without beta-carotene because of the increased risk of lung cancer, but this regimen lacks good evidence to fully support its use
Simplicity	OTC formulation (comparable to the AREDS formulation) is available for $10 a month

AMD = age-related macular degeneration; AREDS = Age-Related Eye Disease Study; OTC = over the counter.

2. Intravitreal drug therapy
    a. Bevacizumab (Avastin)
    b. Pegaptanib (Macugen)
    c. Ranibizumab (Lucentis)
    d. Aflibercept (Eylea)

Table 3. Intravitreal Therapy STEPS

Safety	Increased IOP Stroke, MI, or thrombotic event Endophthalmitis and retinal detachment
Tolerability	Endophthalmitis (erythema, photophobia, vision changes) Conjunctival hemorrhage Corneal edema (pegaptanib) Vitreous floaters (pegaptanib)
Efficacy	Reduced visual acuity loss (< 15 letters on Snellen chart) Significantly more individuals gaining visual acuity (≥ 15 letters on Snellen chart)
Preference (Pearls)	These agents should only be used for neovascular (wet) AMD First class of agents to improve visual acuity in patients with neovascular (wet) AMD Ranibizumab is the most extensively studied of the three options Bevacizumab is not FDA labeled for AMD; however, it is more widely used and is covered by third-party payers because of its major cost advantage over ranibizumab
Simplicity	Intravitreal injections (traumatic) performed once monthly to once every 3 mo Ranibizumab costs $2100 per month Bevacizumab costs $30/dose Periodic eye examinations are needed

FDA = U.S. Food and Drug Administration; IOP = intraocular pressure; MI = myocardial infarction.

3. Other considerations
    a. Photodynamic therapy
        i. Verteporfin infusion followed by laser therapy
        ii. Reduces visual acuity loss (greater than 15 lines on Snellen chart) at 24 months
        iii. Questionable benefit of adding intravitreal triamcinolone to therapy
    b. Laser photocoagulation
    c. Surgery
    d. Over-the-counter (OTC) vitamin preparations also include lutein and zeaxanthin, but there is no evidence to support their supplementation (outside dietary intake) to prevent the progression of macular degeneration.
    e. Self-management and problem-solving treatment sessions may help patients adjust to life with macular degeneration.

II. GLAUCOMA

A. Professional Treatment Guidelines *(Domain 3)*
   1. AAO 2015 guidelines on primary open-angle glaucoma (POAG)
   2. 2010 American Optometric Association care of the patient with open-angle glaucoma
   3. National Institute for Health and Clinical Excellence 2009 review on diagnosis and management of chronic open-angle glaucoma and ocular hypertension

B. Types of Glaucoma *(Domain 1)*
   1. POAG (most common)
   2. Acute angle-closure glaucoma
   3. Congenital glaucoma
   4. Secondary glaucoma

C. Factors Associated with Developing POAG – Prediction tool available through Ocular Hypertension Treatment Study for 5-year risk of conversion from ocular hypertension to glaucoma *(Domains 1, 2 and 3)*
   1. Advanced age
   2. African ancestry or Latino/Hispanic ethnicity
   3. Family history and genetic predisposition
   4. Elevated IOPs (ocular hypertension)
   5. Thinner central cornea
   6. Low ocular perfusion pressures
   7. Various optic nerve characteristics (size and shape of optic cup, thickness of neuroretinal rim, and symmetry of optic cups)
   8. Myopia
   9. Type 2 diabetes (controversial)

D. Disease Prevention *(Domains 1 and 2)*
   1. The AAO does not recommend community screenings because this is not a cost-effective intervention.
   2. May be beneficial to target high-risk populations for screening instead of screening the general population
      a. Older adults
      b. Diabetes
      c. Family history of glaucoma

E. Presentation and Diagnosis *(Domain 1)*
   1. Patient findings
      a. Ocular hypertension (21 mm Hg or greater) often precedes the diagnosis of (chronic) open-angle glaucoma.
      b. POAG is usually asymptomatic in early stages, but it develops to noticeable tunnel vision and scotomas (visual field defect) over time.
      c. Patients with acute angle-closure glaucoma present with ocular pain, blurry vision, halos, and headache.
      d. Congenital glaucoma causes patients to have light sensitivity and excessive lacrimation.
   2. Screening procedures for glaucoma may include, but are not limited to, the following:
      a. Goldmann applanation tonometry is the reference standard for diagnosis and should be performed before pupil dilation to assess IOP.
         i. Normal IOP is 13–18 mm Hg.
         ii. IOP and time of day should be recorded to assess for diurnal variations.

   b. Gonioscopy should be used to evaluate the anterior chamber angle as well as to identify/rule out secondary causes of glaucoma and IOP.
   c. Pachymetry measures central corneal thickness and is indicated in evaluating patients with glaucoma or suggestion of glaucoma.
   d. Use of a biomicroscope with ancillary lens is the preferred method to assess the optic nerve (preferably through a dilated pupil).
3. Diagnosis is based on several factors.
   a. Physical examination will reveal an increased cupping diameter in the optic nerve.
   b. IOP is usually elevated, though some patients may have a normal value.
4. Disease severity is usually related to disease duration. Follow-up examination of patients with a diagnosis of POAG should occur within the first 1–2 years.

Patient Case

2. E.K. is a 67-year-old woman with a medical history significant for type 2 diabetes, hypertension, osteoarthritis, hypothyroidism, asthma, and osteopenia. At her most recent ophthalmologist appointment, she had increased IOPs and findings consistent with POAG. Her IOP is 35 mm Hg, and she has optic nerve changes. Her ophthalmologist recommends therapy to decrease her IOPs and prevent the progression of glaucoma. Which regimen is best for E.K. to start?

   A. Travoprost eyedrop; one drop in each eye at bedtime.
   B. Travoprost eyedrop; two drops in each eye at bedtime.
   C. Timolol eyedrop; one drop in each eye twice daily.
   D. Timolol eyedrop; two drops in each eye twice daily.

F. Treatment of POAG *(Domain 1)*
   1. IOP lowering is individually determined but typically targets a reduction of 20%–30% from baseline IOP to delay visual field loss.
   2. Early, aggressive management of elevated IOP may delay progression.
   3. Topical ocular rules
      a. Only one drop is necessary per dosing.
      b. Wait about 5 minutes between agents if using several drops.
   4. At each patient contact, counsel patient regarding treatment adherence and proper administration of eyedrops (including nasolacrimal occlusion techniques).

Table 4. Therapeutic Considerations for Drug Classes

Reduce Aqueous Outflow Resistance	Decrease Aqueous Production
Prostaglandin analogs Adrenergic agents (epinephrine) Miotics (pilocarpine) Adrenergic agonists	β-Blockers Carbonic anhydrase inhibitors Adrenergic agonists (primary)

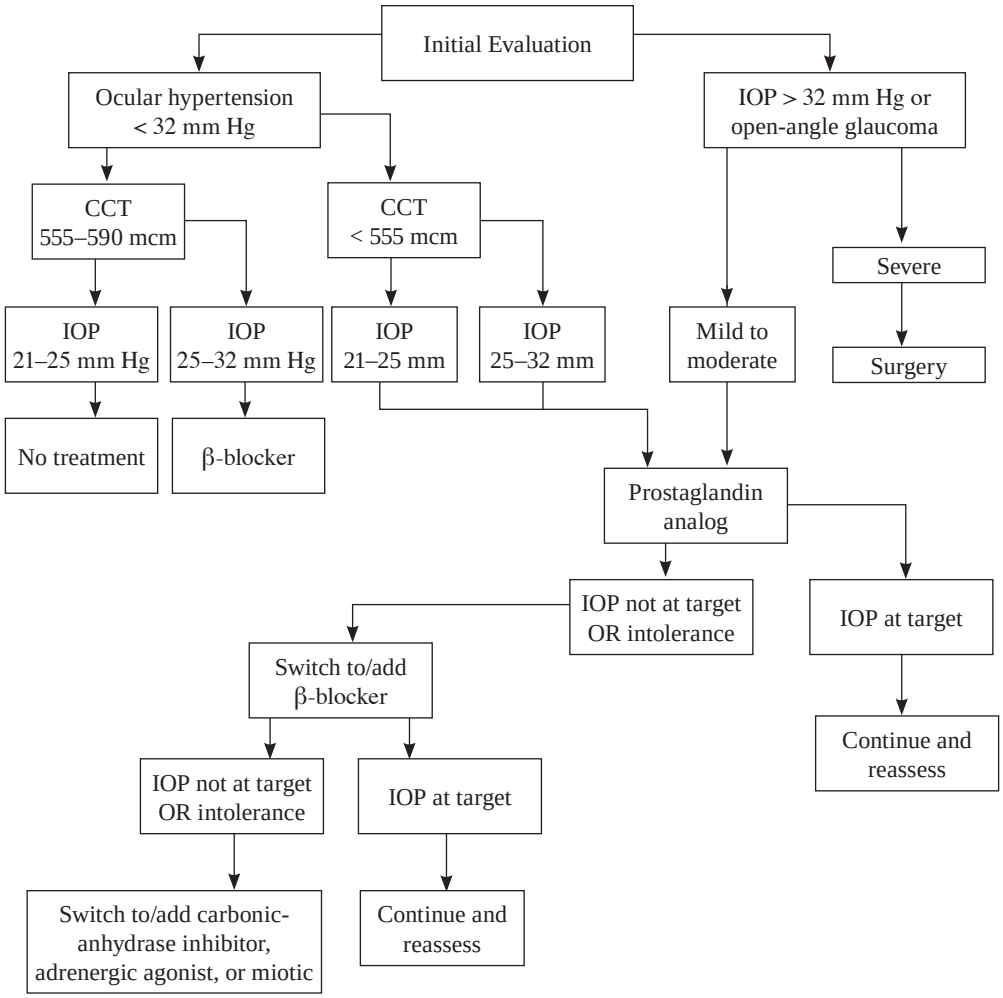

Figure 1. Ocular hypertension and primary open-angle glaucoma treatment algorithm.

CCT = central corneal thickness; IOP = intraocular pressure.

5. Prostaglandin analogs
    a. Bimatoprost (Lumigan)
    b. Latanoprost (Xalatan)
    c. Tafluprost (Zioptan)
    d. Travoprost (Travatan)
    e. Unoprostone (Rescula)

Table 5. Ocular Prostaglandin Analog STEPS

Safety	Contraindicated in macular edema or those with a history of herpetic keratitis
Tolerability	Increased brown pigmentation of iris (especially blue or multicolored irises) Increased number, thickness, curvature, and pigmentation of eyelashes Ocular pruritus/dryness/blurring Eyelid erythema
Efficacy	Greatest IOP reduction potential of all available pharmacologic agents
Preference (Pearls)	In patients who do not achieve adequate IOPs with a single agent, add a second agent (from a different class) to further lower IOP Caution when using with ophthalmologic NSAIDs because they may decrease the therapeutic effect of the prostaglandin analog
Simplicity	Once-daily application in the evening Available as a combination with a topical β-antagonist for patients who require additional therapy Administer 15 min before inserting contact lenses secondary to benzalkonium chloride (will adsorb to contact lenses)

NSAID = nonsteroidal anti-inflammatory drug.

6. β-Antagonists (topical)
    a. Betaxolol (Betoptic S)
    b. Timolol (Timoptic)
    c. Levobunolol (Betagan)
    d. Metipranolol (OptiPranolol)
    e. Carteolol (Ocupress)

Table 6. Ocular β-Antagonists STEPS

Safety	Severe cardiovascular and respiratory events reported with topical β-antagonists Not to be used as monotherapy in patients with angle-closure glaucoma
Tolerability	Ocular burning and stinging with application Reported bradycardia, depression, and bronchospasm
Efficacy	Adding to a prostaglandin analog appears to decrease the variations in IOP throughout the day
Preference (Pearls)	May be used as monotherapy, but would be best used as add-on therapy for patients without adequate IOP lowering with a prostaglandin analog
Simplicity	Once- or twice-daily application Available as a combination with a prostaglandin analog for patients who require additional therapy Administer 15 min before inserting contact lenses secondary to benzalkonium chloride (will adsorb to contact lenses)

7. Selective α_2-agonists
   a. Apraclonidine (Iopidine)
   b. Brimonidine (Alphagan P)

Table 7. Selective α-Agonists STEPS

Safety	Caution with use around children < 5 yr secondary to serious systemic adverse events with ingestion Use with caution in patients with cardiovascular disease, cerebrovascular disease, depression, orthostatic hypotension, or Raynaud phenomenon Ocular hypersensitivity reactions (hyperemia, swelling, pruritus)
Tolerability	Tearing Foreign body sensation Ocular inflammation Dry mouth Altered taste
Efficacy	Reported to have IOP-lowering properties similar to β-antagonists
Preference (Pearls)	Third-line agent for treating glaucoma (brimonidine preferred) May be efficacious for a limited time (less than 1 mo; apraclonidine)
Simplicity	Application three times daily Administer 15 min before inserting contact lenses secondary to benzalkonium chloride (will adsorb to contact lenses)

8. Carbonic anhydrase inhibitors
   a. Topical brinzolamide (Azopt)
   b. Topical dorzolamide (Trusopt)
   c. Oral acetazolamide (Diamox)
   d. Oral methazolamide (Neptazane)

Table 8. Carbonic Anhydrase Inhibitor STEPS

Safety	Systemic agents may cause serious dermatologic adverse events; recommend to avoid or discontinue topical preparation if the patient has a history of Stevens-Johnson syndrome or toxic epidermal necrolysis with systemic agent Contraindications (mainly systemic use) include aplastic anemia, nephrolithiasis, sulfonamide allergy, thrombocytopenia
Tolerability	Stinging Blurry vision Corneal edema Altered taste sensation
Efficacy	Least potential for IOP lowering of all available classes to treat glaucoma Agents in this class are equally effective and may switch within class if the patient develops adverse reactions to one
Preference (Pearls)	Third-line agent for treating glaucoma Topical formulations are typically used before oral formulations Oral formulations are reserved for patients who have an inadequate response or cannot tolerate the topical formulations
Simplicity	Available as a combination with a β-antagonist for patients who require additional therapy Application two or three times daily

9. Marijuana – IOP-lowering effects last about 3 hours with each marijuana cigarette (3000 marijuana cigarettes per year).
10. Surgical intervention
    a. Trabeculectomy
        i. Consider when two or more agents fail to control rising IOPs.
        ii. Increased risk of developing cataracts
    b. Laser trabeculoplasty
    c. Implantable valves

III. DRY EYES (XEROPHTHALMIA)

A. Professional Treatment Guidelines: 2013 AAO Preferred Practice Pattern: Dry Eye Syndrome *(Domain 3)*

B. Factors Associated with Developing Dry Eye Syndrome *(Domain 1)*
1. Advanced age (older than 65 years)
2. Female sex
3. Concurrent use of medications that have anticholinergic effects
4. Postmenopausal estrogen therapy
5. LASIK (laser-assisted in situ keratomileusis) and refractive excimer laser surgery
6. Vitamin A deficiency
7. May be associated with the following medical conditions:
    a. Rheumatoid arthritis
    b. Sarcoidosis
    c. Sjögren syndrome
    d. Systemic lupus erythematosus

C. Presentation and Diagnosis *(Domain 1)*
1. Patient will have dry and irritated eyes, redness, excess watering, photophobia, gritty, scratchy, burning, or a foreign body sensation.
2. Physical examination will reveal an irritated (red) but otherwise normal-looking eye.
3. Diagnostic tests include the following:
    a. Tear break-up time test
    b. Ocular surface dye staining
    c. Aqueous tear production (Schirmer test)
    d. Fluorescein clearance test/tear function index
    e. Lacrimal gland function test
    f. Tear osmolarity test

D. Potential Complications *(Domains 1 and 2)*
1. Corneal ulceration
2. Functional vision loss
3. Infections
4. Neovascularization
5. Scarring

E. Treatment *(Domain 1)*
   1. Nonpharmacologic interventions include the following:
      a. Avoiding medications with anticholinergic or diuretic properties
      b. Smoking cessation and avoidance of secondhand smoke
      c. Avoiding drafts or low-humidity environments
      d. Hot compresses
      e. Frequent breaks from reading/television/computer screen
      f. Eyelid scrub/massage

Table 9. Severity Classification for Dry Eye Syndrome

Dry Eye Severity	1	2	3	4
Discomfort, severity, and frequency	Mild and/or episodic; occurs under environmental stress	Moderate episodic or chronic; stress or no stress	Severe frequent or constant without stress	Severe and/or disabling and constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity limiting, episodic	Annoying, chronic, and/or constant, limiting activity	Constant and/or possibly disabling
Conjunctival injection	None to mild	None to mild	+/–	+/++
Conjunctival staining	None to mild	Variable	Moderate to marked	Marked
Corneal staining (severity/location)	None to mild	Variable	Marked central	Severe punctate erosions
Corneal/tear signs	None to mild	Mild debris, decrease meniscus	Filamentary keratitis, mucus clumping, increased tear debris	Filamentary keratitis, mucus clumping, increased tear debris, ulceration
Lid/meibomian glands	MGD variably present	MGD variably present	Frequent	Trichiasis, keratinization, symblepharon
TFBUT, seconds	Variable	≤ 10	≤ 5	Immediate
Schirmer score, mm/5 min	Variable	≤ 10	≤ 5	≤ 2

MGD = meibomian gland disease; TFBUT = fluorescein tear break-up time.

Reproduced with permission from: The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf 2007;5:75-92.

Patient Case

3. When classifying patients with xerophthalmia in order to choose the best treatment, which patient would be best suited to receive ophthalmologic cyclosporine?
   A. A 63-year-old woman with bothersome dry eyes once weekly who receives adequate relief from artificial tears solution.
   B. A 54-year-old woman with daily dry eyes who receives adequate relief from artificial tears ointment.
   C. A 58-year-old woman with twice-weekly dry eyes unrelieved with artificial tears, leading to lost productivity.
   D. A 61-year-old woman with dry eyes, dry mouth, fatigue, and other dry mucous membranes.

Table 10. Treatment Recommendations Based on Dry Eye Syndrome Severity[a]

Mild	Education and environmental modifications Elimination of offending topical or systemic medications Aqueous enhancement using artificial tear substitutes, gels/ointments Eyelid therapy (warm compresses and eyelid hygiene) Treatment of contributing ocular factors such as blepharitis or meibomianitis Correction of eyelid abnormalities
Moderate[b]	Anti-inflammatory agents (topical cyclosporine and corticosteroids), systemic omega-3 fatty acid supplements Punctal plugs Spectacle side shields and moisture chambers Lymphocyte function-associated antigen-1 (LFA-1) antagonist
Severe[b]	Systemic cholinergic agents Systemic anti-inflammatory agents Mucolytic agents Autologous serum tears Contact lenses Permanent punctual occlusion Tarsorrhaphy

[a]Note: Tear replacement therapy is often unsuccessful when used as the sole treatment for dry eye syndrome if additional causative factors are not concomitantly addressed.

[b]In addition to the above treatments.

Reproduced with permission from: Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye Workshop (2007). Ocul Surf 2007;5:163-78.

2. Artificial tears usually consist of normal saline, methylcellulose, or hydroxypropyl methylcellulose.
   a. Available in liquid, gel, and ointment forms
   b. Preservative-free forms are often recommended; however, they may be more expensive.
3. Topical cyclosporine (0.1%, 0.05%)

Table 11. Topical Cyclosporine STEPS

Safety	Remove contact lenses before use and wait 15 min before reinserting them	
Tolerability	Blurry vision Burning sensation Foreign body sensation	Hypersensitivity reaction Large, evident conjunctiva blood vessels
Efficacy	Effective for patients with moderate to severe disease that is refractory to conventional therapy 0.1% concentration may be more effective than 0.05% formulation for patients with moderate to severe symptoms	
Preference (Pearls)	0.05% formulation is FDA approved in the United States Higher-dose formulations may require special preparation and compounding	
Simplicity	Dosed every 12 hr May use artificial tears concurrently, allowing a 15-minute interval between administration of the two products	

4. Topical lymphocyte function-associated antigen-1 (LFA-1) antagonist (lifitegrast 5%)
5. Systemic cholinergic agonists – U.S. Food and Drug Administration (FDA) approved to treat xerostomia in patients with Sjögren syndrome, but also appear to improve tear production
   a. Cevimeline
   b. Pilocarpine

Table 12. Topical LFA-1 Antagonist STEPS

Safety	Remove contact lenses before use and wait 15 minutes before reinserting them
Tolerability	Dysgeusia (foul, salty, rancid, or metallic taste in mouth) Local irritation Decreased visual acuity
Efficacy	Indicated to treat the signs and symptoms of DES Clinical trials showed significant improvement in eye dryness and corneal staining
Preference (Pearls)	Approved in 2016 and the first in its class with this MOA
Simplicity	Dosed every 12 hours

Table 13. Systemic Cholinergic Agonist STEPS

Safety	Use with caution in patients with a history of: cardiovascular disease, cholelithiasis, nephrolithiasis, respiratory disorders	
Tolerability	Abdominal pain Diaphoresis Dyspepsia Edema Excessive salivation Flushing/headache	Nausea Sinusitis Upper respiratory tract infection symptoms Urinary tract infection Vomiting
Efficacy	Improves symptoms of dry eyes better than artificial tears	
Preference (Pearls)	Most research for treating dry eye symptoms was with patients with Sjögren disease and other symptoms of hyper-anticholinergic activity (e.g., xerostomia, fatigue)	
Simplicity	Dosed three or four times daily	

6. Topical pilocarpine (2%) is also an option for patients who cannot tolerate or afford topical cyclosporine or systemic cholinergic agonists.
7. Oral omega-6 fatty acid (6 capsules per day of evening primrose oil) showed benefit in a small cohort of women who wore contact lenses.
8. Topical tamarind seed polysaccharide (0.5%, 1%) is effective for short-term symptoms.

IV. VERTIGO

A. Professional Treatment Guidelines *(Domain 3)*: 2017 American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) clinical practice guideline on benign paroxysmal positional vertigo (BPPV)

B. Vertigo: A Symptom of Another Underlying Condition – Is not a lone treatable condition *(Domain 1)*

C. The Condition May Be Caused by the Following: *(Domain 1)*
   1. Centrally originating causes (cerebral ischemia such as stroke, carotid artery stenosis, migraine headaches, tumors, neurodegenerative disorders, epilepsy, intoxication, positional changes)
   2. Peripherally originating causes (BPPV, vestibular neuronitis, Ménière disease, otosclerosis, whiplash)
   3. Medications such as Mysoline, carbamazepine, and phenytoin; antihypertensives; and cardiovascular medications

D. Benign Paroxysmal Positional Vertigo *(Domain 1)*
   1. Most common disorder of the inner ear's vestibular system; benign condition
   2. Presents most often in men in their 50s; lasts an average of 3–4 years and then subsides
   3. Typically, there are no precipitating events or findings leading up to symptom presentation.
   4. Symptoms tend to present in episodes and last for less than 1 minute.
   5. Complications of the condition may include falls, nausea, vomiting, or dehydration.
   6. Treatment
      a. First-line therapy is repositioning and vestibular exercises and rehabilitation.
      b. Antihistamines and benzodiazepines should not be used routinely to treat BPPV.

E. Ménière Disease *(Domain 1)*
   1. First presentation generally occurs between age 20 years and 50 years and affects both sexes equally.
   2. Patients will present with episodes of sustained vertigo, (progressive) hearing loss, and/or tinnitus.
   3. May be caused by genetic predisposition, trauma, viral infection, and/or vasculopathies
   4. Symptoms may be triggered by barometric changes, allergies, hormonal changes, or increased sodium intake.

Table 14. American Academy of Otolaryngology–Head and Neck Surgery Diagnostic Criteria for Ménière Disease

Diagnosis	Criteria	Staging
Possible	Other causes excluded and … episodic vertigo without documented hearing loss	N/A
Probable	Other causes excluded and … one definitive episode of vertigo, one or more episodes of hearing loss, tinnitus, or aural fullness	
Definite	Other causes excluded and … two or more definitive spontaneous episodes of vertigo lasting > 20 min, one or more episodes of hearing loss, tinnitus, or aural fullness	Audiogram findings Stage 1: < 25 dB Stage 2: 26–40 dB Stage 3: 41–70 dB Stage 4: > 70 dB
Certain	All criteria for definite Ménière disease plus confirmation of endolymphatic hydrops (excess endolymph fluid in ears)	

N/A = not applicable.

5. Treatment options *(Domain 1)*
   a. Nonpharmacologic interventions include the following:
      i. Watchful waiting/observation
      ii. Education/information/counseling
      iii. Reduce or restrict sodium, alcohol, and caffeine intake
      iv. Affects mainly women between their fifth and seventh decades
      v. Repositioning treatments
   b. Thiazides (hydrochlorothiazide), in addition to sodium restriction, may be of benefit in reducing symptoms of dizziness and hearing loss.
   c. Betahistine (not available in the United States) has shown effective reduction of vertigo, but no effect on hearing loss, in Ménière disease.
   d. Intratympanic injections include the following:
      i. Gentamicin: Will reduce vertigo, but may cause decreased auditory response
      ii. Dexamethasone: Will reduce vertigo less effectively than gentamicin, but may have only a small effect on patient hearing
      iii. Options such as latanoprost and lidocaine show positive results in small studies (of 10 and 40 patients).
   e. Surgery may be necessary for patients whose condition does not respond to dietary, activity, and pharmacologic interventions.
   f. Positive pressure devices (deliver air pulsations to inner ear periodically throughout the day) showed a significant reduction in vertigo symptoms and sick days.

F. Patient Resources: National Institute on Deafness and Other Communication Disorders (www.nidcd.nih.gov/)

V. ALLERGIC RHINITIS

A. Professional Guidelines and Published Reviews *(Domain 3)*
   1. AAO allergic rhinitis clinical practice guideline 2015
   2. Joint Task Force on Practice Parameters for Allergy and Immunology: The Diagnosis and Management of Rhinitis: An Updated Practice Parameter 2008
   3. British Society for Allergy and Clinical Immunology guidelines for the management of allergic and nonallergic rhinitis 2008

B. Types of Allergic Rhinitis *(Domain 1)*
   1. Seasonal
   2. Perennial
   3. Occupational

Table 15. Factors Associated with Developing Symptoms of Rhinitis

Allergic Irritants	Nonallergic Irritants
Dust mites (late fall and throughout winter) Trees (oak or maple in late winter and spring) Grasses (spring and early summer) Mold (summer) Ragweed (late summer and early fall) Insect debris (throughout the year) Pet dander	Infection Pollution Stress Tobacco smoke Weather

Table 16. Presentation and Diagnosis of Rhinitis

Age at onset	Onset of allergic rhinitis is common in childhood, adolescence, and early adult years, with a mean age onset of 8–11 yr In childhood, it is more common in boys than in girls, but in adulthood, it is more common in women In 80% of cases, allergic rhinitis develops by age 20 yr About 50% of patients with allergic rhinitis can manage without medications within 10 yr of their initial diagnosis	
Symptoms	Nasal congestion/obstruction Sneezing Thin rhinorrhea Pruritus	Ocular discharge (lacrimation) Decreased or loss of smell, taste, or both Postnasal drip with or without nausea
Physical findings	Mouth breathing at rest Swollen turbinates with evidence of clear secretions Conjunctival swelling	

   a. Presence of purulent discharge or fever probably indicates a nonallergic disease.
   b. Diagnosis is best made using the skin prick test.
      i. Current recommendation is to make the diagnosis on the basis of symptoms, examination, and response to therapy.
      ii. Unreasonable to perform on everyone with concerns consistent with allergic rhinitis
   c. May consider the following tests for individuals thought to have atypical disease:
      i. Skin testing
      ii. IgE (immunoglobulin E) (blood) evaluation
      iii. Pulmonary function test (asthma)
      iv. Sweat test (cystic fibrosis)
      v. Computed tomography of sinuses

C. Nonpharmacologic Treatment *(Domains 1 and 2)*
   1. Control for dust mites and other insect refuse
   2. Control moisture to reduce likelihood of mold spores

3. Pet management
   a. Removal of pet
   b. Limiting pet areas (not in bedroom or on furniture)
4. Manage pollen exposure

Patient Case

4. T.B. is a 21-year-old college student presenting to his local urgent care clinic for allergic rhinitis. He has taken intranasal fluticasone (2 sprays in each nostril once daily) and oral loratadine as needed for the past 6 years with success. However, during the past 1–2 weeks, his symptoms have been unrelieved by scheduled intranasal fluticasone and daily loratadine. He knows his symptoms are out of control because his roommate is cat-sitting for his parents, but he cannot ask his roommate (and cat) to leave. His roommate has to cat-sit for only 1 more week. Yet he cannot live with this degree of discomfort any more. In addition to household hygiene and dander management, which is the best short-term option to help T.B. control his symptoms?

   A. Double the intranasal corticosteroid dose until the feline is out of the house.
   B. Change loratadine to fexofenadine plus pseudoephedrine twice daily until the allergen is gone.
   C. Add prednisone 10 mg once daily to his current regimen and continue for the duration of the cat-sitting.
   D. Add montelukast 10 mg once daily to his regimen for the next 7 days.

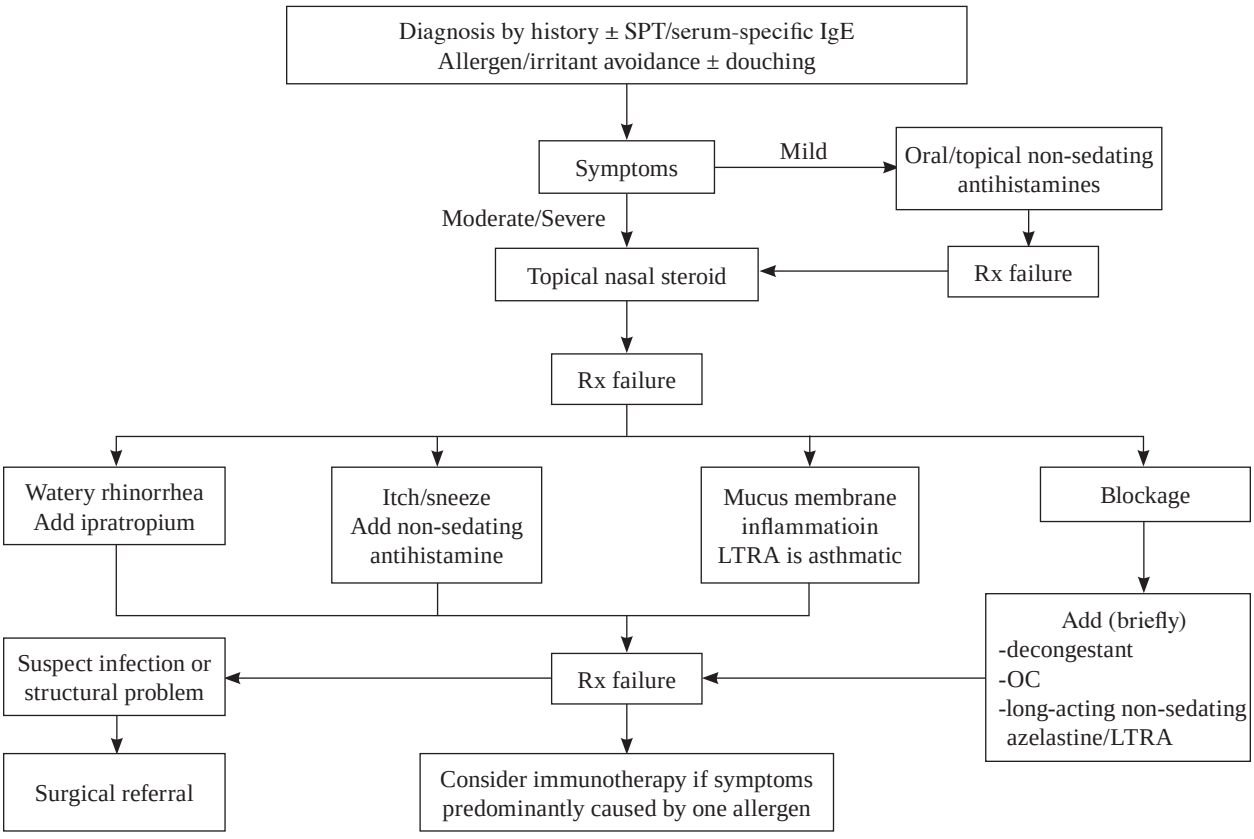

Figure 2. BSACI 2008 allergic rhinitis treatment algorithm.

BSACI = British Society for Allergy & Clinical Immunology; IgE = immunoglobulin E; LTRA = leukotriene receptor antagonist; OC = oral corticosteroid; Rx = prescription; SPT = skin prick test.

Reprinted with permission from: Scadding GK, Durham SR, Mirakian R, et al. BSACI guidelines for the management of allergic and non-allergic rhinitis. Clin Exp Allergy 2008;38:19-42.

D. Topical Pharmacologic Treatment *(Domain 1)*
   1. Intranasal antihistamines
      a. Azelastine (Astepro)
      b. Olopatadine (Patanase)

Table 17. Intranasal Antihistamines STEPS

Safety	Although topical, associated with somnolence and drowsiness
Tolerability	Abnormal taste (bitter) Postnasal drainage Sneezing
Efficacy	Less effective than intranasal corticosteroids for nasal symptoms Possibly better than systemic antihistamines for symptoms of allergic rhinitis
Preference (Pearls)	Recommended as first-line therapy for patients with mild disease Reserve for patients with a preference for non-corticosteroid treatment options or for those with mucosal irritation or nosebleeds with intranasal corticosteroids
Simplicity	Once- or twice-daily dosing

   2. Intranasal corticosteroids
      a. Beclomethasone (Beconase AQ; Qnasl)
      b. Budesonide (Rhinocort Aqua)
      c. Ciclesonide (Omnaris; Zetonna)
      d. Fluticasone (Flonase; Veramyst)
      e. Mometasone (Nasonex)
      f. Triamcinolone (Nasacort AQ-Rx; Nasacort Allergy 24 Hour-OTC)
      g. Flunisolide

Table 18. Intranasal Corticosteroids STEPS

Safety	Safe for use in pregnancy Intranasal corticosteroids are not associated with increased likelihood of fractures in postmenopausal women Conflicting evidence regarding growth deceleration in adolescents (mometasone, fluticasone, and triamcinolone approved < 6 yr)
Tolerability	Epistaxis (appears to be directly related to agent potency) Headache Cough Pharyngitis
Efficacy	Most effective treatment for seasonal and perennial allergic rhinitis Treatment of choice for patients with moderate to severe allergic rhinitis Has shown efficacy over oral/intranasal antihistamines, oral leukotriene inhibitors, and a combination of these
Preference (Pearls)	Patients may receive benefit with as-needed use, but maximal efficacy occurs when used on a schedule No intranasal steroid has been proved superior to another, so choice should be based on formulary, cost, and response to therapy
Simplicity	Once- or twice-daily dosing

E. Systemic Pharmacologic Options *(Domain 1)*
   1. Oral antihistamines, second generation
      a. Cetirizine (Zyrtec)
      b. Levocetirizine (Xyzal)
      c. Fexofenadine (Allegra)
      d. Loratadine (Claritin)
      e. Desloratadine (Clarinex)

Table 19. Oral Antihistamine, Second-Generation STEPS

Safety	Loratadine and cetirizine are FDA pregnancy category B
Tolerability	Dry mouth Headache Somnolence
Efficacy	Recommended as first-line agent, but most expert guidelines note they are ineffective for nasal congestion alone Most agents are effective for treating symptoms of seasonal or perennial allergic rhinitis Continuous use is most effective, but appropriate for PRN use
Preference (Pearls)	Second-generation agents are preferred to first-generation agents because they cause less sedation and fewer anticholinergic adverse effects All second-generation oral antihistamines are equally efficacious, except for desloratadine because it has not yet shown equal efficacy to other agents in the class Combining first-generation antihistamines (bedtime dosing) with second-generation antihistamines (daytime dosing) has not been well studied, and next-day sedation has been observed
Simplicity	Once- or twice-daily dosing Some in combination with decongestants

PRN = as needed.

   2. Oral decongestants
      a. Phenylephrine (Sudafed PE)
      b. Pseudoephedrine (Sudafed)

Table 20. Oral Decongestants STEPS

Safety	Caution in use with patients with preexisting cardiovascular disease, diabetes, hyperthyroidism, closed-angle glaucoma, or bladder neck obstruction
Tolerability	Insomnia Palpitations Irritability
Efficacy	Effective in relieving nasal congestion symptoms
Preference (Pearls)	Pseudoephedrine is preferred to phenylephrine to relieve symptoms of nasal congestion
Simplicity	Extended-release formulations Available as combination Federal regulations limit the amount of pseudoephedrine a person may purchase with a valid photo ID: 3.6 g daily or 9 g monthly

3. Leukotriene receptor antagonists
    a. Montelukast (Singulair)
    b. Zafirlukast (Accolate) – FDA-approved asthma treatment
    c. Zileuton (Zyflo) – FDA-approved asthma treatment

Table 21. Leukotriene Receptor Antagonists for Allergic Rhinitis STEPS

Safety	Neuropsychiatric disorders have been reported in postmarketing reports, but they are considered rare events
Tolerability	Headache Abdominal pain/discomfort Nasal congestion/cold-like symptoms
Efficacy	Less effective than intranasal corticosteroids, but as effective as oral antihistamines
Preference (Pearls)	May be used in combination with an oral antihistamine, but the clinical significance of this improvement is not well evaluated In general, recommended for patients who lack adequate symptom control with an oral antihistamine, intranasal corticosteroid, or combination Montelukast is approved for both rhinitis and asthma and may therefore be useful for patients with both conditions
Simplicity	Once-daily (montelukast) or twice-daily (zafirlukast, zileuton) administration Zileuton requires regular monitoring of hepatic transaminases

4. Systemic corticosteroids
    a. Oral steroids may be recommended for patients with an insufficient response to all other treatment options.
    b. Limit treatment to 5–7 days.
    c. Depot corticosteroid therapy is not recommended.
5. Allergen immunotherapy
    a. Consider for patients who have the following:
        i. Symptoms despite systemic corticosteroid therapy
        ii. An inadequate response to high-dose medication, several medications, or both
        iii. Coexisting conditions such as sinusitis, asthma, or both
    b. Provided as subcutaneous injection, sublingual tablet, or transcutaneous skin prick
        i. Effective for the treatment of allergic rhinitis
        ii. Treatment options for patients with identifiable and relevant allergens (consistent exposure) who require high doses of medications to avoid symptoms
        iii. Treatment for less than 5 years increases the chance of symptom relapse.
    c. Systemic adverse reactions have been reported in 5%–10% of individuals receiving allergen immunotherapy.
6. Other pharmacologic options
    a. Intranasal cromolyn (available only OTC as NasalCrom)
    b. Intranasal ipratropium (Atrovent)
7. Herbal medicines
    a. Butterbur (*Petasites hybridus*)
    b. Guduchi (*Tinospora cordifolia*)
    c. Green shiso (*Perilla frutescens*)
    d. Huáng qí (*Astragalus propinquus*)

VI. URTICARIA ("HIVES")

A. Professional Treatment Guidelines *(Domain 3)*
   1. American Academy of Allergy, Asthma & Immunology: the diagnosis and management of acute and chronic urticaria 2014
   2. European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network/European Dermatology Forum/World Allergy Organization (EAACI/GA(2)LEN/EDF/WAO) guideline on management of urticaria 2009
   3. British Association of Dermatologists guidelines for evaluation and management of urticaria in adults and children 2007

Table 22. Identifiable Causes of Urticaria *(Domains 1 and 3)*

Immunologic Causes	
Type 1 IgE mediated	Foods Tree nuts, legumes, shellfish, eggs, milk, soy, wheat
	Organic substances Preservatives, latex
	Medications Penicillins and penicillin-like agents, aspirin, NSAIDs
	Aeroallergens Dust mites, pollen, animal dander, molds
Type 2 cytotoxic-antibody mediated	Transfusion reaction
Type 3 antibody-antigen mediated	Serum sickness reaction
Type 4 delayed hypersensitivity	Medication, food handling, animal exposure
Autoimmune disease	Hashimoto disease, systemic lupus erythematosus, vasculitis, hepatitis
Infection	Viral, parasitic, bacterial, fungal
Nonimmunologic causes	
Physical stimuli	Exposure to sun, water, or extreme temperatures, delayed pressure, or vibration
Mast cell degranulation	Opiates, vancomycin, aspirin, radiocontrast media, dextran, muscle relaxants, bile salts, NSAIDs
Foods (histamine containing)	Strawberries, tomatoes, shellfish, cheese, spinach, eggplant

Patient Case

5. J.T. is a 13-year-old male adolescent presenting to his pediatrician with his father. It is spring, and the family has just opened the pool for the season. J.T. has been swimming daily for the past 4 days, but he has been getting out after 15 minutes because of excessive itching all over his body. His father describes J.T.'s symptoms as "giant welts" on his arms, legs, and stomach that are erythematous on the border. They cause J.T. significant discomfort, and the "welts" (wheals) last 4–6 hours. He has no significant medical history and no recent vaccinations, illness, or exposure to sick individuals. He takes no medications for chronic therapy; has not changed clothing materials, soaps, or detergents; and has no other symptoms. He once before developed these symptoms during the winter months when he was wet from playing in the melting snow. The pediatrician gives J.T. a diagnosis of acute cold urticaria and would like to prescribe a drug for him that he can take 60 minutes before swimming to decrease the chances or intensity of the symptoms. Which is the best choice of drug in this situation?

   A. Diphenhydramine 25 mg.
   B. Loratadine 10 mg.
   C. Prednisone 50 mg.
   D. Famotidine 10 mg.

B. Additional Causes May Include the Following: *(Domains 1 and 3)*
   1. Alcohol
   2. Connective tissue diseases
   3. Menses
   4. Stress

C. Physical Presentation and Evaluation *(Domain 1)*
   1. Well-defined wheals on the skin
      a. Pruritic with or without burning sensation
      b. Central swelling with or without surrounding erythema
      c. Skin returns to "normal" within 24 hours.
   2. When collaborating with a diagnostician, be sure to rule out dermatologic reactions that are more serious.
   3. Consider some testing if the cause is not readily identifiable (American College of Allergy, Asthma, and Immunology).
      a. Complete blood cell count
      b. Erythrocyte sedimentation rate
      c. Urinalysis
      d. Liver function testing

D. Nonpharmacologic Treatment *(Domains 1 and 2)*
   1. Discontinue and avoid triggers to urticarial reactions.
   2. When a trigger is unavoidable and the result is severe (e.g., exercise induced, cold induced), use pharmacologic treatment options to prevent symptoms and ensure that patient is not alone.

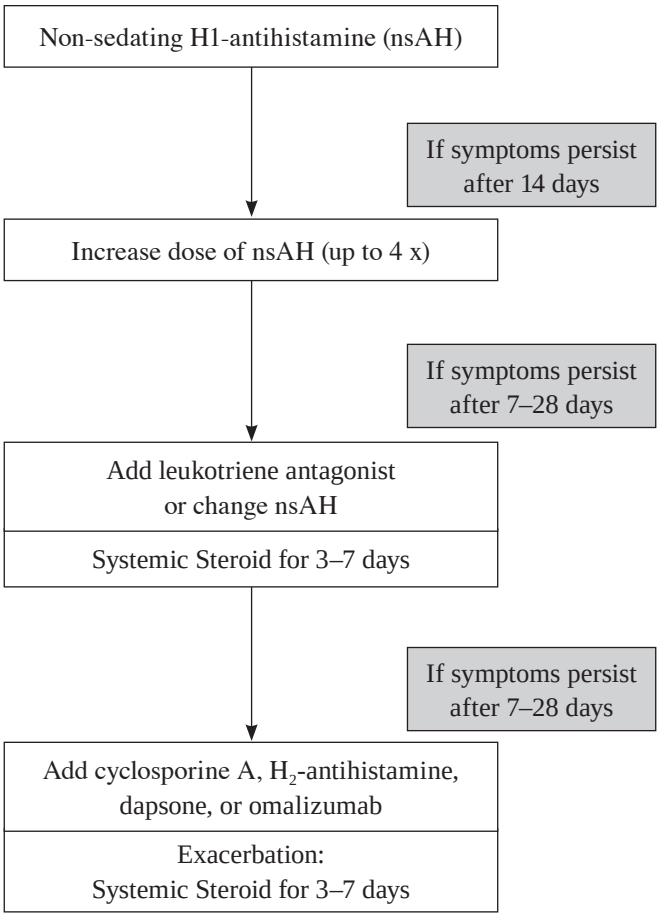

Figure 3. Urticaria treatment algorithm.
Source: EAACI/GA2LEN/EDF/WAO guideline: management of urticaria. Allergy 2009;64:1427-43.

E. Pharmacologic Options *(Domain 1)*
   1. All professional treatment guidelines recommend a nonsedating histamine-1 (H_1) antihistamine (nsAH) as first-line therapy.
   2. In patients with an inadequate response to an nsAH, consider adding the following:
      a. First-generation (sedating) H_1 antihistamine
      b. Histamine-2 (H_2) receptor antagonist
      c. Corticosteroids
      d. Tricyclic antidepressants
      e. Leukotriene modifier
   3. First-line options: nsAHs – Loratadine (Claritin), cetirizine (Zyrtec), fexofenadine (Allegra), levocetirizine (Xyzal), desloratadine (Clarinex)

Table 23. Nonsedating H_1 Antihistamine STEPS

Safety	In pregnancy, loratadine and cetirizine are FDA pregnancy category B
Tolerability	Dry mouth Headache Somnolence
Efficacy	Appears that most agents in this class are equally effective for treating urticaria, though few head-to-head comparisons exist
Preference (Pearls)	May need to increase dose to greater than recommended (up to 4 times) to achieve desired effect
Simplicity	Once-daily dosing with limited adverse drug reactions Available OTC

4. Second-line or additional options
   a. (First-generation) H_1 antihistamines – Diphenhydramine (Benadryl), chlorpheniramine (Chlor-Trimeton), clemastine (Tavist Allergy), hydroxyzine (Atarax), cyproheptadine

Table 24. (First-Generation) H_1 Antihistamine STEPS

Safety	Contraindications in pregnancy (hydroxyzine) or breastfeeding (diphenhydramine) Chlorpheniramine is FDA pregnancy category C
Tolerability	Excessive sedation Discoordination Dry mouth or secretions (anticholinergic adverse effects)
Efficacy	As effective as the nonsedating antihistamines for treating urticaria
Preference (Pearls)	N/A
Simplicity	Require many daily doses Most available OTC

   b. H_2 antagonists – Ranitidine (Zantac), famotidine (Pepcid), nizatidine (Axid), cimetidine (Tagamet)

Table 25. H_2 Antagonists

Safety	Associated with an increased risk of developing community-acquired pneumonia
Tolerability	Constipation or diarrhea Dizziness Headache
Efficacy	Significant increase in resolution when added to histamine-1 (H_1) antagonist
Preference (Pearls)	Not justified to add to nsAH therapy initially Reserve for patients whose condition does not sufficiently respond to nsAH or (first-generation) H_1 antihistamine
Simplicity	Once- or twice-daily dosing Available OTC

nsAH = nonsedating H_1 antihistamine.

c. Corticosteroids (short-term or "burst" therapy)

Table 26. Corticosteroid (burst) STEPS

Safety	Gastrointestinal toxicity Prolonged use increases risk of osteoporotic fracture
Tolerability	Acute hyperglycemia Appetite changes Mood and sleep disturbance
Efficacy	May expedite time to remission (< 3 days) for patients with acute urticaria
Preference (Pearls)	Studied doses were 50 mg of prednisone daily for 3 days, but may be possible to use lower doses Follow with H_1 receptor antagonist
Simplicity	Once-daily dosing for 3–7 days, followed by step-up therapy

5. Other agents to consider
   a. Tricyclic antidepressants (doxepin, oral) – May use doses of up to 75 mg daily for patients with insufficient response to H_1 receptor antagonists
   b. Leukotriene modifier – Inconsistent evidence from small-scale studies to support use of montelukast and zafirlukast in urticaria
   c. Omalizumab is an FDA-approved treatment for chronic, refractory idiopathic urticaria in patients 12 years and older who remain symptomatic despite H_1 antihistamine treatment. Cyclosporine also has evidence supporting its use in these patients.

VII. ANGIOEDEMA

A. Professional Treatment Guidelines *(Domain 3)* – 2012 International Collaboration in Asthma, Allergy and Immunology consensus document on hereditary and acquired angioedema

B. Classification of Angioedema *(Domain 1)*
   1. Acquired component (C)1 inhibitor (C1 INH) deficiency
   2. Allergic
   3. Hereditary angioedema (HAE) type 1 – Low C1 INH values and function; type II – Normal C1 INH values but low function
   4. Idiopathic
   5. Medication induced

C. Risk Factors and Patient Presentation *(Domains 1 and 2*)
   1. Typically caused by exposure to the following:
      a. Foods: Peanuts, tree nuts, wheat, eggs, milk, seafood
      b. Medications: Angiotensin-converting enzyme (ACE) inhibitors, fibrinolytics, NSAIDs, oral contraceptives, paroxetine, or risperidone
         i. NSAIDs may be most likely to cause angioedema.
         ii. Angioedema occurs in less than 1% of the population using ACE inhibitors (occurs more commonly in ACE inhibitor users who are female, smokers, or of African American descent).

2. May not require instigation and may be strictly hereditary
    a. C1 INH
    b. Estrogen-related HAE
3. Other risk factors include the following:
    a. African American race
    b. History of drug rash or seasonal allergies
    c. Patients older than 65 years
4. Patients will present with the following:
    a. Skin swelling that may occur on the body
        i. Mucus membranes are usually involved.
        ii. ACE inhibitor–induced angioedema will present only on the face, lips/mouth, and tongue.
    b. Urticaria
    c. Dyspnea, wheezing, or both
    d. Others that occur less than 10% of the time: Nasal congestion, pain, loss of consciousness (or fainting), and abdominal pain

D. Diagnostic Evaluation *(Domain 1)*
1. C1 INH deficiency screening
2. C4 complement will help if C1 INH deficiency screening is unremarkable and angioedema continues.
3. In patients with other suspected rheumatologic conditions, may consider checking the following:
    a. Antinuclear antibody
    b. Rheumatoid factor
    c. C3/C4 complement
    d. C1q antibodies

E. Treatment Strategies *(Domains 1 and 2)*
1. Remove patient from instigating factor.
2. Emergency care (if needed)
    a. Rapid fluid replacement (1–2 L of normal saline)
    b. Epinephrine (0.2–0.5 mg intramuscularly) every 5–10 minutes, as needed
    c. Diphenhydramine (25–50 mg intravenously or intramuscularly)
    d. Ranitidine (50 mg intravenously) administered for 5 minutes
    e. Systemic corticosteroids may be included, but use not supported with evidence
3. Acute symptoms (but not emergency) may be treated with nonsedating antihistamines.
4. Plasma-derived C1 INH (Berinert or Cinryze)
5. Recombinant C1 INH (Ruconest)

Patient Case

6. C.R. is a 13-year-old male adolescent with HAE. He was given the diagnosis at 6 years of age and has episodes of laryngeal edema and constriction about once a year. He has icatibant at home that he is supposed to take each time he begins to have these symptoms. After the medication is administered, which is the next best step for him (and his family) to follow?

    A. Immediately seek emergency medical care.
    B. Take diphenhydramine 25–50 mg and closely monitor symptoms.
    C. Begin taking prednisone 40 mg and continue once daily for the next 14 days.
    D. If syncope occurs, lie down on a flat surface.

Table 27. Plasma-Derived C1 Inhibitor STEPS

Safety	Thrombosis/thrombotic event Severe hypersensitivity reactions during or after administration Donor screening required to reduce likelihood of bloodborne disease transmission	
Tolerability	Abdominal pain Dizziness Erythema	Headache Nausea
Efficacy	Used for the routine prophylaxis of HAE (Cinryze) or the acute management of angioedema (Berinert)	
Preference (Pearls)	Patients may self-administer both of these medications with training and instruction If patients administer the medication for an acute episode of angioedema, they should then seek immediate medical attention	
Simplicity	Estimated to cost $5000 every 3–4 days for prophylaxis	

HAE = hereditary angioedema.

Table 28. Recombinant C1 Inhibitor STEPS

Safety	Contraindicated in patients allergic to rabbits Arterial/venous thrombosis events Severe hypersensitivity reaction may occur (can mimic HAE attack)
Tolerability	Headache, nausea, and diarrhea
Efficacy	Used for acute attacks in adult and adolescent patients with HAE
Preference (Pearls)	Patients may self-administer with training and instruction After administration, the patient should seek immediate medical attention Patient assistance program available
Simplicity	Available as powder that must be reconstituted for injection in a single-use vial

6. Selective bradykinin B_2 receptor antagonist (Icatibant [Firazyr])

Table 29. Selective Bradykinin B_2 Receptor Antagonist STEPS

Safety	Acute airway obstruction may occur during HAE May attenuate the antihypertensive effects of ACE inhibitors	
Tolerability	Injection-site reaction (97% of patients) Increased transaminase values	Pyrexia
Efficacy	Used in the treatment of HAE	
Preference (Pearls)	If patients administer the medication for an acute episode of angioedema, they should then seek immediate medical attention	
Simplicity	Should be injected subcutaneously in the abdomen, 2–4 inches below the umbilicus, with a 25-gauge needle Inject for ≥ 30 s 30-mg dose costs around $8900	

ACE = angiotensin-converting enzyme.

7. Kallikrein inhibitor (Ecallantide [Kalbitor])

Table 30. Kallikrein Inhibitor STEPS

Safety	FDA black box warning: Serious hypersensitivity reactions, including anaphylaxis	
Tolerability	Diarrhea Fatigue Fever	Headache Nausea Upper respiratory tract infection
Efficacy	For use in the acute management of HAE attack	
Preference (Pearls)	Must be administered in the presence of a medical provider because of the risk of a hypersensitivity reaction	
Simplicity	Three doses (10 mg/mL/dose) given subcutaneously in the abdomen, upper arm, or thigh Separate injections by 2 inches; rotation of injection sites is not necessary About $4200 per 10-mg/mL dose	

8. Other considerations for patients who have more than one severe event per month include the following:
   a. 17-α-Alkylated androgens: Recommended only at the lowest dose that decreases attack frequency because the efficacy may be offset by the likelihood of adverse events
   b. Antifibrinolytics: Less efficacious than 17-α-alkylated androgens for long-term treatment
9. Recommend the hepatitis B vaccine series for any person who will be receiving human blood products to manage HAE.

F. Patient Information: U.S. Hereditary Angioedema Association (www.haea.org)

VIII. ACNE

A. Professional Treatment Guidelines *(Domain 3)*
   1. Guidelines of care for acne vulgaris management; American Academy of Dermatology (AAD) 2016
   2. Global Alliance to Improve Outcomes in Acne Group guideline on management of acne 2009

B. Types of Acneiform Presentation *(Domain 1)*
   1. Acne conglobata – Burrowing and interconnecting abscesses and irregular scars
   2. Acne mechanica – Lesions on areas of friction from protective sports gear
   3. Acne rosacea – Erythema and telangiectasias without comedones
   4. Comedogenic acne – Many comedones with minimal inflammation
   5. Common acne – Variety of pustules and comedones
   6. Cystic acne – Cystic presentation with infection, leading to scars

Table 31. Factors Associated with Developing Acne

Hormone Abnormalities or Fluctuations	Physical Occlusion or Damage	Medications
Excess androgen in men Menstruation Pregnancy Stress	Cosmetics Excessive exfoliation Occlusive dressings/bodyguards Pimple popping	Anabolic steroids Azathioprine Corticosteroids Cyclosporine Lithium Phenytoin Vitamin B_1, B_6, B_{12}

C. Presentation and Diagnosis *(Domain 1)*
   1. Open (blackhead) and/or closed (whitehead) comedones
   2. Pustules or papules at the core
   3. Usually on upper torso, neck, face, and back
   4. Distribution of comedones, physical presentation, and associated risk factors aid in acne classification.

D. Additional Testing *(Domain 1)*
   1. Not necessary unless trying to rule out hyperandrogenism
   2. Endocrinologic evaluations
      a. Testosterone, free
      b. Dehydroepiandrosterone sulfate
      c. Luteinizing hormone
      d. Follicle-stimulating hormone

E. Treatment *(Domains 1 and 2)*
   1. Nonpharmacologic interventions
      a. None has proved drastically effective for improving acne.
         i. Avoid popping pimples.
         ii. Face washing with non-comedogenic soap
         iii. Sunlight exposure
      b. Dietary changes (e.g., avoiding chocolate, fatty foods) have not been shown to improve or prevent acne.
      c. Severity classification will guide therapy choices.

Table 32. Classification of Acne Severity

Severity	Definition
Mild	< 20 comedones OR < 15 inflammatory lesions OR < 30 total lesions
Moderate	20–100 comedones OR 15–50 inflammatory lesions OR 30–125 total lesions
Severe	> 5 cysts OR Total comedone count > 100 OR Total inflammatory lesion count > 50 OR > 125 total lesions

	Mild	Moderate	Severe
First choice	TR or BPO -OR- Topical combination therapy[a]: TR + BPO *or* BPO + tATB *or* TR + BPO + TA	Topical combination therapy[a]: BPO + TA *or* TR + BPO *or* TR + BPO + TA -OR- OA + TR + BPO *or* OA + TR + BPO + TA	OA + topical combination therapy [a]: BPO + TA *or* TR + BPO + TA -OR- OI
Alternatives	Add TR or BPO (if not already taking) -OR- Consider alternative TR -OR- Consider topical dapsone	Consider alternative combination therapy -OR- Consider change in OA -OR- Add combined OAAn (females) -OR- Consider OI	Consider change in OA -OR- Add combined OAAn (females) -OR- Consider OI

Figure 4. Acne treatment algorithm.

aIndicates that the medication may be prescribed as a fixed combination product or a separate component.

BPO = benzoyl peroxide; OA = oral antibiotic; OAAn = oral antiandrogenic; OI = oral isotretinoin; TA = topical antimicrobial; TR = topical retinoid.

Adapted from: Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol 2016;74:945-73.

Additional graphic algorithm available in: Dreno B, Bettoli V, Ochsendorf F, et al. An expert view on the treatment of acne with systemic antibiotics and/or oral isotretinoin in the light of the new European recommendations. Eur J Dermatol 2006;16:565-71.

2. Pharmacologic interventions (mild to moderate acne)
    a. Retinoids, topical
        i. Adapalene (Differin, Differin XP)
        ii. Tazarotene (Tazorac)
        iii. Tretinoin (Avita, Retin-A)

Table 33. Topical Retinoids STEPS

Safety	Significant photosensitivity and sunburn risk Topical retinoids should be avoided in pregnancy, and women of childbearing age should use adequate contraception (two different methods are recommended [i.e., barrier and hormonal])
Tolerability	All versions are irritating to skin, but some preparations appear to be more tolerable because of formulation (microspheres) Use of other OTC medications may increase irritation (salicylic acid scrubs or astringents)
Efficacy	Reduce the presence of mild to moderate noninflammatory lesions Used in combination with topical antibiotics and benzoyl peroxide, considerably increases likelihood of lesion changes with no additional adverse events May take up to 3 mo to see an effect, and therapy should be continued until no new lesions develop Often used as maintenance therapy after discontinuing oral agents
Preference (Pearls)	Recommended as first-line therapy and the foundation for treatment of all forms/severity levels of acne except severe (nodular/conglobate) acne May see an initial worsening of symptoms, but they usually resolve in 2–4 wk Patients should use at least SPF 15 sunscreen for outdoor activities Counsel patients that their skin may be more sensitive to weather extremes (wind, cold) Not recommended to be used as spot therapy; divide into four equal aliquots and smooth over entire face Tretinoin unstable in UV light and with benzoyl peroxide; non-issue with adapalene Differin (adapalene) 0.1% available OTC
Simplicity	Once-daily application, in the evening

OTC = over-the-counter; SPF = sun protection factor.

b. Antimicrobials, topical
   i. Clindamycin
   ii. Erythromycin

Table 34. Topical Antimicrobial STEPS

Safety	Pseudomembranous colitis and hypersensitivity reactions have rarely been reported (less than 1%) in patients using clindamycin	
Tolerability	Dry skin Erythema	Itching Scaling or peeling
Efficacy	Best efficacy when used in combination with topical retinoids and/or benzoyl peroxide Clindamycin 1% solution or gel is the preferred topical antibiotic for acne treatment; topical erythromycin 2% has reduced efficacy because of resistance	
Preference (Pearls)	Used predominantly for the treatment of mild to moderate inflammatory or mixed acne If patients are using the topical clindamycin foam, dispense the dose into the cap or onto a cool surface and then administer small amounts to the affected area Because of concerns of *Propionibacterium acnes* resistance, should never be used as monotherapy	
Simplicity	Available co-formulated with benzoyl peroxide May be applied once or twice daily after facial cleansing	

c. Benzoyl peroxide, topical

Table 35. Benzoyl Peroxide STEPS

Safety	May disfigure skin with edema, blistering, and crusting Photosensitivity to UV light	
Tolerability	Dry skin Pruritus	Scaling of skin Skin bleaching
Efficacy	Bactericidal against *P. acnes* and therefore provides benefit to individuals with both comedonal and inflammatory acne Efficacy comparable with that of tetracycline and minocycline without evidence of bacterial resistance No resistance has been reported	
Preference (Pearls)	Used in combination with oral or topical antimicrobials because of concerns about resistance For patients experiencing skin irritation secondary to benzoyl peroxide use, decrease the frequency of application or temporarily discontinue until irritation resolves Counsel patients to wash away the drug after a few hours to help skin grow to tolerate its presence 10% lotion/gel is only minimally better than 2.5% and 5% preparations and is much less tolerated Will cause discoloration/bleaching of fabric (e.g., pillowcases, towels) that come in contact with the face or treated area	
Simplicity	Twice-daily application Co-formulated with other topical acne treatment options, including adapalene, clindamycin, and erythromycin	

d. Azelaic acid cream, 20% topical (Azelex) – (Azelaic acid 15% gel [Finacea] is FDA approved for treatment of rosacea.)

Table 36. Azelaic Acid STEPS

Safety	Avoid contact with eyes or other mucous membranes
Tolerability	Skin irritation (e.g., burning, stinging) is reported in a few individuals Isolated reports of hypopigmentation with use
Efficacy	Reported to possess comedolytic and antibacterial properties Mildly effective as a comedolytic, antibacterial, and anti-inflammatory agent Once-daily application is equal to twice-daily application for treatment response Adding it to topical antimicrobials and/or cleansers is more effective than using either component alone
Preference (Pearls)	Despite success in clinical trials, experts believe the drug has limited efficacy and applicability for treating acne If patients experience continual skin irritation with twice-daily use, decrease the dose to once daily or discontinue use until the irritation resolves May cause skin lightening in individuals with darker skin pigmentation or postinflammatory hyperpigmentation
Simplicity	Applied to skin once or twice daily

e. Oral contraceptives (estrogen containing)

Table 37. Oral Contraceptives for Acne STEPS

Safety	VTE risk Estrogen dose directly related to VTE (doses > 30 mcg associated with higher risk of VTE) Levonorgestrel appears to be a progestin least associated with VTE; levonorgestrel (second generation) < drospirenone (fourth generation) < desogestrel (third generation) Premenopausal breast cancer risk Cervical cancer risk Cerebrovascular disease risk Smoking after age 35 yr increases risk of VTE
Tolerability	Abnormal vaginal bleeding Headaches Abdominal cramping
Efficacy	Reduced severity of inflammatory and noninflammatory acne
Preference (Pearls)	Recommended for use as an alternative agent for women with moderate to severe acne Low to moderate dose of ethinyl estradiol (20–35 mcg) appears to be the target dose Second- and third-generation progestins have the least androgenic activity Drospirenone (fourth generation) appears to have antiandrogenic activity Patient should have annual health evaluations while using oral contraceptives, including a Papanicolaou smear and a physical examination Smoking cessation counseling for patients who smoke or use cigarettes infrequently at bars, recreational events, or social gatherings May be used to treat other conditions, including dysmenorrhea and polycystic ovarian syndrome May be used to prevent pregnancy in patients using isotretinoin
Simplicity	Once-daily dosing

VTE = venous thromboembolism.

f. Dapsone 5% topical gel (Aczone)

Table 38. Topical Dapsone STEPS

Safety	Associated concerns are much less severe with topical dapsone therapy than with oral dapsone therapy Changes suggestive of mild hemolysis have been observed in some patients with G6PD deficiency who are using dapsone gel Photosensitivity
Tolerability	Oiliness/peeling Dryness Erythema
Efficacy	Significantly higher reductions in inflammatory lesions, noninflammatory lesions, and total lesions at 6 and 12 wk than with placebo
Preference (Pearls)	Still undergoing studies that evaluate long-term efficacy as monotherapy and safety when combined with other anti-comedonal agents Localized discoloration of the skin and facial hair (yellow or orange) if benzoyl peroxide is used after dapsone gel
Simplicity	Apply only a small amount (pea size) to skin and gently rub in Patients may notice gritty appearance or particles after application

G6PD = glucose-6-phosphate dehydrogenase.

g. Salicylic acid, topical

Table 39. Salicylic Acid STEPS

Safety	Risk of salicylate toxicity when topical therapy is used for a long period on a large surface area of the body
Tolerability	Excessive erythema and/or peeling of the skin Scaling of skin Burning Contraindicated if patient has used isotretinoin therapy within the past 6 mo
Efficacy	Comedolytic properties are considered less potent than those of topical retinoids
Preference (Pearls)	Used when patient has skin irritation with a topical retinoid
Simplicity	Many topical application choices including gel, foam, pads, patches, and liquid cleansers Several times per day application (three or four times daily) Available to patients OTC

Patient Case

7. D.M. is a 17-year-old male adolescent with inflammatory nodular acne on his face, shoulders, and back that becomes increasingly irritated during football season secondary to friction from his helmet strap and shoulder pads. His current acne medications include an oral antibiotic, a topical retinoid, and benzoyl peroxide. He is beginning to develop scarring because of this irritation and would like something new. Which is the best alternative regimen for the patient to try?

   A. Oral isotretinoin.
   B. Topical retinoid plus azelaic acid.
   C. Oral antiandrogen (spironolactone).
   D. Topical retinoid plus topical antibiotic.

h. Other topical agents to consider
   i. Spironolactone 50–200 mg orally
   ii. Gluconolactone (α-hydroxy fruit acid) 14%

3. Pharmacologic interventions (moderate to severe acne)
   a. Combination treatment should be used to target as many of the pathophysiologic mechanisms of acne as possible.
      i. Improves acne resolution efficacy
      ii. Increases speed of lesion healing/resolution
      iii. Decreases the chance of antibiotic resistance
   b. Oral antibiotics should be used in combination with topical retinoids, benzoyl peroxide, or both.
   c. Oral antibiotics (tetracycline, doxycycline, minocycline)

Table 40. Oral Antibiotics for Acne STEPS

Safety	Tooth discoloration and enamel hypoplasia in children < 8 yr (tetracyclines) Fetal and infant toxicity (tetracyclines and SMZ/TMP) Photosensitivity
Tolerability	Nausea Vomiting Diarrhea
Efficacy	Used for moderate to severe acne Minocycline, doxycycline, tetracycline, and erythromycin are all efficacious for acne symptoms The AAD recommends reserving oral antibiotics for moderate to severe inflammatory acne and limiting the duration of use, when possible Because of potential for bacterial resistance, benzoyl peroxide should be added to any regimen with an oral antibiotic
Preference (Pearls)	Minocycline and doxycycline are more effective than tetracycline, but neither is superior Save erythromycin and azithromycin for patients who receive a recommendation against using tetracyclines (e.g., pregnancy, < 8 yr) Bacterial resistance most commonly reported with erythromycin TMP/SMZ or TMP alone may be used for individuals who cannot use the above-mentioned oral antibiotics Use of systemic antibiotics other than the tetracyclines and macrolides is discouraged because data are limited for their use in acne Patients may try probiotics or yogurt to prevent vaginal candidiasis, but evidence for efficacy is inconclusive
Simplicity	Once- or twice-daily dosing Oral formulations Available agents are less expensive than other agents (non-contraceptives) for moderate to severe acne

TMP/SMZ = trimethoprim/sulfamethoxazole.

d. Isotretinoin, oral (Claravis, Amnesteem, Sotret)

Table 41. Isotretinoin STEPS

Safety	Highly teratogenic (iPledge program) Suicidal ideations Pancreatitis
Tolerability	Hypertriglyceridemia Arthralgias, myalgias Possible scarring Excessive drying of skin and/or mucus membranes
Efficacy	Approved for the treatment of severe recalcitrant nodular acne Effectively reduces inflammatory lesions and acne cysts Reserved for severe acne, treatment-resistant acne, or acne resulting in physical or psychological scarring
Preference (Pearls)	iPledge program is for prescribers, distributors, patients, and pharmacists (see below) All pregnancies need to be referred to a reproductive toxicity specialist for evaluation Treat for up to 20 wk and discontinue sooner if acne resolution is ≥ 70% Prescriptions should only be for a 1-mo supply and should be filled within 7 days of prescription date Oral retinoids carry the same risk of sunburn as the topical retinoids, so recommend sunscreen (at least SPF 15) for all patients during outdoor activities Patients should be instructed not to donate blood during treatment and for 1 mo after discontinuing treatment
Simplicity	Once- or twice-daily dosing Weight-based dosing (0.5–1 mg/kg divided) Requires monthly monitoring for complete blood cell count (with differential), glucose, lipids, creatine phosphokinase, liver function, and psychiatric/mood changes

SPF = sun protection factor.

F. iPledge Program (www.ipledgeprogram.com)
   1. Single resource for all individuals and businesses involved with isotretinoin to document patient safety data
   2. Wholesalers, pharmacies, prescribers, and patients must enroll in the program.
   3. Creates a single resource to create a "verifiable link between the negative pregnancy test and the dispensing of the isotretinoin prescription to the female patient of childbearing potential"
   4. Requires monthly provider documentation that a patient has been counseled on the risks of isotretinoin therapy
   5. Before starting therapy, iPledge requires two consecutive blood or urine test results to be negative for pregnancy.
   6. Patients commit to using two forms of contraception 1 month before, throughout, and 1 month after therapy with isotretinoin.
   7. The above information must be documented monthly in the iPledge online recordkeeping program.

G. Supportive Therapy
   1. Discuss therapeutic expectations – Up to 6 weeks for decreased or resolved symptoms
   2. During the first 4–8 weeks of therapy, the patient's acne may worsen, but it will improve or resolve with time.
   3. Remind the patient of appropriate hygiene (though not a contributor to acne), moisturizers, and sunscreen.
   4. Psychological counseling has weak evidence for a possible benefit.

IX. PSORIASIS

A. Professional Treatment Guidelines – AAD Guidelines on Management of Psoriasis and Psoriatic Arthritis (J Am Acad Dermatol 2008;58:851-64) *(Domain 3)*

B. Types of Psoriasis *(Domain 1)*
   1. Plaque psoriasis (most common; about 80%–90% of cases)
   2. Pustular psoriasis (von Zumbusch variant)
   3. Guttate psoriasis
   4. Erythrodermic psoriasis (life-threatening emergency)
   5. Inverse psoriasis

Patient Case

8. J.W. presents to his primary care provider's office for his annual physical examination. He is a 25-year-old man with a medical history significant for bipolar disease with rapid cycling. His medications include quetiapine, valproic acid, sertraline, and lithium. Today, he presents with new, itchy, and painful skin lesions on his knees. He was involved in a car accident about 12 months ago, which resulted in several contusions on his upper legs from hitting the dashboard. Since then, lesions have developed, and he asks his primary care provider to identify them. The patient is given a diagnosis of psoriasis, and the provider believes the patient's mental health agents may be contributing to the development of these lesions. Which agent is most likely causing the psoriatic lesions?
   A. Quetiapine.
   B. Valproate.
   C. Sertraline.
   D. Lithium.

C. Factors Associated with Developing Psoriasis *(Domains 1 and 2)*
   1. Various genetic factors, as evidenced by the higher incidence reported between first- and second-degree relatives and monozygotic twins
   2. Skin trauma, concurrent skin disorders, and infection are environmental factors that affect the onset of psoriasis.
   3. Smoking is also a predisposing factor to developing psoriasis.
   4. Medication induced (NAILS)
      a. NSAIDs
      b. Antimalarials or ACE inhibitors
      c. Inderal (and other β-blockers)
      d. Lithium
      e. Steroid withdrawal

D. Medical Comorbidities Associated with Psoriasis *(Domains 1 and 2)*
   1. Autoimmune disease
   2. Cardiovascular disease
   3. Metabolic syndrome
   4. Lymphoma, melanoma, and nonmelanoma skin cancer
   5. Depression/suicide

E. Presentation and Diagnosis – Chronic Plaque Psoriasis *(Domain 1)*
   1. Red, raised scaly patches with well-defined borders that are symmetric
   2. Lesions may begin to form after an acute skin injury (Koebner phenomenon)
   3. May occur anywhere on the skin, including the following:
      a. Arms and legs
      b. Buttocks
      c. Genitals
      d. Palms/soles
      e. Scalp
      f. Trunk
      g. Face
   4. About 50% of patients will have evidence of fingernail involvement (and 35% will have toenail involvement).
   5. Diagnosis is usually made by visualizing the lesions, and testing is rarely indicated.
   6. PASI (Psoriasis Area Severity Index) commonly used in clinical trials to assess psoriasis, but not routinely used in clinical practice

F. Pretreatment Evaluation *(Domain 1)*
   1. Classified as mild, moderate, or severe on the basis of percentage of body involvement
      a. Mild: Less than 3% of the body
      b. Moderate: 3%–10% of the body
      c. Severe: Greater than 10% of the body
   2. Given the potential agents for treating, may consider the following:
      a. Metabolic profile
      b. Complete blood cell count
      c. Hepatic function panel
      d. Hepatitis and tuberculosis evaluation

G. Treatment Options – Nonpharmacologic *(Domains 1 and 2)*
   1. Smoking cessation
   2. Saline spa water therapy (limited efficacy)
   3. UV radiation/phototherapy (UVB or UVA) for psoriasis cases that fail to respond to topical treatments
   4. Moisturizers

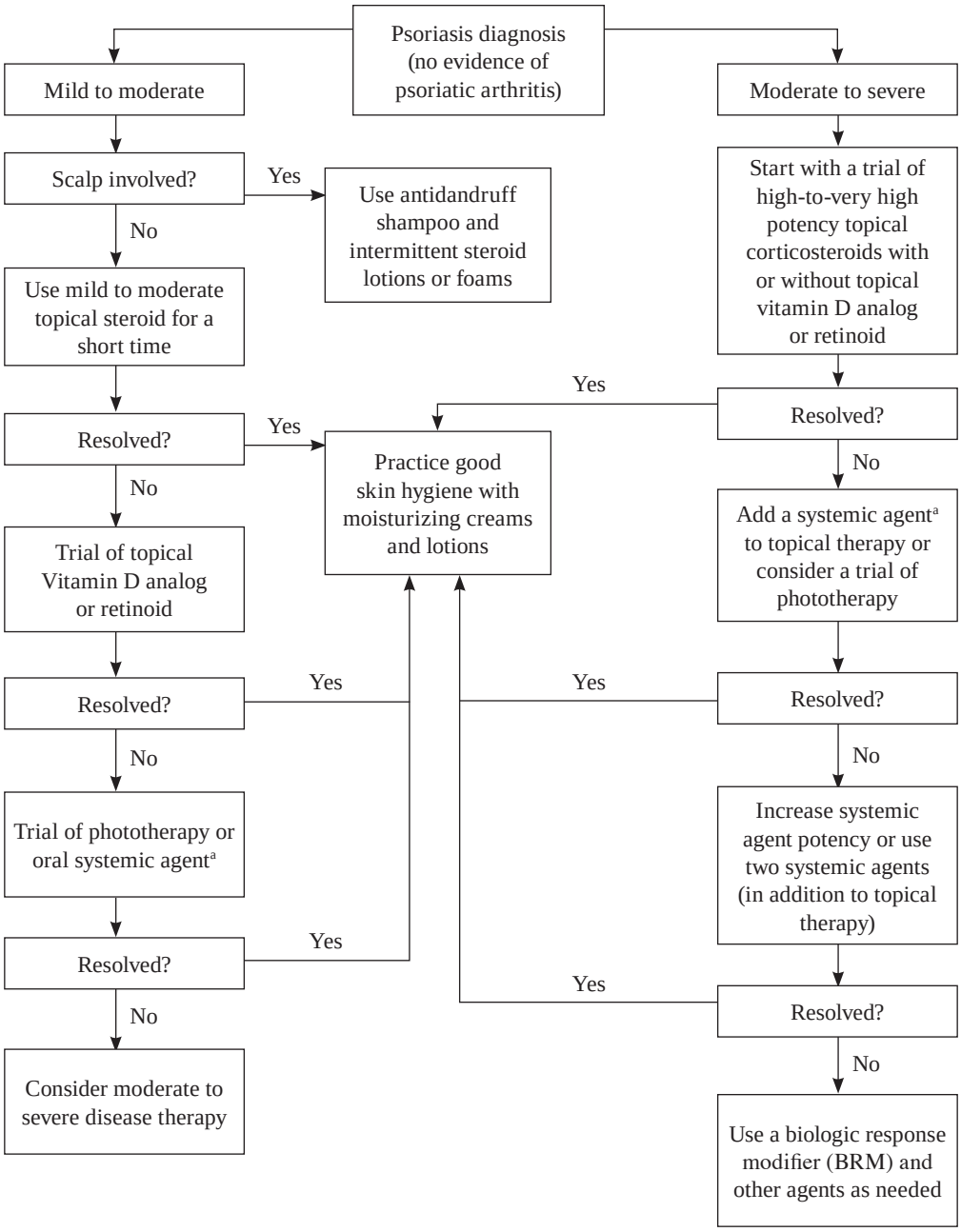

Figure 5. Psoriasis treatment algorithm.

[a]Systemic agents include T-cell inhibitors and tumor necrosis factor inhibitors.

BRM = biologic response modifier.

H. Pharmacologic Agents *(Domain 1)*
   1. Topical therapy and targeted phototherapy are the first choice for mild to moderate disease (accounts for around 80% of cases).
   2. For extensive, severe, disabling, or plaque psoriasis, systemic therapy may be necessary to control symptoms.
   3. Consider biologic agents for moderate to severe disease or for patients whose response to topical or targeted phototherapy is insufficient.
   4. Considerations with topical agents. Choice of vehicle will alter medication penetration and relative efficacy – The optimal choice is usually the vehicle the individual patient will most likely use. Consider patient preference and limitations with each dosing vehicle.
      a. Hair-bearing areas may be best treated with foams, shampoos, gels, and sprays because these are less likely to leave a residue on the hair.
      b. Creams are ideal for daytime application because they are less likely to glisten and stain clothes.
      c. Consider ointments for nighttime application because they have less cosmetic appeal.
      d. Dosing recommendations using "fingertip units" (ribbon of cream/ointment from tip of finger to distal-interphalangeal joint) – One fingertip unit is about 500 mg.

Table 42. FTU Needs to Various Anatomic Regions

Area	FTUs[a]	Area	FTUs[a]
Scalp	3	Leg (one)[b]	8
Face and neck	2.5	Buttocks	4
Hand (one)[b]	1	Knees	1
Arm (one)[b]	4	Trunk	8
Elbows	1	(anterior)	8
Both soles	1.5	Trunk	0.5
Foot (one)[b]	1.5	(posterior)	
		Genitalia	

[a]Two FTUs are about 1 g of topical agent.

[b]Includes anatomy peripheral to noted site (i.e., arm includes hands and fingers).

FTU = fingertip unit.

   5. Corticosteroids, topical
      a. Cornerstone of treatment for most patients with psoriasis, particularly those with limited disease
      b. Many topical corticosteroids are classified as having several potencies, depending on their percentage concentration, application vehicle, and formulation.
      c. The AAD classifies corticosteroids from the Stoughton-Cornell classification system (1–7).
         i. 1 = superpotent and 7 = least potent
         ii. Potency is defined by vasoconstrictive, not anti-inflammatory, properties.

Table 43. Topical Corticosteroid STEPS

Safety	Skin atrophy Telangiectasia Striae distensae Exacerbation of dermatologic infections (rosacea, tinea infections)
Tolerability	Pustular or vesicular lesions Hyperesthesia Telangiectasia
Efficacy	Treatment of choice for patients with mild to moderate psoriatic disease Efficacy rates vary widely, even among agents in the same potency class (41%–92%) Ultra–high-potency agents or ointment-based preparations are associated with greater efficacy
Preference (Pearls)	Corticosteroids are as effective as the vitamin D analogs, but with fewer adverse drug reactions To minimize adverse reactions and maximize adherence, application site needs to be considered in choosing the appropriate corticosteroid potency As clinical use continues, reduce potency or agent use to the minimal required for a clinical response Taper (do not abruptly discontinue) to avoid psoriasis rebound Limit ultra–high-potency topical steroids to 50 g weekly for up to 2–4 wk
Simplicity	Once- or twice-daily local application May be used in conjunction with occlusive therapy to boost efficacy for low to medium potency Can be combined with other topical agents, UV light, and systemic agents

6. Vitamin D analog, topical (calcipotriene – Dovonex ; calcitriol – Vectical)

Table 44. Vitamin D Analog STEPS

Safety	Photosensitivity and an increased risk of UV-induced skin tumors Acute psoriatic eruptions of the scalp with direct application Topical solution and foam are flammable (51% isopropyl alcohol) Appears safe for pediatric use (studied in ages 2–14 yr)
Tolerability	Hypercalcemia (applying > 100 g weekly) Worsening psoriasis Skin irritation
Efficacy	Calcipotriene is as effective as topical corticosteroids, but with more frequent adverse drug reactions Greatest efficacy when used in combination with betamethasone (combination product available)
Preference (Pearls)	Recommend use in combination with topical corticosteroid for added efficacy NOT contraindicated for use with UVB phototherapy; however, inactivated by UVA; apply after, not before, UVA exposure
Simplicity	Twice-daily application to affected areas; not to exceed 30% of body surface area

7. Retinoid, topical (tazarotene – Tazorac)

Table 45. Topical Retinoid STEPS

Safety	Pregnancy category X Photosensitivity
Tolerability	Increased sensitivity to environmental factors (wind, cold, heat) Skin burning, stinging, irritation
Efficacy	Achieves > 50% improvement in symptoms at 12 wk in about half of treated patients
Preference (Pearls)	Recommended to use with topical corticosteroids for improved efficacy and improved tolerability To reduce the incidence of irritation: Use cream formulation Use the lower-concentration product Combine use with moisturizers Apply on alternating days Limit exposure (30–60 min) Apply with topical corticosteroids to reduce skin irritation and improve outcomes
Simplicity	Once-daily application

8. Additional topical agents to treat psoriasis
    a. Salicylic acid
        i. Usually used in addition to topical corticosteroid or immunosuppressive agents for additive effect
        ii. Avoid using topical salicylic acid in UVB phototherapy because it will decrease the efficacy of the phototherapy.
        iii. Contributes to total daily salicylate intake (potential toxicity)
    b. Anthralin (Dritho-Creme)
        i. Not as effective as topical corticosteroids or vitamin D analogs
        ii. Apply at increasing contact intervals (starting at 1 minute), and increase as tolerated.
        iii. Less cosmetically appealing secondary to staining of lesions, surrounding skin, hands, nails, clothing
    c. Coal tar
        i. 1% lotion is preferred to 5% extract for symptom improvement.
        ii. Often avoided secondary to cosmetic staining and undesirable odor
    d. Topical immunosuppressive agents (tacrolimus, pimecrolimus)
        i. No FDA-approved indications for psoriasis
        ii. Primary off-label use for facial symptoms or intertriginous (skinfold) areas
        iii. Black box warning issued by the FDA for increased risk of lymphoma
        iv. Approved for patients 2 years and older
    e. Nonmedicated topical moisturizers
        i. Accepted standard of care for patients with psoriasis
        ii. Limited evidence to support their benefit, but placebo has a 15%–47% response rate in clinical trials
        iii. Considered safe with few or no adverse events
    f. Less common topical agents
        i. Capsaicin
        ii. Indigo naturalis
        iii. Mahonia aquifolium bark extract

9. Combination topical therapy – Consider combination therapy for patients who do not achieve the desired effect with one agent.
    a. Topical corticosteroids plus salicylic acid
    b. Topical corticosteroids plus vitamin D analogs (co-formulated)
    c. Topical corticosteroids plus tazarotene
    d. Tacrolimus plus salicylic acid

I. Systemic (Biologic) Pharmacologic Agents
1. T-cell inhibitors: Alefacept (Amevive) – No longer manufactured
2. Tumor necrosis factor (TNF) inhibitors
    a. Adalimumab (Humira)
    b. Etanercept (Enbrel)
    c. Infliximab (Remicade)
    d. Other TNF inhibitors are used primarily in the treatment of psoriatic arthritis (golimumab, certolizumab pegol).

Table 46. TNF Inhibitor STEPS

Safety	Increased risk of serious bacterial and fungal infections (contraindicated in patients with active, serious infections) Associated with reactivation of tuberculosis (Note: Recommendations for initial and periodic testing for tuberculosis with TNF inhibitors and other biologics can be found in the Bone/Joint and Rheumatology chapter) May increase risk of malignancy, including melanoma, leukemia, and lymphoma Linked with new or worsening heart failure and possibly death in patients with heart failure
Tolerability	Headache Abdominal pain Injection-site reactions Upper respiratory tract infection
Efficacy	A small percentage of patients may lose efficacy after 12 wk of therapy with adalimumab Patients who decrease their etanercept dose from twice weekly to once weekly experience a decrease in therapeutic effect Infliximab appears to produce the greatest decrease in symptoms in the shortest time (10 wk vs. 12 wk)
Preference (Pearls)	Patients who discontinue adalimumab, etanercept, or infliximab abruptly are not at risk of rebound symptoms, but they may have a diminished effect when restarting therapy TNF inhibitors have been combined with methotrexate to lessen the likelihood of patients developing resistance to therapy Highly effective, but very costly, therapeutic interventions Do not use with live vaccines; immune response of inactive vaccines may also be compromised
Simplicity	Adalimumab maintenance doses are administered subcutaneously every other week Etanercept maintenance doses are administered subcutaneously twice weekly x 12 wk, followed by once weekly thereafter Infliximab intravenous maintenance infusions are administered every 6–8 wk

TNF = tumor necrosis factor.

3. Phosphodiesterase-4 enzyme inhibitor
   a. Apremilast (Otezla)

Table 47. Phosphodiesterase-4 Enzyme Inhibitor STEPS

Safety	Neuropsychiatric effects (such as depression, suicidal ideation, mood changes) reported; use with caution May cause weight loss; monitor Dosage reduction required in patients with CrCl <30mL/min
Tolerability	Diarrhea, nausea, vomiting Decreased appetite Tension headache
Efficacy	Comparative studies are lacking, but efficacy appears to be lower than that of TNF-α inhibitors
Preference (Pearls)	Advantages include oral administration, minimal drug interaction potential, and minimal adverse effect profile, especially when compared to other biologics and MTX
Simplicity	10mg by mouth every morning; titrate to maintenance dose of 30mg BID starting on day 6

J. Biologic Response Modifiers
   1. Should be reserved for patients with moderate to severe disease or refractory disease because the risks associated with therapy may be greater than those associated with the disease
   2. Questionable whether as efficacious as T-cell inhibitors or TNF inhibitors
   3. Methotrexate

Table 48. Methotrexate STEPS

Safety	Contraindicated in pregnancy and breastfeeding; women who are planning to become pregnant should discontinue use 3 mo before conception Significantly diminishes ability to generate an immune response Increased incidence of the following: • Any malignancy • Lung cancer • Melanoma • Non-Hodgkin lymphoma Avoid in patients with the following: • CrCl < 30 mL/min • Platelet count < 50,000/mm^3 • White blood cell count < 3 x 10^3 cells/mm^3 • Liver transaminase values > 2 times the upper limit of normal	
Tolerability	Abdominal cramping Anorexia Bone marrow suppression Hypersensitivity pneumonitis	Increased aminotransferase values Infections Nausea Stomatitis
Efficacy	Effective for reducing symptoms of psoriasis, but may be less effective than cyclosporine	
Preference (Pearls)	Reserved for use in severe, intractable, and disabling psoriatic symptoms and psoriatic arthritis Reported as being slightly less effective than cyclosporine for psoriasis, but with fewer adverse events that require discontinuing therapy	
Simplicity	Administered with folic acid therapy (once daily)	

CrCl = creatinine clearance.

4. Cyclosporine

Table 49. Cyclosporine STEPS

Safety	Nephrotoxicity Do not use concurrently with UV phototherapy Cutaneous squamous cell carcinoma Avoid in patients receiving methotrexate, immunosuppressive agents, or coal tar Avoid use in patients with renal insufficiency, poorly controlled hypertension, malignancy, major infection, or poorly controlled diabetes Hypertriglyceridemia (triglycerides > 750 mg/dL) Increased risk of infections (bacterial, viral, fungal)
Tolerability	Flu-like symptoms Gingival hyperplasia Headaches
Efficacy	Despite being considered more efficacious than methotrexate, the greater number of serious adverse events limits its use
Preference (Pearls)	Reserved for patients whose condition does not respond to at least one systemic agent and who cannot use or tolerate biologic therapy Increase frequency of blood pressure monitoring after each dosage alteration
Simplicity	Twice-daily dosing for up to 1 yr of therapy

5. Acitretin (Soriatane)

Table 50. Acitretin STEPS

Safety	Pregnancy category X Avoid using in individuals who plan, or are actively trying, to become pregnant Should continue oral contraceptive therapy for at least 3 yr after discontinuing therapy Men or women using acitretin should not donate blood during, or up to 3 yr after discontinuing, therapy because of the risk of a pregnant woman receiving the donation
Tolerability	Mucocutaneous reactions Unstable psoriasis-like reaction (“retinoid dermatitis”) Dyslipidemia
Efficacy	Considered less effective than other systemic therapies for psoriasis Often used in combination with UVB or PUVA
Preference (Pearls)	Efficacy is dose-dependent, and optimal treatment dose is 50 mg daily Do Your PART Program (www.soriatane.com/patient/part.aspx)
Simplicity	Once-daily dosing

PART = Pregnancy Prevention Actively Required During and After Treatment; PUVA = psoralen plus ultraviolet light therapy.

6. Interleukin (IL) inhibitors
    a. Ustekinumab (Stelara) targets IL-12 and IL-23
    b. Secukinumab (Cosentyx) and ixekizumab (Taltz) target IL-17A whereas brodalumab (Siliq) targets IL-17
    c. Guselkumab (Tremfya) targets IL-23

Table 51. Interleukin Inhibitor STEPS

Safety	Increased risk of serious bacterial and fungal infections (contraindicated in patients with active, serious infections) Associated with reactivation of tuberculosis Risk of serious skin conditions, exfoliative dermatitis, and erythrodermic psoriasis
Tolerability	Nasopharyngitis Fatigue Headache Diarrhea Upper respiratory infections
Efficacy	May be used as first line for moderate to severe chronic plaque psoriasis These agents have all shown efficacy over etanercept
Preference (Pearls)	Secukinumab may exacerbate Crohn disease Ustekinumab has been associated with malignancies and reversible posterior leukoencephalopathy syndrome (RPLS) Ixekizumab may cause Crohn disease and ulcerative colitis Do not use with live vaccines; immune response of inactive vaccines may also be compromised Highly effective, but very costly
Simplicity	Given subcutaneously into top of thigh, abdomen, upper arms, or buttocks; rotate sites Ustekinumab given at weeks 0, 4; then every 12 wk thereafter Secukinumab dosed every 4 wk after initial doses once weekly during weeks 0–4 Laboratory monitoring not necessary Ixekizumab injected every 2 wk after initial dose; then every 4 wk Guselkumab given at weeks 0, 4; then every 8 weeks thereafter Brodalumab dosed initially at weeks 0, 1, and 2; then biweekly thereafter

7. Second-tier agents – Considered for patients whose condition does not respond to, or for patients who cannot tolerate, systemic therapy and who cannot afford or be treated with biologic agents
    a. Azathioprine
    b. Fumaric acid esters
    c. Hydroxyurea
    d. Leflunomide
    e. Mycophenolate mofetil
    f. Sulfasalazine
    g. Tacrolimus
    h. Thioguanine
8. Other agents – Apremilast (Otezla)
    a. Phosphodiesterase type 4 inhibitor
    b. Oral medication approved for active psoriatic arthritis

9. After many treatment failures, patients and providers may consider the following:
    a. Goeckerman therapy (coal tar plus UVB for 3–5 weeks)
    b. Ingram regimen (dithranol/salicylic acid/zinc oxide paste [with or without coal tar] plus UVB for 3 weeks)

X. INFESTATIONS

A. Additional Resources *(Domain 3)*
    1. *American Family Physician*. Pediculosis and Scabies: A Treatment Update 2012
    2. American Academy of Pediatrics Clinical Report on Head Lice 2015
    3. Am J Clin Dermatol 2002;3:9-18
    4. N Engl J Med 2006;354:1718-27

B. Scabies *(Domain 1)*
    1. Types
        a. Common scabies
        b. Crusted scabies (Norwegian scabies): Commonly found in immunocompromised, debilitated, or malnourished individuals
        c. Nodular scabies
    2. Factors associated with contracting scabies *(Domain 2)*
        a. Person-to-person contact
            i. Higher likelihood in crowded communities
            ii. Hospitals, nursing homes, homeless shelters, jails/prisons, and schools have increased person-to-person contact and risk of mass infection.
        b. Impoverished areas
    3. Presentation *(Domain 1)*
        a. Symptom onset
            i. May take 4–6 weeks for onset of symptoms in patients who have never had scabies
            ii. Symptoms may manifest as follows:
                (a) Be worse during evening hours and while sleeping
                (b) Worsen for 1–2 days after starting treatment
                (c) Persist for up to 1 week after resolving infestation
            iii. Subsequent re-infestations may present with symptoms as soon as 24 hours.
        b. Itching and lesions (common sites)
            i. Areola and nipples
            ii. Axillary folds
            iii. Extensor (outer) of elbows
            iv. Finger webs
            v. Flexor (inner) of wrists
            vi. Lower buttocks
            vii. Genitalia
        c. Primary lesions may develop into secondary lesions or bacterial infections.
            i. May persist for weeks or months after the infestation is eradicated
            ii. If crusted scabies develops, patients may appear to have psoriasis or seborrheic dermatitis.

4. Diagnostic studies *(Domains 1 and 3)*
    a. A definitive diagnosis can be made when a clinician identifies mites, eggs, mite pellets, or egg fragments under magnification (skin shaving).
    b. The Burrow Ink Test may also be used to identify tracks left by the mite as it burrows under the skin.
    c. Epiluminescence microscopy is a newer in vivo technique that allows a detailed inspection of the superficial papillary dermis.
    d. Empiric therapy for generalized itching is not recommended; should only be used in those with a history of exposure with or without typical eruptions

Patient Case

9. P.F. is the 26-year-old mother of two children (6 and 8 years old) who contracted scabies after spending the night at a neighborhood friend's house. The two daughters developed symptoms about 2 weeks after the exposure, and the family's primary care provider gave them a prescription for permethrin 5%. However, permethrin did not eradicate the infestation, and the symptoms recurred 1 month later. Which factor most likely caused the treatment failure?

    A. Increasing resistance patterns for scabies in the United States.
    B. The prescriber ordering an inappropriate dose of permethrin for the children (pediculosis dose).
    C. Not applying permethrin to areas such as the soles of feet or unexposed areas.
    D. Not evaluating infested/symptomatic areas and removing nits (eggs).

5. Treatment *(Domains 1 and 2)* – Patients with a scabies infestation and their close physical contacts should be treated at the same time, regardless of whether symptoms are present.
    a. Nonpharmacologic
        i. Evaluate all close contacts within the past 30 days for symptoms of infestation.
        ii. Identify all items in contact with the patient having a scabies infestation for the past 72 hours.
            (a) Decontaminate all bedding, clothing, and toys using machine washer (at least 140°F water) and heated dryer.
            (b) Isolate items that cannot be put in a machine washer using an insecticide powder and sealed plastic bag for at least 72 hours.
            (c) Pesticide sprays and powders are not recommended; little evidence of benefit of vacuuming
        iii. In-hospital or nursing home situations
            (a) Isolate patients with an infestation (may require prolonged isolation to ensure eradication).
            (b) Provide education and therapy for family, staff, and residents in contact with the person.
            (c) May require treatment of the entire at-risk population
        iv. Remove children with an infestation from school until the infestation is adequately treated.
    b. Family members, household contacts, and other close contacts
        i. All individuals who have had close personal contact with the patient in the past 30 days should be evaluated and treated for scabies.
        ii. Symptoms may take days to weeks to present, and transmission is possible during the initial asymptomatic period.

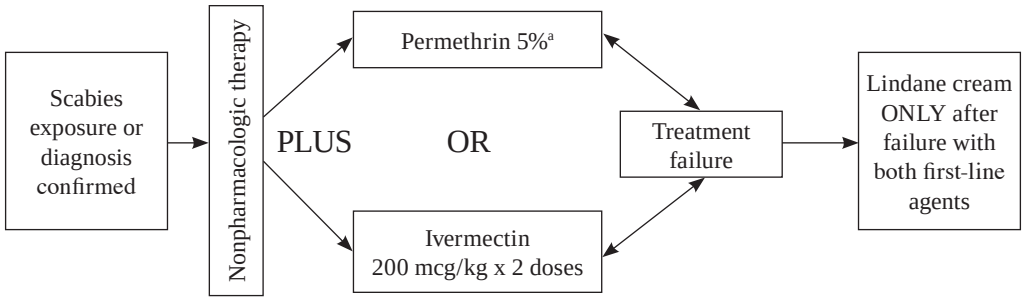

Figure 6. Scabies treatment algorithm.

[a]Primary choice

c. Topical pharmacologic agents
   i. Permethrin 5%, topical (Elimite)

Table 52. Permethrin 5% STEPS

Safety	Photosensitivity
Tolerability	Burning and stinging Erythema and pruritus Numbness and tingling
Efficacy	5% cream is the efficacious dose (1% OTC formulation is ineffective) Most effective agent and first-line recommendation from the American Academy of Pediatrics and the CDC Counsel patients to be sure to cover all areas of the body (e.g., soles of feet, hands, under nails) because missing these areas may allow a recurrence of infestation and symptoms
Preference (Pearls)	Total body (below head) application is required FDA approved for use in those ≥ 2 mo Recommended as well-tolerated alternative treatment for those who cannot use lindane (infants and small children, patients with seizures or neurologic complications, therapeutic failure, or resistance to lindane) Pregnancy category B Reasonable cost: About $10 per bottle
Simplicity	Apply from head to toe, leave on for 8–14 hr before washing off with water; may reapply in 1 wk if live mites appear

CDC = Centers for Disease Control and Prevention.

ii. Ivermectin, oral (Stromectol)

Table 53. Ivermectin STEPS

Safety	Symptomatic postural hypotension Life-threatening dyspnea (three individuals) Association between 6-mo mortality and ivermectin in long-term care residents
Tolerability	Peripheral edema Tachycardia Gastrointestinal effects Transaminase elevations Pruritus Fever Skin involvement (edema, urticarial rash)
Efficacy	Appears less effective than permethrin, but more effective than lindane
Preference (Pearls)	Not FDA approved for scabies treatment, but endorsed by the CDC May consider in patients whose infestations are not eradicated by permethrin Alternative for those who cannot completely cover body with topical treatments Administer on an empty stomach with water
Simplicity	Single oral dose 200 mcg/kg; may be repeated in 14 days

iii. Lindane, topical

Table 54. Lindane STEPS

Safety	Black box warning secondary to neurologic toxicity (seizures and death) with prolonged or repeated exposure
Tolerability	May cause pruritus lasting several weeks after infestation is eradicated
Efficacy	Appears to be less effective than permethrin for treating scabies
Preference (Pearls)	Not recommended as first-line therapy and should be used cautiously as a second-line agent for those who lack response to permethrin Total body (below head) application is required Apply to dry skin, leave on for 8–12 hr, and then wash off in warm shower or bath (do not exceed 12 hr) Be aware of thumb sucking in children Do not re-treat if infestation is not eradicated Must be dispensed with FDA-approved patient mediation guide
Simplicity	One application Conduct a 2- and 4-wk follow-up to evaluate for new lesions High cost: About $125 per bottle

iv. Crotamiton, topical – Second-line topical agent because its efficacy is lower than that of other agents; has high resistance and increased reports of persistent itch after use

v. Malathion, topical – Use is discouraged because it contains 78% isopropyl alcohol, causing skin and genital irritation.

vi. "Natural" options (not proven effective in the United States)
(a) Tea tree oils
(b) Extracts of neem and turmeric
(c) Bush tea
(d) Coconut oil
(e) Melaleuca oil plus lavender oil

C. Pediculosis ("Lice")
1. Types *(Domain 1)*
a. Pediculus capitis (head)
b. Pediculus corporis (body)
c. *Phthirus pubis* (pubic)
2. Factors associated with contracting pediculosis *(Domain 2)*
a. Adults with poor hygiene
b. Direct hair-to-hair contact
c. Sharing contaminated objects (toys, bedding, clothing, hats, hairbrushes)
d. Overcrowded living conditions
3. Presentation and diagnosis *(Domains 1 and 2)*
a. Initially, patients may be asymptomatic, and diagnosis is based on physical findings (nits).
b. Pruritus of the scalp and a feeling that something is "crawling" on the head
c. Intense itching leads to scratching, with subsequent excoriations and secondary cellulitis.
d. Usually asymptomatic, but may also see the following:
i. Irritability
ii. Rash
iii. Malaise
iv. Headache
e. Nits (eggs) may be seen where hair exits scalp.
f. Definitive diagnosis occurs by finding at least one live louse on visual inspection.
i. Run a fine-toothed comb through wet hair, and identify lice on comb.
ii. Lice are commonly found behind the ears and on the back of the neck.
iii. Finding nits (louse eggs) on examination is not enough to indicate current infestation.
g. Symptoms may persist for about 1 week after infestation is eradicated.

Patient Case

10. Y.M. is a 17-year-old female adolescent who contracted lice after sharing a hat with one of her softball teammates. She was sent home from school after excessive scalp itching, and the school nurse identified nits at the proximal end of her hair follicles. She was treated with permethrin 1% at home but experienced pruritus and abnormal scalp tingling with the treatment. The lice infestation was not completely resolved with this treatment, and her family physician recommended a second course of therapy. Y.M. is extremely upset because her junior prom is only 2 weeks away, and she cannot have "lice" for her junior prom. Aside from manual removal of lice by fine-toothed combs, which would be the best addition to permethrin to enhance therapy and decrease the chance of another course of therapy?

A. Add oral ivermectin 300 mcg/kg for two doses, separated by 7 days.
B. Add topical malathion 0.5%, applied the day after treatment with permethrin.
C. Apply a suffocation-based pediculicide after washing out permethrin.
D. Add oral trimethoprim/sulfamethoxazole twice daily for 10 days.

4. Treatment

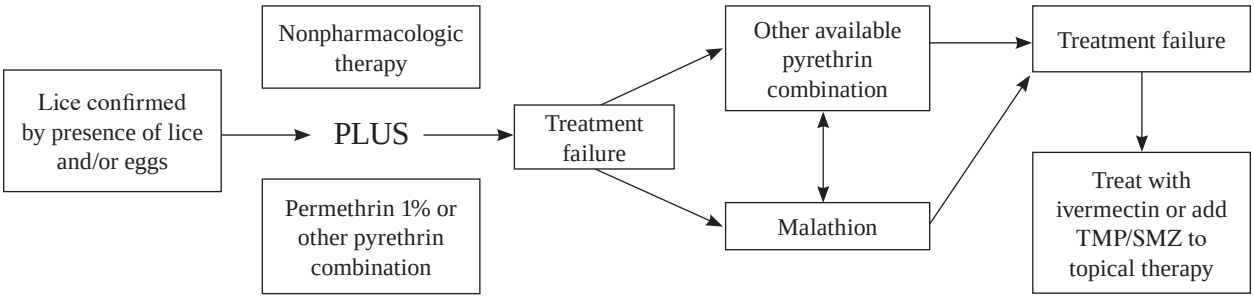

Figure 7. Lice treatment algorithm.

TMP/SMZ = trimethoprim/sulfamethoxazole.

Note: Lindane no longer recommended; spinosad is not included in treatment recommendations.

a. Nonpharmacologic *(Domains 1 and 2)*
   i. Nit removal using a fine-toothed comb ("nit picking")
   ii. Use a conditioner or olive oil in hair to remove tangles.
   iii. Use a comb from a pediculicide product to comb hair, starting at the scalp.
   iv. Repeat every 2–3 days until no nits or eggs are found.
   v. Machine wash items (linens, clothing) in hot (140°F) water and high-heat dry.
   vi. Seal non-washable items in plastic bag for 14 days.
   vii. Centers for Disease Control and Prevention recommends against the use of lice bedding sprays.
   viii. Neon Nits is not recommended by the American Pediculosis Association.
   ix. The American Academy of Pediatrics does not recommend removing students from school because most children will have had lice for about 1 month before diagnosis.
      (a) Discourage close contact with other students.
      (b) Maintain patient privacy.

b. Topical pharmacologic *(Domain 1)*
   i. Pyrethrins
      (a) Permethrin 1% (Nix) or pyrethrins 0.33% and piperonyl butoxide 3%–4% (RID; Pronto, Clear Lice System)
      (b) See STEPS analysis in Scabies section.
      (c) Permethrin 1% formulation should be used for pediculosis (American Academy of Pediatrics).
      (d) May be used as prophylaxis in household contacts and areas where greater than 20% of the population is affected
      (e) Apply to washed and towel-dried hair, and rinse after 10 minutes. May repeat in 7–10 days if nits still present
      (f) Resistance to permethrin and pyrethrins/piperonyl butoxide can be significant in various communities, necessitating the use of malathion.

ii. Malathion 0.5% (Ovide)

Table 55. Malathion STEPS

Safety	0.5% lotion is flammable secondary to high isopropyl alcohol content (avoid use near source of ignition) Contraindicated in children < 24 mo
Tolerability	Irritation of scalp and skin Avoid use for *Phthirus pubis* because of high alcohol content (irritation)
Efficacy	Evidence of resistance to malathion preparations in the United Kingdom, but malathion in the United States has a different formulation (terpineol, dipentene, and pine needle oil) without similar documentation of resistance
Preference (Pearls)	Use in individuals > 24 mo when permethrin resistance is suspected Safety data are not reported for children < 6 yr Pay attention to regional resistance patterns when selecting treatment High cost: About $125 per bottle
Simplicity	Apply to dry hair enough to sufficiently wet the hair and scalp, allow to dry, and remove after 8–12 hr One-time treatment (may be repeated in 7–9 days if live lice still present) Remove dead lice with a fine-toothed comb

iii. Spinosad 0.9% (Natroba)

Table 56. Spinosad STEPS

Safety	Not recommended for use in infants < 6 mo secondary to benzyl alcohol (gasping syndrome)
Tolerability	Application site erythema and irritation Alopecia
Efficacy	Limited randomized controlled trial data suggest spinosad is markedly superior to permethrin for 14-day lice-free outcome
Preference (Pearls)	Not included in the 2010 American Academy of Pediatrics treatment recommendations because approved for use in the United States in January 2011
Simplicity	Single application Apply to dry hair, leave on for 10 min, and then rinse May repeat application in 7 days if nits are still present May be used without nit combing, although best results occur with nit combing

iv. Other topical formulations
   (a) Lindane – See STEPS analysis in Scabies section.
      (1) Is no longer recommended by the American Academy of Pediatrics and is banned in the California
      (2) Instruct patients to leave it on their scalp for no longer than 4 minutes.

(b) Suffocation-based pediculicide
(1) Petrolatum shampoo applied to scalp, dried with a hair dryer, left on overnight, and then washed out in the morning
(2) Thorough hair washing for 7–10 days is required to remove the petrolatum residue.
(3) Requires manual removal of lice and nits with fine-toothed comb

c. Oral agents
i. Trimethoprim and sulfamethoxazole (Bactrim, Septra)

Table 57. Trimethoprim/Sulfamethoxazole STEPS

Safety	Electrolyte (potassium) abnormalities Contraindicated in children < 2 mo or pregnant/nursing women Contraindicated in patients with a history of anaphylaxis to sulfa-containing antibiotics
Tolerability	Nausea Vomiting Rash
Efficacy	Adding TMP/SMZ to permethrin has higher success rates than either agent alone
Preference (Pearls)	Add to traditional therapy (permethrin only) if nits and lice are found 2 wk after first course of therapy
Simplicity	Twice daily for 10 days

ii. Ivermectin, oral – See Ivermectin, oral in Scabies section. As effective as malathion lotion

d. "Natural" options
i. Coconut oil plus anise spray
ii. Coconut oil, anise oil, and ylang ylang oil (Hair-Clean 1-2-3)
iii. Melaleuca oil plus lavender oil

5. Follow-up (for scabies and pediculosis) *(Domain 2)*
a. Confirm treatment success with patient and family.
b. Re-treat with different agent if treatment is ineffective 1 month after final scheduled treatment.
c. Identify causes of treatment failure.
i. Nonadherence to or inappropriate treatment instructions
ii. Not re-treating as recommended
iii. Wrong product selected
iv. Acquired resistance

XI. MINOR BURNS

A. Professional Treatment Guidelines *(Domain 3)*
1. No professional treatment guidelines are published for minor burn management.
2. Review article: Am Fam Physician 2012;85:25-32

Table 58. Severity Classification for Burn Injuries

Degree	Characteristics and/or Criteria	Healing Times
First (superficial burn)	Involves only the epidermis Skin findings include red color, dry, and painful The burn rarely blisters	3–10 days
Second (partial-thickness burn)	Superficial, partial-thickness burn • Involves all of the epidermis and part of the underlying dermis • Skin findings include erythema, painful, and wet/weeping skin • Blisters are clear • Blanching when touched Deep partial-thickness burn • Involves deeper layers of the dermis (reticular dermis) • Skin findings include pale white or fixed red color and blanching absent with pressure • Blisters present • Patient has dull sensation or lack of pain with stimulation • Often results in scarring and contractures	2 wk
Third (full-thickness burn)	Destroys all skin layers, including underlying subcutaneous fat Skin findings include leathery feel; white, brown, or tan appearance; charred and dry or hard and waxy feel; and blanching absent with pressure No blistering Skin grafting is usually required	> 3 wk
Fourth	Destroys all skin layers and extends into muscle, tendon, or bone	

Table 59. Common Causes of Minor Burns

Thermal Burns	Chemical Burns	Others	Medications[a]
Scalding (food/water) Fire (flash/flame) Hot surfaces	Alkalis/acids Petroleum Phosphorus Airbags Hair dyes Fabric detergents OTC pain products (menthol related)	UV radiation Particle radiation Electrical burn/injury	Amiodarone Doxycycline Hydrochlorothiazide Fluoroquinolones NSAIDs Retinoids Tetracycline Voriconazole

[a]Note: Medications usually increase the risk of burn and are not the primary cause.

B. Complications Are Usually Infectious, Resulting in Cellulitis. *(Domain 1)*
   1. *Acinetobacter* spp.
   2. *Klebsiella* spp.
   3. *Pseudomonas aeruginosa*
   4. *Staphylococcus aureus*
   5. *Streptococcus pyogenes*

C. Treatment *(Domains 1 and 2)*
   1. Most minor burns (first degree and superficial, partial-thickness second degree) can be managed in the outpatient setting.
   2. Nonpharmacologic interventions
      a. Remove heat/burning source from skin (if safe to do so).
      b. Try to cool the burned area with cool, running water.
      c. Avoid using ice to cool burn because it can worsen the burn and symptoms.
      d. Wash (do not scrub) the burned area and loose skin.
      e. Do not remove blisters that are less than 6 mm and intact.
   3. Pain management
      a. NSAIDs may provide sufficient relief.
      b. Topical diclofenac (0.1%) reduced spontaneous pain and provoked pain and erythema with sunburn.
      c. If NSAIDs are insufficient, the patient may require a short course of opioid analgesia.
   4. Cover burns with moist dressing to promote healing (occlusive dressings for more serious burns).
   5. For first-degree burns, consider using topical agents such as the following:
      a. Aloe vera
      b. Antibiotic ointments
      c. Lotions
      d. Honey
   6. For second-degree burns, use topical antimicrobials or antiresorptive, occlusive dressings.
      a. Silver sulfadiazine (SSD)
         i. New occlusive dressings should be considered instead of SSD because of faster healing, decreased pain, fewer dressing changes, and improved patient satisfaction.
         ii. Use SSD cautiously in patients with sulfa allergy.
      b. Non-silver treatment options include the following:
         i. Biobrane (biosynthetic dressings)
         ii. Silicone-coated nylon dressings (Mepitel)
         iii. Antimicrobial-releasing biosynthetic dressings (Hydron)
         iv. Hydrofiber dressing (Aquacel-Ag)
         v. Hydrocolloid dressing (DuoDERM)
   7. Patients with more than a first-degree burn should be considered for a tetanus booster.

D. Education Tips for Households and Families *(Domain 2)*
   1. Cook on rear burners when children are present.
   2. Test bathwater temperature.
   3. Do not hold a child while working with hot items.
   4. Set water heaters to less than 130°F (54°C).
   5. Use sunscreen with SPF (sun protection factor) 40 for prolonged exposure to UV light.

XII. DECUBITUS ULCERS

A. Professional Guidelines *(Domain 3)*
   1. European and US National Pressure Ulcer Advisory panels (EPUAP and NPUAP): 2014 International Pressure Ulcer Guidelines
   2. 2012 Institute for Clinical Systems Improvement pressure ulcer prevention and treatment protocol (2014 update, but no changes were made)

B. Classification of Pressure Ulcers (National Pressure Ulcer Advisory Panel—European Pressure Ulcer Advisory Panel) *(Domain 1)*
   1. Category/stage I: Nonblanchable erythema of intact skin
   2. Category/stage II: Partial-thickness loss of dermis, appearing as open ulcer with red-pink wound bed without slough or bruising
   3. Category/stage III: Full-thickness tissue loss; subcutaneous fat may be visible, but bone, tendon, or muscle not exposed
   4. Category/stage IV: Full-thickness tissue loss with exposed bone, tendon, or muscle visible or directly palpable
   5. In the United States, two additional stages are used in classification.
      a. Unstageable/unclassified: Full-thickness tissue loss (with depth unknown) in which base of ulcer is covered by slough and/or eschar in the wound bed
      b. Suggestion of deep tissue injury, depth unknown – Purple or maroon localized area of discolored intact skin or blood-filled blister

C. Risk Factors for Developing Decubitus Ulcer *(Domain 2)*
   1. Several risk assessment scales available; most commonly used is the Braden Scale for Predicting Pressure Sore Risk ("Braden Scale"). The Braden Q Scale is a modified Braden Scale for use in pediatric patients up to 18 years of age.
   2. Levels or risk
      a. Mild risk: 15–18
      b. Moderate risk: 13–14
      c. High risk: 10–12
      d. Very high risk: 9 or less
   3. The Braden Scale considers the following information:
      a. Sensory perception: Ability to respond meaningfully to pressure-related discomfort
      b. Moisture: Degree to which the skin is exposed to moisture
      c. Activity: Degree of physical activity
      d. Mobility: Ability to change and control body position
      e. Nutrition: Usual food intake pattern
      f. Friction and shear
   4. Risk factors for developing decubitus ulcer
      a. Aging skin
      b. Comorbidities (type 1 or 2 diabetes, vasculitis, peripheral arterial disease, heart failure, malignancy, end-stage kidney disease, dementia or cognitive impairment, sensory disorder)
      c. Friction or pressure from any hard surface (bed, stretcher, wheelchair)
      d. Moist skin or environment in contact with skin
      e. Patients in long-term care facilities
      f. Patients with limited mobility, including those with coma/sedation, fractures, neurologic disorders, spinal cord injury, or stroke
      g. Poor nutrition (anorexia, dehydration, poor dentition)
      h. Previous ulcer

Table 60. Potential Complications of Decubitus Ulcer

Infectious	Noninfectious
Bacteremia	Amyloidosis (rare)
Cellulitis	Perineal-urethral fistula
Endocarditis	Pseudoaneurysm
Meningitis	Squamous cell carcinoma (in the ulcer)
Osteomyelitis	
Sepsis	

D. Patient Presentation and Diagnosis *(Domain 1)*
   1. Usually presents with significant pain radiating from the site of the ulcer or infection
   2. Evidence of any of the following on examination of the ulcer:
      a. Exudate
      b. Necrosis
      c. Foul odor
      d. Granulation or new skin formation
      e. Tunneling or undermining
   3. Blood tests (hemoglobin, albumin, iron studies) will help serve as markers for malnutrition.
   4. It is not necessary to swab and culture the wound. Aspiration may be necessary for wounds that do not heal with initial treatments.
   5. In certain instances, it may be necessary to conduct testing to rule out osteomyelitis (white blood cell count, erythrocyte sedimentation rate, blood culture, probe-to-bone test).

E. Nonpharmacologic Treatment *(Domains 1 and 2)*
   1. Minimize/eliminate friction and shear.
   2. Minimize pressure (offloading).
   3. Use specialty support surfaces.
   4. Reposition patient often.
      a. Patients in bed
         i. Use pillows or wedges to decrease pressure on bony prominences.
         ii. Turn patients every 2 hours (minimum).
      b. Patients in sitting position
         i. Encourage patients to weight shift every 15 minutes.
         ii. Avoid use of “donuts.”

F. Treatment *(Domain 1)*
   1. Wound management
      a. Surgical debridement of necrotic tissue
      b. Hydrocolloid dressings
      c. Evidence is insufficient to support wound cleaning with cleaners or antiseptics. These agents tend to destroy new tissue and are not helpful.
   2. Dietary considerations
      a. Recommended to take in 35–40 kcal/kg/day of energy and 1–1.5 g/kg/day of protein
      b. The evidence is not robust for nutritional intervention, but this may contribute to faster wound healing.

Patient Case

11. Becaplermin is used to help accelerate the speed of ulcer healing in patients with pressure ulcers. The medication is applied topically, but it carries with it a high risk of mortality in certain patient populations. Which patient is most at risk of experiencing life-threatening adverse events when using becaplermin?
    A. A 28-year-old woman using oral contraceptives for dysmenorrhea.
    B. A 36-year-old man with a history of epilepsy.
    C. A 48-year-old woman with a history of breast cancer.
    D. A 56-year-old man treated with tiotropium for chronic obstructive pulmonary disease.

3. Becaplermin

Table 61. Becaplermin STEPS

Safety	Do not apply if there is a known neoplasm at the application site Increases risk of mortality because of malignancy with use of > 3 tubes of drug
Tolerability	Erythematous rash
Efficacy	Will accelerate the speed of ulcer healing, but must weigh risk of serious adverse events (malignancy) vs. decreased ulcer healing time
Preference (Pearls)	If not at least a 30% reduction in ulcer size at 10 wk or complete resolution at 20 wk, discontinue use of drug
Simplicity	To determine dose, measure the greatest width and length of the ulcer[a]: 15-g tube: (ulcer length [inches] x ulcer width [inches]) x 0.6 = length of gel (inches); 2-g tube: (ulcer length [inches] x ulcer width [inches]) x 1.3 = length of gel (inches)

[a]Recalculate the dose every 1–2 wk.

4. Antibiotics are not considered first-line treatment options and should be reserved as follows:
    a. Oral antibiotics for patients with bacteremia, cellulitis, or osteomyelitis
    b. Topical antibiotics for patients without wound healing, despite 2 weeks of wound care
5. Pain management is especially important because of pain caused by cleaning, movement because of repositioning, and dressing changes after debridement.
    a. Topical agents such as lidocaine/prilocaine during debridement
    b. Topical morphine has shown efficacy for ulceration pain reduction.
6. Other interventions
    a. Pressure relief devices: Static or dynamic devices to reduce contact pressure
    b. Electrotherapy: Electrical stimulation has some evidence of increased wound healing.
    c. Negative pressure wound therapy: Weak evidence for efficacy, and the FDA issued an advisory for providers to be cautious and selective with candidates because of a high number of reported deaths and injuries

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ANSWERS AND EXPLANATIONS TO PATIENT CASES

1. Answer: D

The antioxidant vitamin formulation should most closely match the combination from the AREDS study. This study evaluated the efficacy of vitamin C, vitamin E, beta-carotene, and zinc. However, this patient is a smoker, and beta-carotene use in patients who smoke increases the patient's risk of developing lung cancer. Hence, the patient should take a combination that does not include beta-carotene (Answer D is correct; Answers A–C are incorrect).

2. Answer: A

For this patient, initiating a prostaglandin analog such as travoprost (Answer A or B) is the best choice for therapy. In addition, she has to use only one drop in each eye every evening because the volume of one drop meets or exceeds the maximal volume the eye can retain topically (Answer A is correct). Extra drops would provide the patient no additional benefit (Answer B is incorrect). Although a β-blocker can be used as first-line therapy in patients with POAG, β-blockers are not as potent as prostaglandin analogs for lowering baseline IOPs (Answers C and D are incorrect).

3. Answer: C

In patients with dry eyes, the indication to begin therapy with ophthalmologic cyclosporine is usually the occurrence of symptoms of dry eyes with no relief from artificial tears (Answer C is correct). Despite the 54-year-old patient's daily symptoms (Answer B) and the 63-year-old woman's once-weekly symptoms (Answer A), both are receiving adequate relief from artificial tears. The symptoms of the 61-year-old patient in Answer D with dry mouth, fatigue, and other dry mucus membranes as well as dry eyes appear to be more consistent with Sjögren disease; this would require systemic cholinergic agents.

4. Answer: C

Steroid bursts are an appropriate intervention for acute moderate to severe exacerbations in patients with allergic rhinitis already treated with an oral antihistamine, allowing relatively quick symptom resolution (Answer C is correct). Doubling this patient's intranasal corticosteroid would probably provide no additional relief and would increase the chances of mucosal irritation and epistaxis (Answer A is incorrect). Although pseudoephedrine may be an acceptable alternative to some intranasal corticosteroids or intranasal/oral antihistamines, it is still an inferior intervention, and the goal is to provide maximal relief to this patient (Answer B is incorrect). Finally, montelukast use would not be beneficial because (1) it is not as efficacious as systemic corticosteroids and (2) the short duration of the intervention is not consistent with the appropriate use of montelukast for allergic rhinitis (Answer D is incorrect).

5. Answer: B

The nsAHs are the best first-line option for treating this patient's urticaria. The prednisone dose is too high for an acute urticarial rash in this child, and (if repeated events) it would not be the best choice for continued administration (Answer C is incorrect). Although famotidine affects histamine receptors, it targets the wrong receptor to make it acceptable for first-line therapy (Answer D is incorrect). Finally, loratadine would be the better choice because it is considered an nsAH with fewer central nervous system effects, and it would be safer for the child playing in and around water. Diphenhydramine is a sedating antihistamine and therefore would not be the best choice for a child to take prior to swimming (Answer B is correct; Answer A is incorrect).

6. Answer: A

After being administered a C1 INH or a selective bradykinin B_2 receptor antagonist, patients with HAE should seek immediate medical attention to manage their angioedema (Answer A is correct). These two classes of medications are approved for use in the outpatient management of acute HAE. The kallikrein inhibitors are only approved for in-hospital administration. Antihistamine or corticosteroid therapy may be warranted in these emergencies, but the patient should go directly to the emergency department for additional care (Answers B and C is incorrect). None of the plasma-derived products causes spontaneous syncope, so patients need not account for this adverse event (Answer D is incorrect).

7. Answer: A

The AAD treatment recommendations list oral isotretinoin as an alternative therapy, which, given the patient's nodular acne and lack of response to the first-line therapeutic combination, would be best for him (Answer A is correct). The other options listed for this question are

appropriate drug combinations for treating acne, but none is potent enough or in a strong enough combination to be of use to the patient (Answers B and D are incorrect). Topical retinoid combinations are incorrect for this stage of acne because the pairing of agents is incorrect. Topical retinoids should be combined with an oral antibiotic, with or without benzoyl peroxide and/or azelaic acid. The listed combinations fail to meet these criteria. In addition, the use of antiandrogenic spironolactone (Answer C) would not be beneficial to a male patient (Answer C is incorrect).

8. Answer: D

Lithium is probably contributing to this patient's psoriasis (Answer D is correct). It is not uncommon to see psoriasis first present after trauma to the skin. The acronym NAILS is a helpful reminder of the agents that may cause psoriasis: NSAIDs, antimalarials, ACE inhibitors, Inderal (β-receptor antagonist), lithium, and steroid withdrawal (Answers A–C are incorrect).

9. Answer: C

Permethrin 5% is the appropriate dose for treating scabies infestations in most individuals (Answer B is incorrect). Although resistance patterns for permethrin 1% are developing in the United States for treating pediculosis, permethrin at this concentration is still highly effective for scabies (Answer A is incorrect). In addition, it is not necessary to "nit pick" when patients are using permethrin to eradicate scabies (Answer D is incorrect). For these two patients, treatment failure probably occurred because the children or their mother did not apply the agent to the entire body and missed some areas of infestation during application (Answer C is correct). Patients should be counseled to apply the agent to all surfaces of the body below the neck, including the palms of their hands and the soles of their feet.

10. Answer: D

Adding trimethoprim/sulfamethoxazole to permethrin 1% for pediculosis is appropriate (Answer D is correct). Although the other options are viable, the instructions for use are not appropriate. Ivermectin should be dosed only once, not twice (Answer A). Malathion and suffocation-based pediculicide should be applied in place of (not in sequence with) permethrin 1% (Answers B and C are incorrect).

11. Answer: C

Becaplermin use has been associated with an increased risk of advanced malignancy and mortality in patients with an existing malignancy, such as the patient in Answer C with breast cancer. Even though this medication is topical (locally applied), the malignant effects of the drug may be seen remotely from the application site. No negative outcomes are associated with becaplermin for patients who have seizure disorders (Answer B) or who take oral contraceptives (Answer A) or inhaled anticholinergics (Answer D).

ANSWERS AND EXPLANATIONS TO SELF-ASSESSMENT QUESTIONS

1. Answer: A

In the AREDS study, the supplement combination shown to delay the progression from intermediate disease to advanced disease consisted of vitamin C 500 mg, vitamin E 400 international units, beta-carotene 15 mg, and zinc 80 mg. Certain situations warrant excluding a component of the combination (beta-carotene in patients with a history of lung cancer or in patients who smoke). The combination showed no benefit for patients without macular degeneration (Answer A is correct; Answers B–D are incorrect).

2. Answer: B

Answer B, the ophthalmologic β-blocker, is the best choice to add to this patient's therapy. The patient already takes a prostaglandin analog (decreasing aqueous outflow resistance), and the dose increase is inappropriate because it does not enhance the IOP-lowering effect. According to recommendations from the National Institute for Health and Clinical Excellence, carbonic anhydrase inhibitors and adrenergic agents should be used after an ophthalmologic β-blocker fails to sufficiently decrease the IOP. Answers A, C, and D are options because their mechanism of action (decreased aqueous production) complements the prostaglandin analog, but only betaxolol has clear preference in the treatment recommendations.

3. Answer: A

There are several options for treating and relieving the symptoms of patients with mild to moderate dry eyes. First, assess for and remove any medications or factors that may be causing dry eyes. Next, apply artificial tears and evaluate response. This patient responded, but not for a sufficient period. However, because she did receive some relief, she may need a different formulation that will remain present for a longer period. For this, an ointment application may be the best choice (Answer A is correct). Ophthalmologic cyclosporine would be the next step or should be used if the patient does not receive relief from artificial tears, in a 0.05%, not 0.1%, concentration (Answers B and C are incorrect). Systemic cholinergic agents should be used in patients with other symptoms of dryness, including most mucus membranes, or in those whose condition does not respond to ophthalmologic cyclosporine (Answer D is incorrect).

4. Answer: C

In any patient with symptoms of vertigo, the goal is to identify the underlying cause of the disease, not just react to the symptom. For this patient, it appears that his primary care physician ruled out most causes of vertigo except for medication-induced symptoms. Of the four medications, carbamazepine (Answer C) is the most likely cause of his symptoms (Answer C is correct; Answer B is incorrect). Although the antihypertensive hydrochlorothiazide (Answer A) may be associated with vertigo because of electrolyte abnormalities or blood pressure changes, neither was present during this patient's physical and laboratory evaluations. Metformin (Answer D) may also be a cause, but for hypoglycemia, the symptoms would most often be accompanied by tachycardia, diaphoresis, and possibly confusion.

5. Answer: B

Although an intranasal corticosteroid is the best choice for this patient's symptoms (moderate to severe), her fear of epistaxis and reluctance to use the corticosteroid are a treatment barrier. Fexofenadine (Answer B) should be used in this patient because it is an nsAH and will most likely provide better relief than the other available agents (Answer B is correct; Answer D is incorrect). Although most oral antihistamines are equally effective, clemastine (Answer A) is a first-generation H_1 antihistamine with a greater chance of causing sedation than fexofenadine. According to treatment guidelines, montelukast (Answer C) and other leukotriene inhibitors should be reserved for use until after a patient's treatment with an intranasal corticosteroid and an nsAH has been unsuccessful.

6. Answer: C

Adding famotidine (Answer C) may be the best choice for this patient because adding fexofenadine will ensure antagonism of both the H_1 and H_2 receptors. Agents such as diphenhydramine (Answer B) or doxepin (Answer D) may be effective, but they also cause fatigue, which could interfere with the patient's ability to work. In addition, diphenhydramine would work on the same receptors as fexofenadine (Answer A), probably producing no additional effect. Adding famotidine will broaden histamine receptor antagonism and further decrease the presence and symptoms of urticaria. If given the option,

the patient could also increase her oral antihistamine dose up to 4 times the suggested normal dose for up to 4 weeks to see whether the symptoms improve or resolve.

7. Answer: D

In patients with HAE, one of the primary treatment strategies for preventing symptoms is using plasma-derived C1 INHs (e.g., Cinryze). Because this is a blood product and may be a vector for disease transmission, treatment guidelines recommend immunizing all patients for bloodborne pathogens, including hepatitis B (Answer D is correct; Answers A–C are incorrect).

8. Answer: A

Patients taking an oral retinoid should be enrolled in the iPledge program and be aware of the severe, increased risk of teratogenicity with pregnancy while actively taking the medication (Answer A). Individuals enrolled in the iPledge program are extensively counseled on the risk of teratogenicity with pregnancy and are encouraged to take hormonal and barrier contraceptives. Even though routine monitoring of hepatic transaminase concentrations is recommended until patients reach an effective dose of oral retinoids, missed laboratory visits are no indication to discontinue therapy (Answer C). In addition, patients starting an oral retinoid should be counseled on the increased risk of mental health disorders (suicidality) with use, but they do not need a mental health provider to sign off on therapy (Answer B). Finally, these analogs have no reported impact on night vision (Answer D).

9. Answer: B

Topical corticosteroids are the treatment of choice for individuals with mild to moderate psoriasis. Adding a vitamin D analog such as calcipotriene (Answer B) would be most reasonable because it is more effective in combination with a topical corticosteroid than is either agent alone. The oral corticosteroid burst in Answer A is not indicated for a "flare-up" of psoriasis. Biologic agents (Answer D) and methotrexate (Answer C) should be reserved for individuals with severe or debilitating disease, those with greater than 10% of their body surface area covered with psoriatic lesions, and those with symptoms of psoriatic arthritis. For this patient, use of these agents would be excessive before trying other topical treatment options.

10. Answer: D

The best agent for this patient would be etanercept (Answer D). Cyclosporine (Answer B) would not be a good choice because of her poorly controlled hypertension and cyclosporine's poor efficacy compared with biologic therapy. Methotrexate is an acceptable agent because it can be used in severe disease with or without the presence of arthritis. However, given that methotrexate's efficacy for controlling symptoms in psoriasis is less than that of the TNF inhibitors, it should be reserved for second-line therapy. Methotrexate should be considered to treat psoriasis only in patients whose condition does not respond to a T-cell inhibitor or TNF inhibitor or who cannot afford biologic therapy. Acitretin (Answer C) is a retinoid-like compound effective in the treatment of psoriatic plaques but does not have an effect on psoriasis-related arthritis symptoms (Answer A is incorrect).

11. Answer: B

Permethrin 5% (Answer B) would be the treatment of choice for this patient. Permethrin 1% lotion (Answer A) is too low in concentration to work for a scabies infestation. It may be used for pediculosis (lice), but it would not be effective for this patient's condition. In addition, the degree of resistance to permethrin 5% for scabies is not yet sufficient to warrant a change to malathion (Answer C), given its inferiority to permethrin and high likelihood for dermatologic drying and irritation. The neurotoxicity associated with lindane (Answer D) makes it a less desirable first-line treatment option for the first symptoms of untreated scabies; it should be reserved for patients who cannot be treated with less potentially harmful therapies.

12. Answer: A

All individuals in the household and in close contact with the person with the infestation should be examined and most likely treated for a scabies infestation, even if they are asymptomatic (Answer A is correct; Answers B and C are incorrect). Household and close contacts within the past 30 days need to be evaluated and treated. Given the long period between initial infestation and presence of symptoms, it is unreasonable to wait for individuals to develop symptoms. During the asymptomatic period, these contacts could possibly contaminate those around them (sometimes for a second or third time). An "on-call" prescription for a scabicide is also not feasible because it still requires individuals to be symptomatic and possibly transmit/retransmit the infestation (Answer D is incorrect).

13. Answer: C

The patient's symptoms are consistent with a first-degree UV light burn. This will probably take 5–10 days to completely heal and requires no therapy beyond miniaturization and pain management (Answer C). Silver-based creams such as silver sulfadiazine (Answer A) are not recommended for burns because they delay healing time and (in more serious burns) may result in an increased risk of infection. Topical aloe is an option, but occlusive and wet dressings should be reserved for second-degree and more serious burns (Answer B). The same reasoning is also applicable for not choosing the hydrocolloid dressing (Answer D). This patient should receive sufficient relief from an NSAID such as ibuprofen.

14. Answer: C

The continued use of becaplermin is based on the percentage of wound healing in the first 10 weeks and the resolution at 20 weeks. Although he must continue taking becaplermin, the same dose should not be used (Answer A is incorrect); instead, a new dose should be calculated according to his wound size reduction. Patients who have at least a 30% reduction in wound size after the first 10 weeks of therapy should continue the medication for 20 weeks. In patients without much wound resolution, the medication should be discontinued (Answer D is incorrect). The becaplermin dose is based on a calculation that considers ulcer length and width and should not arbitrarily be increased or decreased on the basis of impression. For this patient, continuing at the same dose or increasing the dose would be excessive. A 35% reduction in wound size would necessitate a new dose of around 75% of his original dose (as the new dose). Doses should be recalculated every 1–2 weeks according to the ulcer size (Answer C is correct; Answer B is incorrect).