GI Health and Its Effect On the Skin Part I

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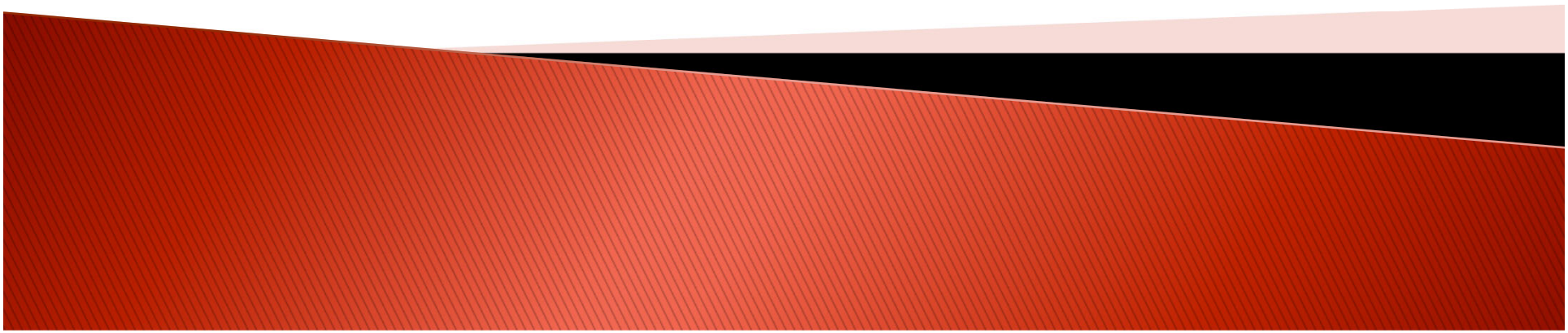
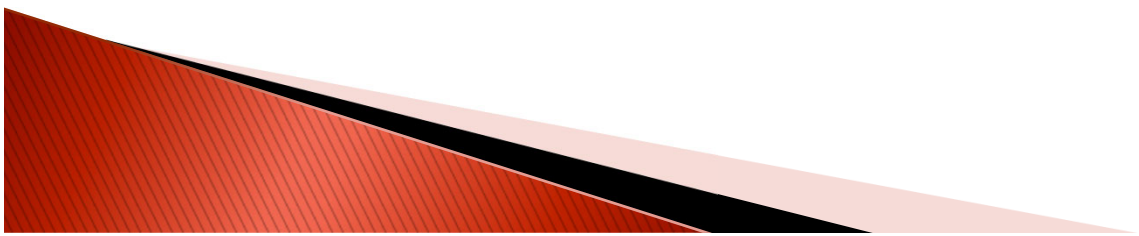


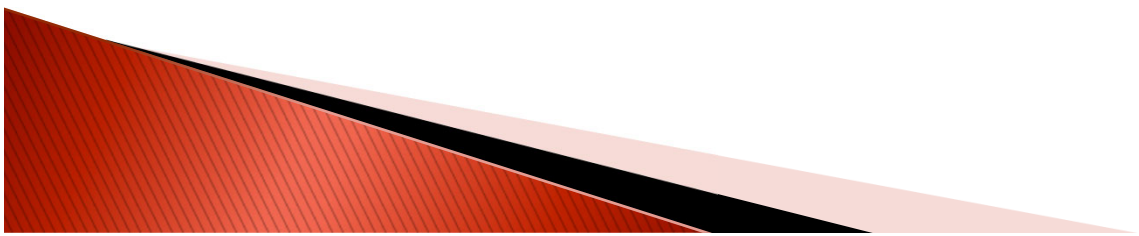
Disclosures

- Disclosure of Financial Relationships:
  - Speaker for Genova, ZRT, Microbiome
- Off-Label Usage
  - None

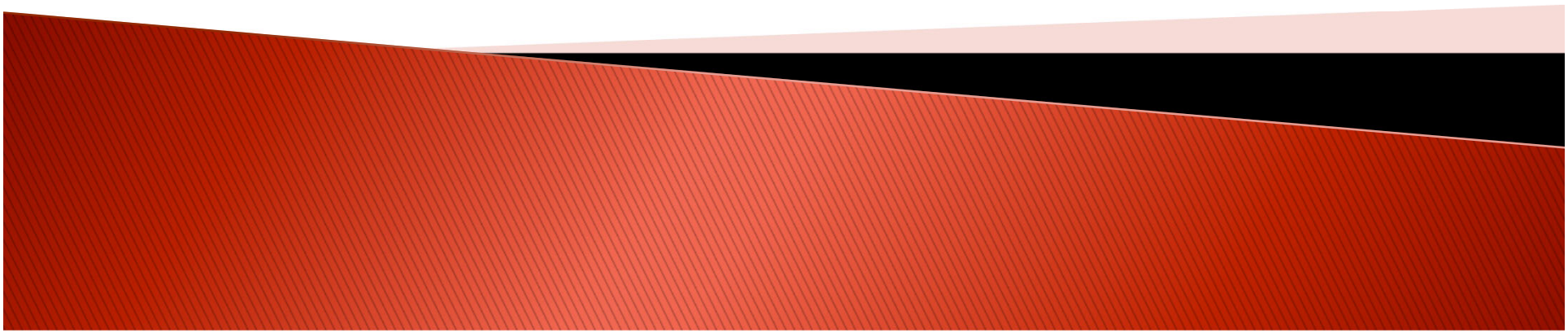


Objectives

- Understand the connection between the health of the GI tract and skin disorders.
- Learn conventional and metabolic therapies for rosacea.
- Recognize conventional and metabolic therapies for acne.
- Review conventional and metabolic therapies for atopic dermatitis.



Rosacea



Reference

- Gaby, A., Rosacea. In Nutritional Medicine. Concord, NH: Fritz Perlberg Publishing, 2017.
- Two, A., et al., “Rosacea: part I. Introduction, categorization, histology, pathogenesis, and risk factors,” Jour Amer Acad Derm 2015; 72(5):748-58.

Rosacea

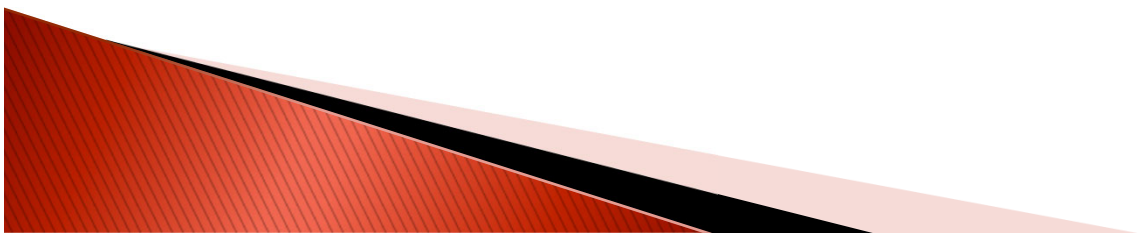
- Rosacea is a chronic inflammatory disease with an unknown cause.
- Recent findings indicate that genetic and environmental components can trigger rosacea initiation and aggravation by dysregulation of the innate and adaptive immune system.
- Trigger factors also lead to the release of various mediators such as keratinocytes (for example, cathelicidin, vascular endothelial growth factor, and endothelin-1), endothelial cells (nitric oxide), mast cells (cathelicidin and matrix metalloproteinases), macrophages (interferon-gamma, tumor necrosis factor, matrix metalloproteinases, and interleukin-26), and T helper type 1 (T_H1) and T_H17 cells.

Rosacea (Cont.)

- Additionally, trigger factors can directly communicate to the cutaneous nervous system and, by neurovascular and neuro-immune active neuropeptides, lead to the manifestation of rosacea lesions.
  - Buddenkotte, J., et al., “Recent advances in understanding and managing rosacea,” F1000Res 2018; 7:F1000 Faculty Rev-1885.

Rosacea (Cont.)

- Rosacea may also be related to H. pylori infection.
  - Utas, S., et al., “Helicobacter pylori eradication treatment reduces the severity of rosacea,” Jour Amer Acad Derm 1999; 40:433-35.
  - Sharma, V., et al., “A study of the prevalence of Helicobacter pylori and other markers of upper gastrointestinal disease in patients with rosacea,” Amer Jour Gastroenterol 1998; 93:220-22.
  - Szlachcic, A., “The link between Helicobacter pylori infection and rosacea,” Jour Eur Acad Dermatol Venerol 2002; 16:328-33.

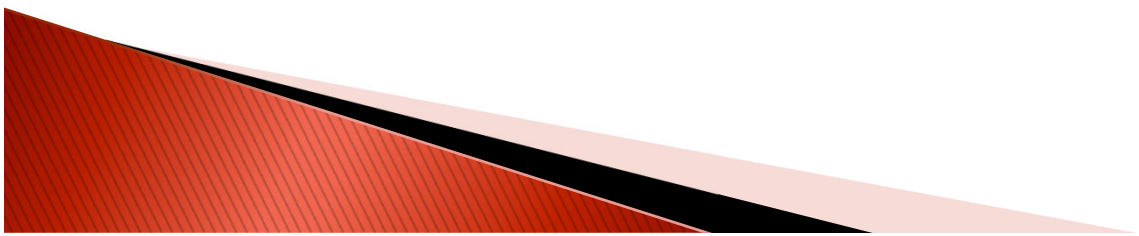


Rosacea (Cont.)

- Physical findings
  - Erythematous papules and pustules and telangiectasia on the cheeks, nose, forehead, and occasionally around the eyes
  - GI symptoms
  - Intermittent flushing occurs in affected areas
  - Irreversible chronic inflammation of nose leas to hypertrophy that is irreversible (rhinophyma)
  - Ocular manifestations
    - Conjunctivitis
    - Dry and burning eyes
    - Corneal abnormalities
    - Blepharitis
      - Steinhoff, M., et al., "New insights into rosacea pathophysiology: a review of recent findings," Jour Amer Acad Dermatol 2013; 69(6 Suppl 1):S15-S26.

Conventional Therapy For Rosacea

- Oral antibiotics
  - Tetracycline
  - Erythromycin
  - Metronidazole
- Oral isotretinoin
- Topical metronidazole
  - Feldman, S., et al., “Current drug therapies for rosacea: a chronic vascular and inflammatory skin disease,” Jour Manag Care Spec Pharm 2014; 20(6):623-29.



Conventional Therapy For Rosacea (Cont.)

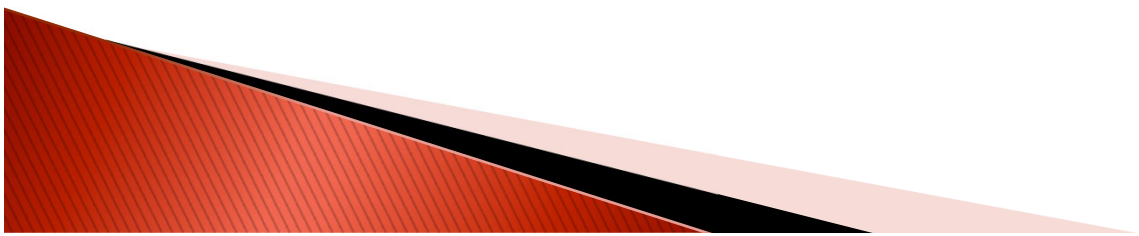
- The newest conventional therapy is ivermectin cream: 1% is use for the treatment of inflammatory lesions of rosacea.
  - Ali, S., et al., "The treatment of rosacea with topical ivermetctin," Drugs Today (Barc) 2015: 51(4):243-50.
- Study found that although ivermectin seems to be more effective than topical metronidazole, with both treatment options about two-thirds of patient relapsed within 36 weeks after discontinuation of treatment.
  - Ebbelaar, C., et al., "Topical ivermectin in the treatment of papulopustular rosacea: A systematic review of evidence and clinical guideline recommendations," Dermatol Ther (Heidelb) 2018; 8(3):379-87.

Metabolic Therapies for Rosacea

- Dietary
- Nutritional
  - Zinc
  - Pancreatic enzymes
  - B vitamins
- Azelaic acid
- Treatment of hypochlorhydria
- Herbal therapies
- Compounded formulas
  - Ibid., Gaby.

Dietary

- The flushing that is associated with rosacea may be triggered by the following.
  - Alcohol
  - Hot beverages
  - Spicy food
- Ask the patient to avoid foods and drink that aggravate rosacea and ones they have an allergy to.
  - Ibid., Gaby.

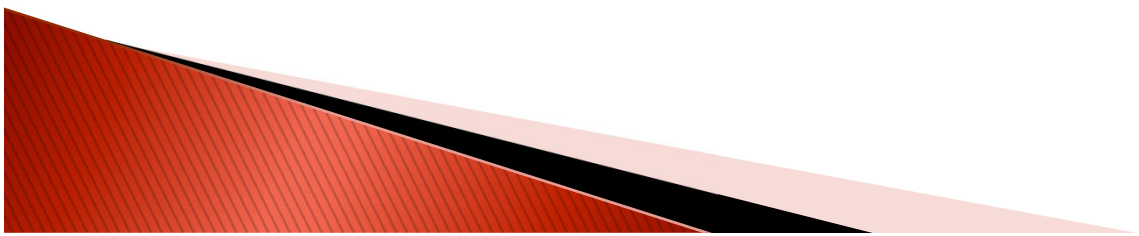


Nutritional Therapies

- Zinc
  - In a double-blind study, zinc supplementation was found to be very helpful.
  - 23 mg of zinc sulfate TID vs. placebo.
  - Zinc picolinate or zinc citrate would have been better absorbed and if used may be able to lower the dose of zinc. With long-term zinc usage, also give copper.
    - Sharquie, K., et al., "Oral zinc sulfate in the treatment of rosacea: a double-blind, placebo-controlled study," Int Jour Dermatol 2006; 45:857-61.
    - Gupta, M., et al., "Zinc therapy in dermatology: A review," Dermatol Res Pract 2014; 2014:709152.

Nutritional Therapies (Cont.)

- Pancreatic enzymes
  - Study showed that patients with rosacea had lower lipase secretion.
  - If the patient with rosacea also has dyspepsia, giving pancreatic enzymes may be useful.
    - Barba, A., et al., "Pancreatic exocrine function in rosacea," Dermatologica 1982; 165:601-06.

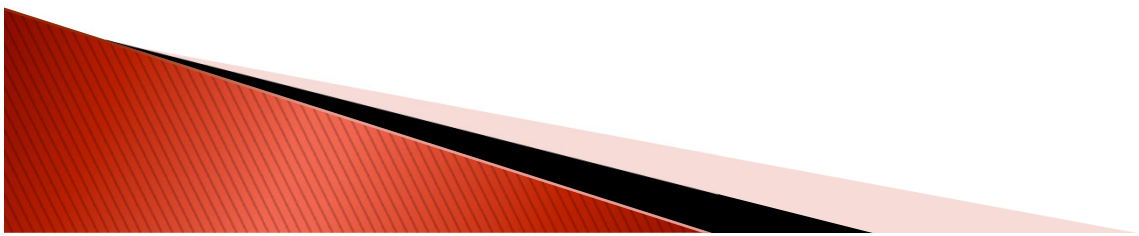


Azelaic Acid

- Azelaic acid has both anti-inflammatory and antibacterial effects.
- Double-blind, randomized study of 20% azelaic acid cream applied to one side of the face vs. metronidazole cream applied to the other side BID for 15 weeks.
- Azeliac acid was more effective.
  - Maddin, S., "A comparison of topical azelaic acid 20% cream and topical metronidazole 0.75% cream in the treatment of patients with papulopustular rosacea," Jour Amer Acad Dermatol 1999; 40:961-65.

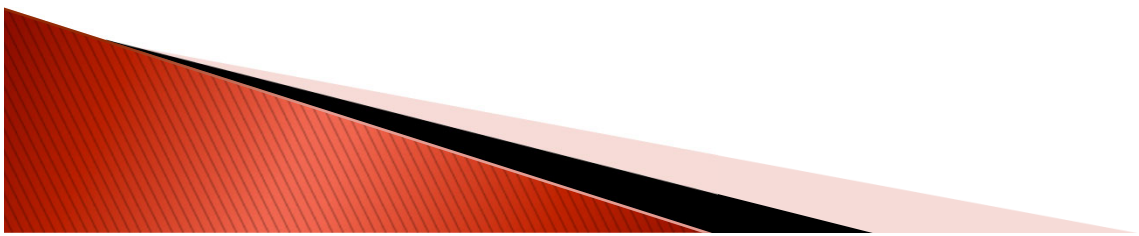
Azelaic Acid (Cont.)

- Another double-blind, randomized study using 15% azelaic acid gel vs. 0.75% metronidazole gel BID for 15 weeks.
- Azelaic was again found to be more beneficial.
  - Elewski, B., et al., "A comparison of 15% azelaic acid gel and 0.75% metronidazole gel in the topical treatment of papulopustular rosacea: results of a randomized trial," Arch Dermatol 2003; 139:1444-50.



Compound Formula for Rosacea

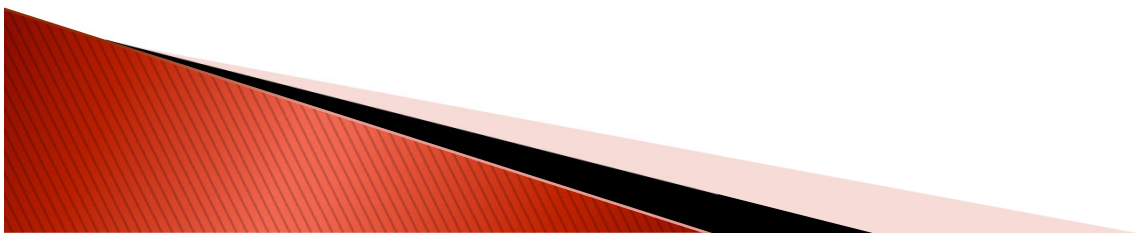
- Azelaic acid 20% in Topical Cream
- #30 grams
- Apply to affected area qd



The Gut Skin Connection: Rosacea

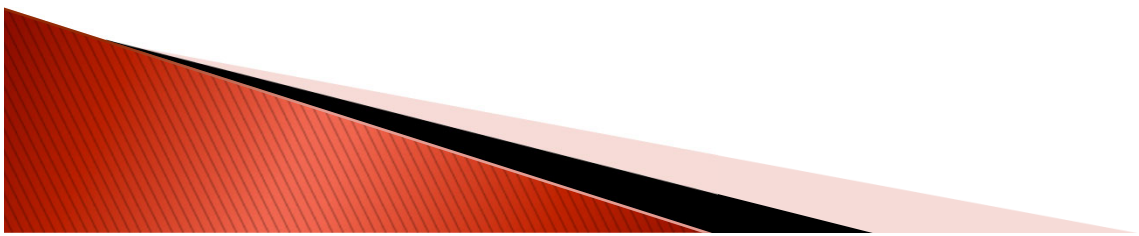
Hypochlorhydria

- Study showed that patients that had both rosacea and dyspepsia: more than 50% had low stomach acid.
  - Ryle, J., et al., "Gastric analysis in acne rosacea," Lancet 1920; 2:1195-96.



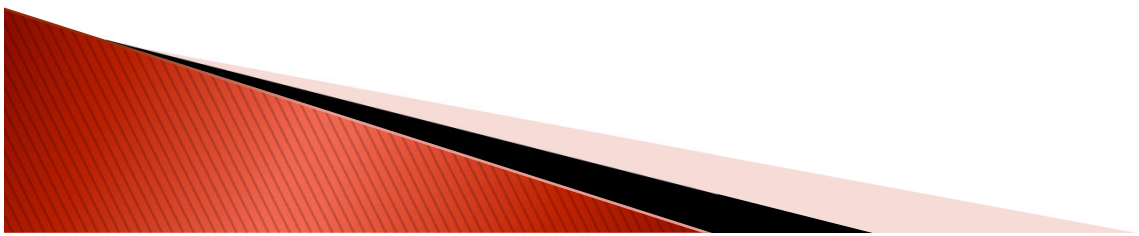
Hypochlorhydria (Cont.)

- In two other studies, patients with rosacea without dyspepsia, the prevalence of hypochlorhydria or achlorhydria was 28%–49%.
  - Usher, B., "Gastroscopic observations in rosacea," Arch Dermatol Syph 1941; 41:251–55.
  - Brown, W., et al., "Fractional gastric analysis in diseases of the skin: Further observation in 316 cases, with special reference to rosacea," Brit Jour Dermatol Syph 1935; 47:181–90.



Hypochlorhydria

- Resolving H. pylori infection restores gastric acid secretion in most people.
  - Iijima, K., et al., "Long-term effect of Helicobacter pylori eradication on the reversibility of acid secretion in profound hypochlorhydria," Aliment Pharmacol Ther 2004; 19:1181-88.

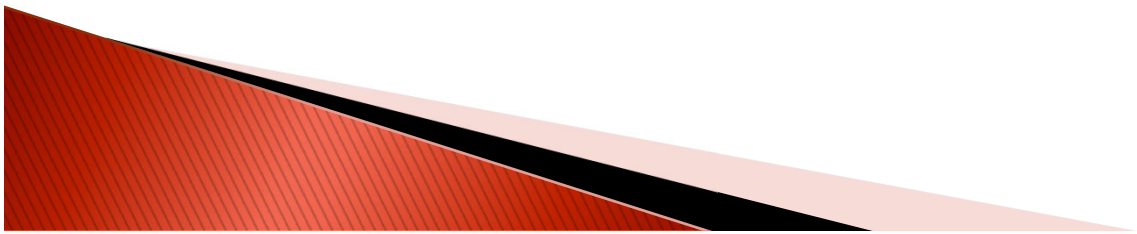


Niacinamide

- In aging skin, topical application of niacinamide improves the surface structure, smooths out wrinkles and inhibits photocarcinogenesis. It is possible to demonstrate anti-inflammatory effects in acne, rosacea and nitrogen mustard-induced irritation.
  - Gehring, W., Nicotinic acid/niacinamide and the skin," Jour Cosmet Dermatol 2004; 3(2):88-93.

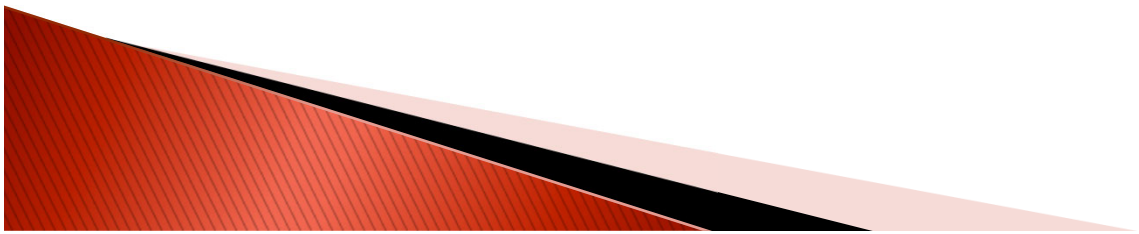
Compounded Formula For Rosacea #1

- Metronidazole 1%/Niacinamide 4% in Topical Cream
- #30 grams
- Sig: apply to affected area qd



Compounded Formula For Rosacea #2

- Niacinamide 5%/Glycosaminoglycans 5%/Dimethyl sulfone 2%/Biotin 0.2% in Topical Cream
- #30 grams
- Sig: apply to affected area qd

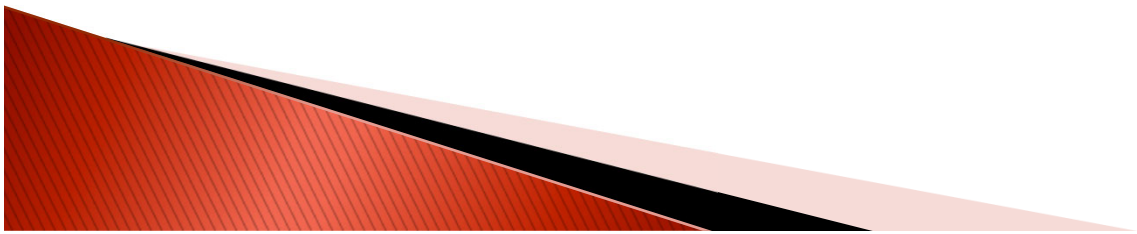


Compounded Formula For Rosacea #3

- Nicotinamide adenine dinucleotide 1% (NADH) in Topical Cream
- #30 grams
- Sig: apply to affected area BID

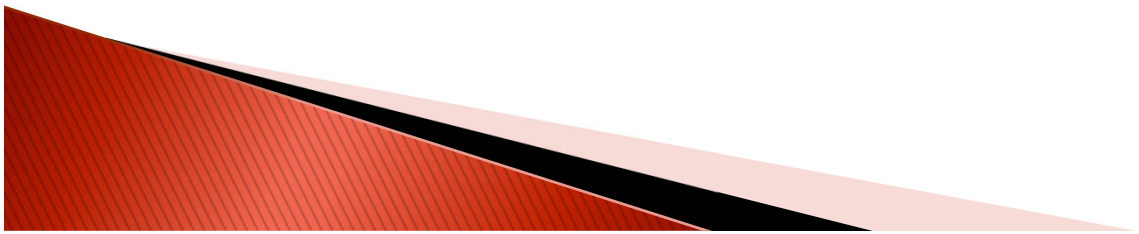
Compounded Formula For Rosacea #4

- Oxymetazoline HCl 0.06% in Facial Lotion
- #30 grams
- Sig: apply to affected area qd to BID



Compounded Formula For Rosacea #5

- Compounded Formula
  - Metronidazole 0.75%/Ketotifen 0.05% in Topical Cream
  - #30 grams
  - Sig: apply to affected area qd to BID

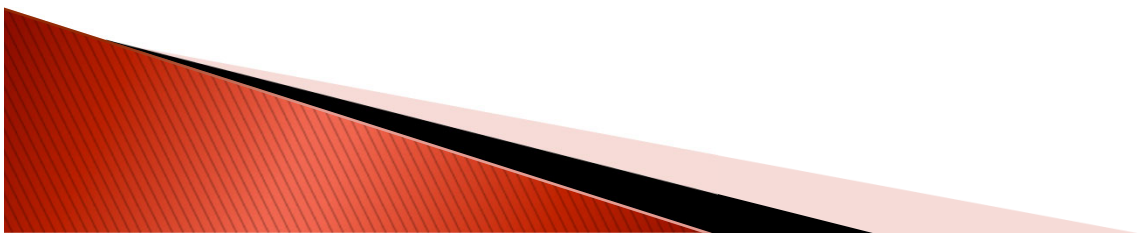


Compounded Formula For Rosacea #6

- Compounded Formula
  - Brimonidine Tartrate 0.5% in Topical Gel
  - #30 grams
  - Sig: apply to affected area qd to BID

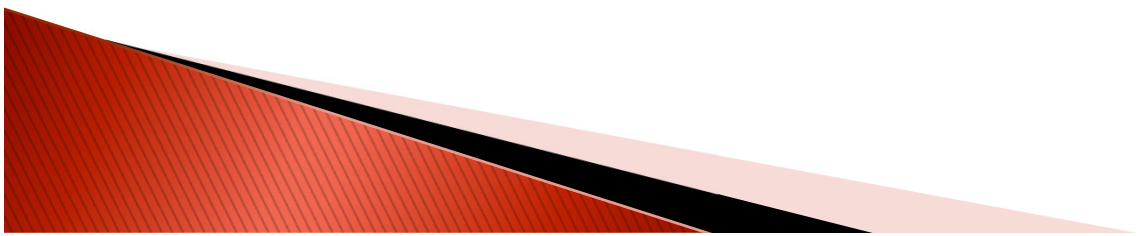
Compound For Pustular Rosacea

- Dapsone 5% in Topical Cream
- #30 grams
- Sig: apply to affected area qd



Vitamins That May Frequently Cause Rosacea Flares

- High doses of vitamin C: orally or any vitamin C topically
- High doses of vitamin E
- High doses of B Vitamins
  - Rosacea sufferers should steer clear from pure niacin and use the “no-flush” form of niacin termed niacinamide.



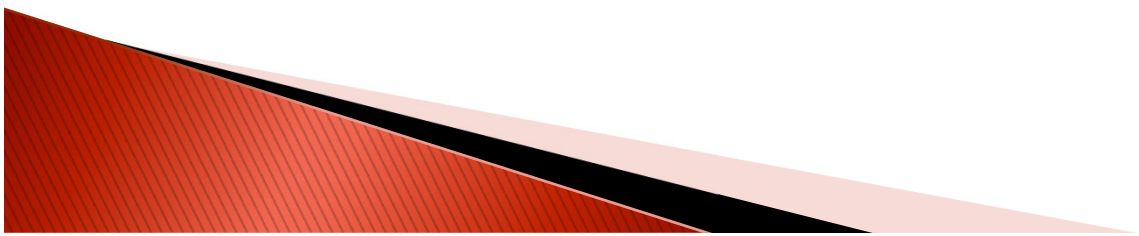
Acne

Reference

- Gaby, A., Urticaria. In Nutritional Medicine. Concord, NH: Fritz Perlberg Publishing, 2017.
- Titus, S., et al., “Diagnosis and treatment of acne,” Amer Fam Physician 2012; 86(8):734-40.
- Oge, L., et al., “Acne vulgaris: diagnosis and treatment,” Amer Fam Physician 2019; 100(8):475-84.

Acne

- Acne vulgaris is a common condition with follicular papules or comedones and inflammatory papules and pustules.
- Contributing factors
  - Infection (Propionibacterium acnes)
  - Tissue inflammation
  - Plugging of hair follicles due to epidermal hyper-proliferation
  - Hormone imbalance
    - Ibid., Gaby.

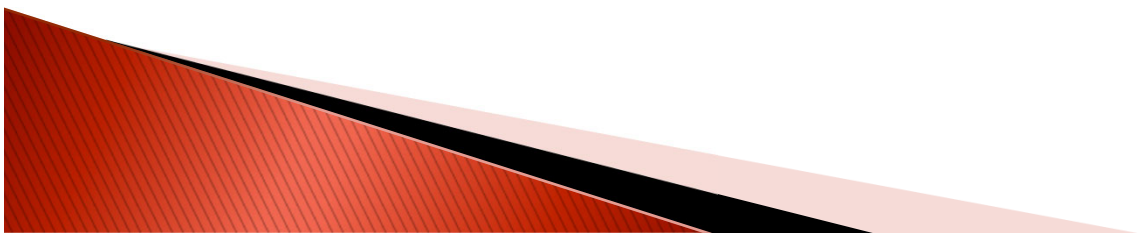


Conventional Therapies For Acne

- Topical therapies
  - Retinoids
    - Tiboutot, D., et al., "Treatment considerations for inflammatory acne: clinical evidence for adapalene 0.1% in combination therapies," Jour Drugs Dermatol 2006; 5(8):785-94.
  - Antibiotics
    - Ghali, F., et al., "Changing the face of acne therapy," Cutis 2009; 83(2 Suppl):4-15.
  - Benzoyl peroxide
    - Sagransky, M., et al., "Benzoyl peroxide: a review of its current use in the treatment of acne vulgaris," Expert Opin Pharmacother 2009; 10(15):2555-62.
  - Combination topical therapies
    - Andres, P., et al., "Adapalene-benzoyl peroxide once-daily, fixed-dose combination gel for the treatment of acne vulgaris: a randomized, bilateral (split-face), dose-assessment study of cutaneous tolerability in healthy participants," Cutis 2008; 81(3):278-84.
    - Weiss, J., et al., "Topical retinoid and antibiotic combination therapy for acne management," Jour Drugs Dermatol 2004; 3(2):146-54.

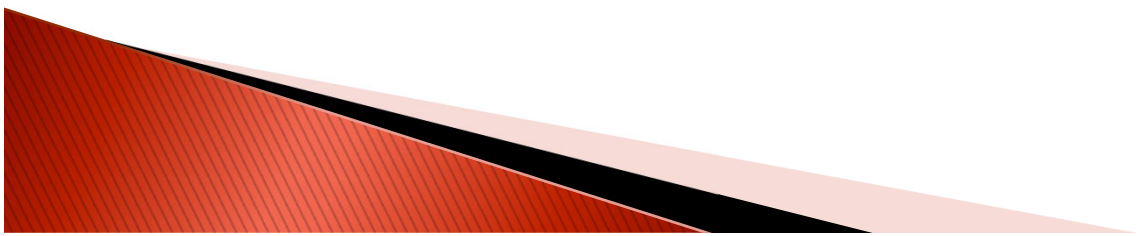
Conventional Therapies For Acne (Cont.)

- Systemic therapies
  - Antibiotics
    - Amin, K., et al., "Common and alternate oral antibiotic therapies for acne vulgaris: a review," Jour Drugs Dermatol 2007; 6(9):873-880.
    - Del Rosso, J., et al., "Optimizing use of oral antibiotics in acne vulgaris," Dermatol Clin 2009; 27(1):33-42.
  - BCP
    - Huber, J., et al., "Treating acne with oral contraceptives: use of lower doses," Contraception 2006; 73(1):23-9.



Conventional Therapies For Acne (Cont.)

- Systemic therapies (Cont.)
  - Isotretinoin (Accutane)
    - Only use in severe cases due to possible side effects that may be severe such as teratogenicity and inconsistent associations with depression, and suicidality.
    - Give B12 and folate if prescribing isotretinoin.
      - Gokalp, H., et al., "Decreased vitamin B12 and folic acid concentrations in acne patients after isotretinoin therapy: A controlled study," Indian Jour Dermatol 2014; 59(6):630.



Conventional Therapies For Acne (Cont.)

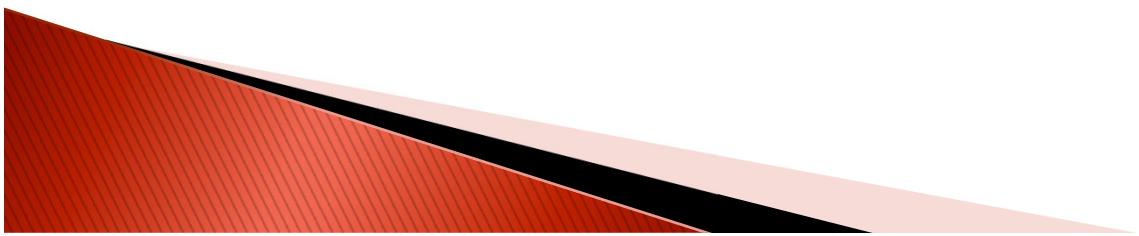
- New approaches favor the limiting of systemic antibiotic use.
  - The rates of antibiotic resistance among isolates of Cutibacterium have been rising.
  - The use of oral antibiotics is associated with disruption of the normal flora, bacterial resistance among other organisms, and increased rates of upper respiratory infection and pharyngitis.
  - Antibiotic use may also be associated with inflammatory bowel disease and collagen vascular disease.
  - There may be an association between the use of oral tetracycline antibiotics and the risk of breast and colon cancer.
    - Barbieri, J., et al., "Approaches to limit systemic antibiotic use in acne: Systemic alternatives, emerging topical therapies, dietary modification, and laser and light-based treatments," Jour Amer Acad Dermatol 2019; 80(2):538-49.

Metabolic Therapies For Acne

- Diet
- Zinc
- Transdermal niacinamide
- Vitamin A
- Vitamin B6 for premenstrual acne
- Pantothenic acid
- Vitamin C
- Selenium
- Azelaic acid
- Hypothyroidism (thyroid replacement)
- Compounded formulas
  - Ibid., Gaby.

Diet

- Study showed that significantly decreasing refined sugar improved acne.
  - Cornbleet, R., et al., “Should we limit sugar in acne? “Arch Dermatol 1961; 83:968-69.
- Compelling evidence shows that high glycemic load diets may exacerbate acne.
  - Kucharska, A., et al., “Significance of diet in treated and untreated acne vulgaris,” Postepy Dermatol Alergol 2016; 33(2):81-6.

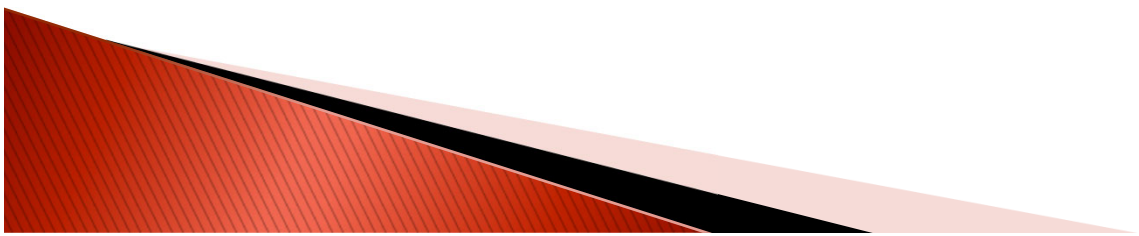


Diet (Cont.)

- Studies have shown that food allergies or sensitivities contribute to acne.
  - Studies have shown a positive correlation between the occurrence of acne and an increased consumption of dairy products.
    - Adebamowo, C., et al., “Milk consumption and acne in teenaged boys,” Jour Amer Acad Dermatol 2008; 58:787–93.
    - Ismail, N., et al., “High glycemic load diet, milk and ice cream consumption are related to acne vulgaris in Malaysian young adults: a case control study,” BMC Dermatol 2012; 12:13.

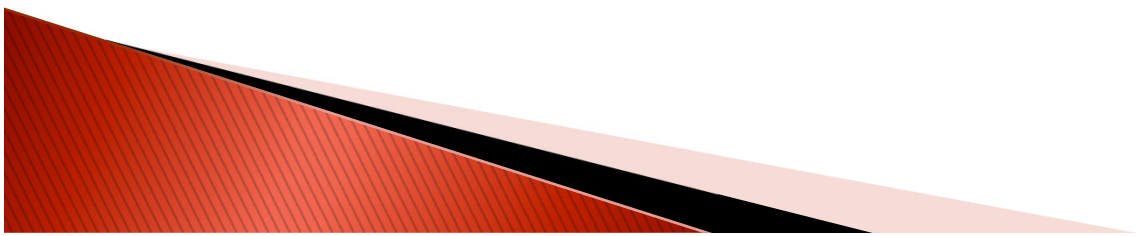
Diet (Cont.)

- Studies have shown that food allergies or sensitivities contribute to acne (cont.).
  - Significant changes in severity of acne occurred among respondents after a single ingestion of chocolate in a medical trial. This allowed the authors to hypothesize that chocolate can exacerbate acne lesions.
    - Block, S., et al., "Exacerbation of facial acne vulgaris after consuming pure chocolate," Jour Amer Acad Dermatol 2011; 65:e114–5.



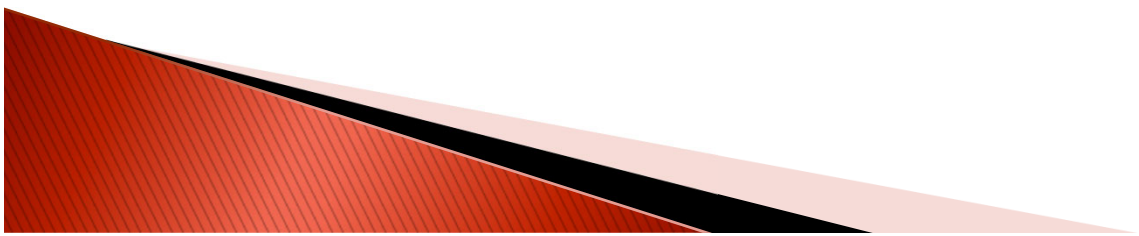
Iodine

- Iodine intake that is too high can cause acne.
  - Harrell, B., et al., "Kelp diet: a cause of acneiform eruption," Arch Dermatol 1976; 112:560.
  - Papa, C., "Acne and hidden iodides," Arch Dermatol 1976; 112:555-56.



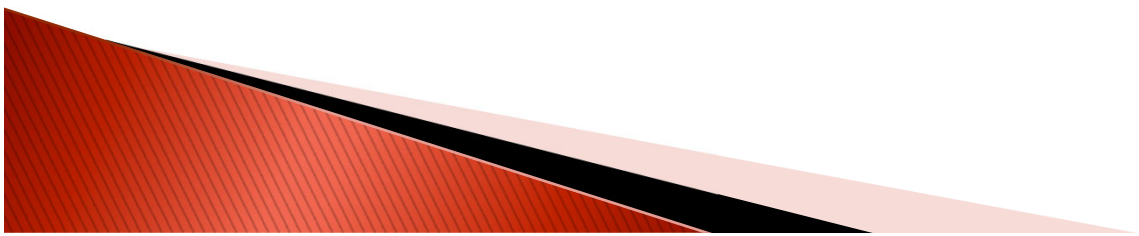
Zinc

- Zinc is a micronutrient that is essential for the development and functioning of the human skin. It has been shown to be bacteriostatic against Propionibacterium acnes, to inhibit chemotaxis and to reduce production of pro-inflammatory cytokine – tumor necrosis factor α (TNF-α).
  - Bowe, W., et al., "Effective over-the-counter acne treatments," Semin Cutan Med Surg 2008; 27:170-76.



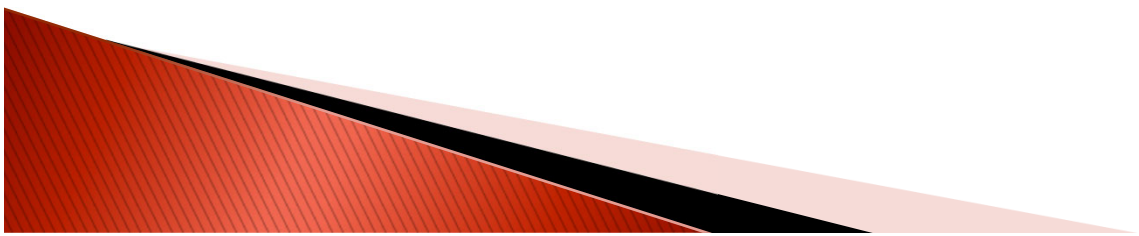
Zinc (Cont.)

- Studies have also shown that patients with acne have a higher rate of zinc deficiency than controls.
  - Amer, M., et al., Serum zinc in acne vulgaris," Inter Jour Dermatol 1982; 21:481-84.
  - Michaelsson, G., et al., "Serum zinc and retinol-binding protein in acne," Brit Jour Dermatol 1977; 96:283-86.



Zinc (Cont.)

- Most trials have shown that supplementing with zinc has been found to be helpful for acne.
- Dose: 30-150 mg of elemental zinc for two to three months.
- Zinc sulfate was used in most studies which is less bioavailable. Instead use zinc picolinate or zinc citrate 20-30 mg qd to TID.
- Zinc and tetracycline should not be used together since zinc inhibits the absorption of tetracycline.
- If zinc is used long-term then also supplement with copper: 10-15 mg zinc: 1 mg copper.
  - Bowe, W., et al., "Diet and acne," Jour Amer Acad Dermatol 2010; 63:124-41.



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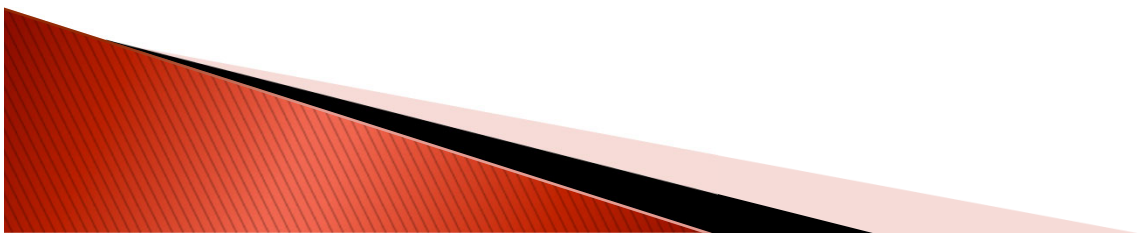
- Dreno, B., et al., “Low doses of zinc gluconate fro inflammatory acne,” Acga Derm Venerol 1989; 69:541-43.
- Michaelsson, G., et al., “A double-blind study of the effect of zinc and oxytetracycline in acne vulgaris,” Bri Jour Dermaol 1977; 97:561-66.
- Hilstrom, L., et al., “Comparison of oral treatment of zinc sulfate and placebo in acne vulgaris,” Brit Jour Dermatol 1977; 97:681-84.

Transdermal Niacinamide

- Niacinamide is anti-inflammatory.
- Study showed that transdermal niacinamide 4% was as effective as transdermal clindamycin 1%.
  - Shalta, A., et al., "Topical nicotinamide compared with clindamycin gel in the treatment of inflammatory acne vulgaris," Int Jour Dermatol 1995; 34:434-37.

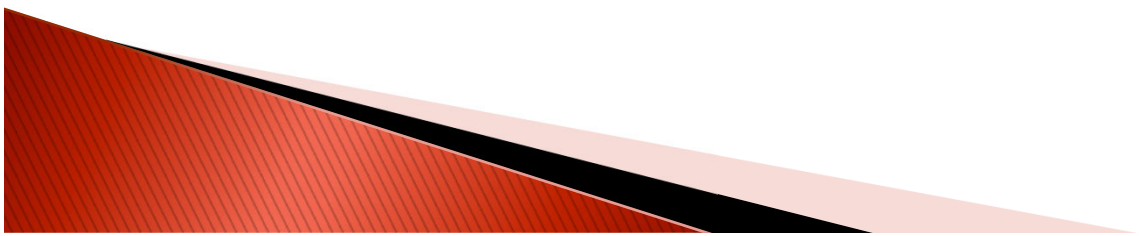
Compound For Acne

- Niacinamide 4% in Topical Cream
- #30 grams
- Sig: apply BID to affected area



Vitamin A

- Studies have shown that patients with acne have lower vitamin A levels in the plasma and skin.
  - El-akawi, Z., et al., "Does the plasma level of vitamins A and E affect acne condition," Clin Exp Dermatol 2006; 31:430-34.
  - Rollman, O., et al., "Vitamin A in skin and serum—studies of acne vulgaris, atopic dermatitis, ichthyosis vulgaris and lichen planus," Brit Jour Dermatol 1985; 113:405-13.

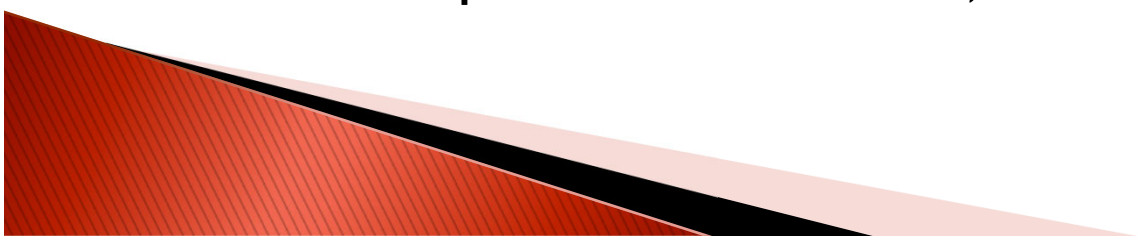


Vitamin A (Cont.)

- A study showed that the more severe the acne the lower the level of vitamin A was in the patients.
- Also patients with severe acne had lower levels of retinol-binding protein than patients with mild acne or no acne.
- If a patient has a lower level of retinol-binding protein then they have less ability to transport vitamin A to the tissues.
  - Kligman, A., et al., "Oral vitamin A in acne vulgaris: preliminary report," Int Jour Dermatol 1981; 20:278-85.

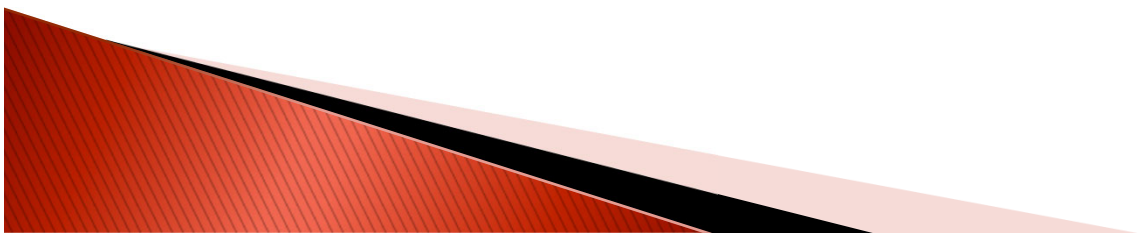
Vitamin A (Cont.)

- Studies using large doses of vitamin A have had varied results but since high doses of vitamin A is potentially toxic, other therapies should be considered first and only use high dose vitamin A as a last resort for treatment.
  - Ibid., Gaby.
  - Saunders, T., "Favorable effects of vitamin A in a case of acne of long duration," Arch Dermatol Symp 1944; 50:199.
  - Labadarios, D., et al., "Vitamin A in acne vulgaris," Clin Exp Dermatol 1987; 12:432-36.



Vitamin B6 For Premenstrual Acne

- An uncontrolled trial showed that pyridoxine 50 mg qd beginning one day prior to the menstrual cycle and continuing during the cycle for three cycles revealed a decrease in acne flares.
  - Snider, B., et al., "Pyridoxine therapy for premenstrual acne flare," Arch Dermatol 1974; 110:130-31.



Pantothenic Acid

- In an uncontrolled trial using high dose pantothenic acid (10 grams qd) in four divided doses produced positive results.
- Patients did have to continue a maintenance dose of pantothenic acid to control their acne.
- They also used a transdermal cream that contained 20% by weight of pantothenic acid to the affected area QID to six times a day.
- No side effects were seen but since the doses of pantothenic acid are very high in this study it may be more advisable to use another therapy.
  - Leung, L., "Pantothenic acid deficiency as the pathogenesis of acne vulgaris," Med Hypotheses 1995; 44:490-92.

Vitamin C

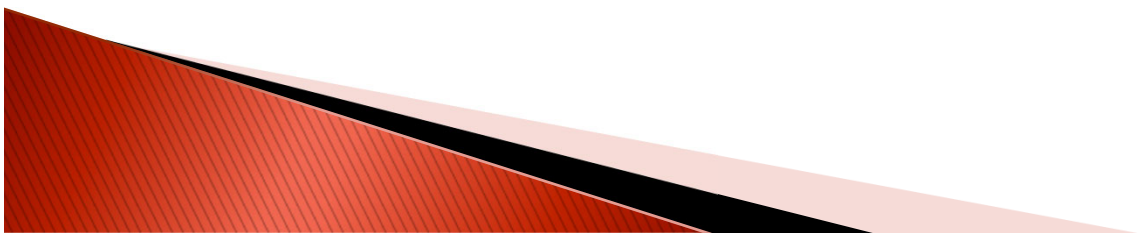
- Vitamin C deficiency has been shown to make acne worse.
- In one study, patients that took vitamin C (3 grams qd) and also drank 16 oz. of citrus juice, many of them had an improvement in their acne.
  - Morris, G., "Use of vitamin C in acne vulgaris," Arch Dermatol 1954; 70:364-64.

Vitamin C and Retinol

- A randomized and double-blind studies on the comparison of the efficacies of topical formulations containing 5% sodium ascorbyl phosphate (SAP) and 0.2% retinol, separately as well as in combination application, were conducted. The resulting data showed that SAP reduced the inflammatory lesion by 20.14% and 48.82% within 4 and 8 weeks respectively.
- The combination treatment significantly reduced the inflammatory lesion by 29.28% after 4 weeks and 63.10% after 8 weeks of application.
  - Ruamrak, C., et al., "Comparison of clinical efficacies of sodium ascorbyl phosphate, retinol and their combination in acne treatment," Jour Cosmetic Sci, 2009.

Selenium

- In an uncontrolled small trial, patients with acne took 400 micrograms of selenium, and 20 IU qd vitamin E for 6 weeks. Many of the patients had their acne improve.
- More trials need to be done.
  - Michaelsson, G., et al., "Erythrocyte glutathione peroxidase activity in acne vulgaris and the effect of selenium and vitamin E treatment," Acta Dermatol Venerol 1984; 64:9-14.



Azelaic Acid

- Azelaic acid is active against Propionibacterium acnes and is antibacterial and anti-inflammatory.
- Studies have shown azelaic acid to be as effective as transdermal tretinoin, benzoyl peroxide, or erythromycin and as effective or almost as effective as oral tetracycline.
- Dose: 20% cream apply qd to affected area for one week and then apply BID for 2-3 months to one year.
  - Kainz, J., et al., "Azelaic acid 20 % cream: effects on quality of life and disease severity in adult female acne patients," Jour Dtsch Dermatol Ges 2016; 14(12):1249-59.

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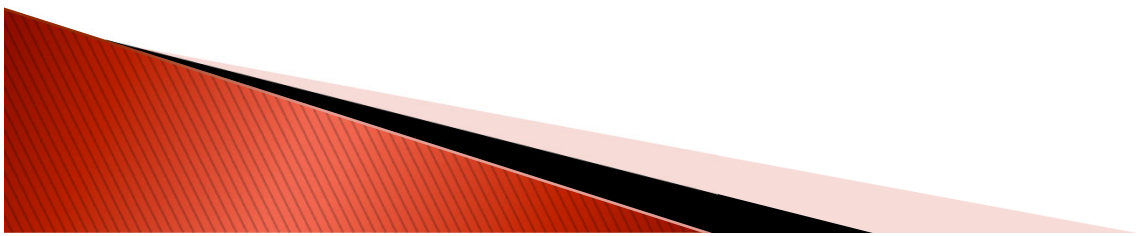
- Norris, J., et al., "Azelaic acid really does work in acne—a double-blind national and international study," Brit Jour Dermatol 1987; 32(Suppl):34-5.
- Bladon, P., et al., "Topical azelaic acid and the treatment of acne: a clinical and laboratory comparison with oral tetracycline," Brit Jour Dermatol 1986; 114:493-99.
- Graupe, K., et al., "Efficacy and safety of topical azelaic acid (20 percent cream): an overview of results from European clinical trials and experimental report," Cutis 1996; 57(1 Suppl):20-35.

Azelaic Acid (Cont.)

- Possible side effects of azelaic acid
  - Lightening of normal skin
  - Reddening of the skin
  - Increased hair growth
  - Worsening of asthma or vitiligo
  - Exacerbation of recurrent herpes labialis
    - Physician's Desk Reference, Montvale, NJ: PDR Network, LLC, 2010, p. 1808-10.

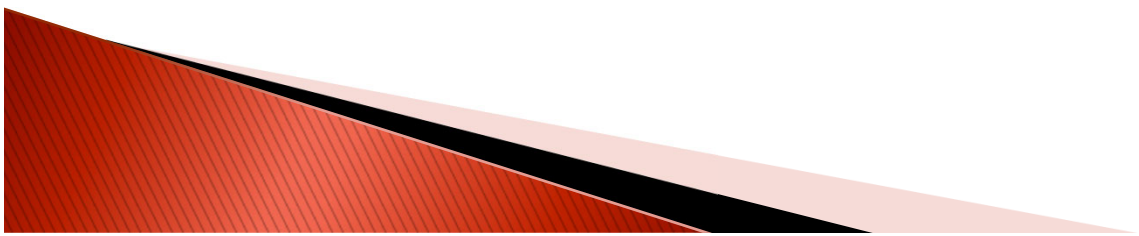


Acne: Post-inflammatory Hyperpigmentation

- Depigmenting agents target different steps in the production of melanin, most commonly inhibiting tyrosinase. These agents include hydroquinone, azelaic acid, kojic acid, arbutin, and certain licorice (glycyrrhiza) extracts.
- Other agents include retinoids, mequinol, ascorbic acid (vitamin C), niacinamide, N-acetyl glucosamine, and soy, and these products depigment by different mechanisms.
  - Callender, V., et al., "Post-inflammatory hyperpigmentation: etiologic and therapeutic considerations," Amer Jour Clin Dermatol 2011; 12(2):87-99.

Hypothyroidism

- One study showed that acne improved in most patients who were treated empirically with desiccated thyroid on the basis of low basal body temperature.
  - Barnes, B., "Thyroid therapy in dermatology," Cutis 1971; 8:581-83.
- The standard of care is to still measure thyroid levels by serum even if you are using basal body temperature to guide the care of the patient.



The Gut Skin Connection: Acne

Gut-Skin Connection

- The proposed causative factors for acne include the following: include insulin resistance, sex hormone imbalances, inflammation, and microbial dysbiosis.
- There is an emerging body of work on the human gut microbiome and how it mediates feedback between the foods the patient eats and the rest of their body.
- The gut microbiome is also an important mediator of inflammation in the gut and systemically.

Gut-Skin Connection (Cont.)

- A low-glycemic load diet, one rich in plant fibers and low in processed foods, has been linked to an improvement in acne, possibly through gut changes or attenuation of insulin levels.
  - Ashley, K., et al., "Edible plants and their influence on the gut microbiome and acne," Int Jour Mol Sci 2017; 18(5):1070.

Gut-Skin Connection (Cont.)

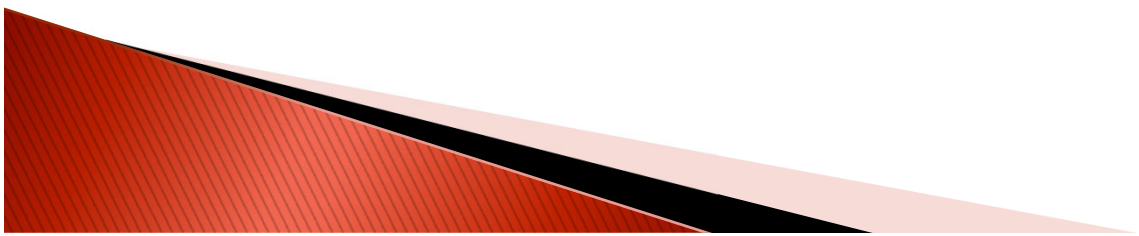
- This study discusses the role of probiotics in the development of the immune system, the treatment of acne and rosacea, and protection against aging and photodamage.
  - Kober, M., et al., "The effect of probiotics on immune regulation, acne, and photoaging," Int Jour Women's Derm 2015; 1(2):85-9.

Gut-Skin Connection (Cont.)

- The gut-brain-skin axis suggests a mechanism that links gastrointestinal health, influenced by interactions with oral probiotics, to the health of the patient's skin.
  - Bowe, W., "Probiotics in acne and rosacea," Cutis 2013; 92:6-7.
  - Bowe, W., et al., "Acne vulgaris, probiotics and the gut-brain-skin axis: back to the future?" Gut Pathog 2011; 3:1.

Compound For Acne #1

- Salicylic acid 2%/Potassium Azelaoyl diglycinate 10% in Topical Foam
- #30 grams
- Sig: apply qd to affected area

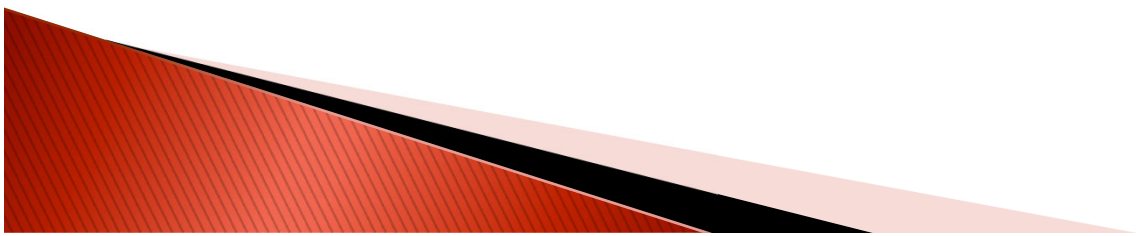


Compound For Acne #2

- Benzoyl peroxide 10%/Biotin 0.1%/Niacinamide 2% in Topical Gel or Cream
- #30 grams
- Sig: apply to affected area qd

Compound For Acne #3

- Benzoyl peroxide 10%/Natapres 6% Topical Lotion
- #30 grams
- Sig: apply to affected area qd

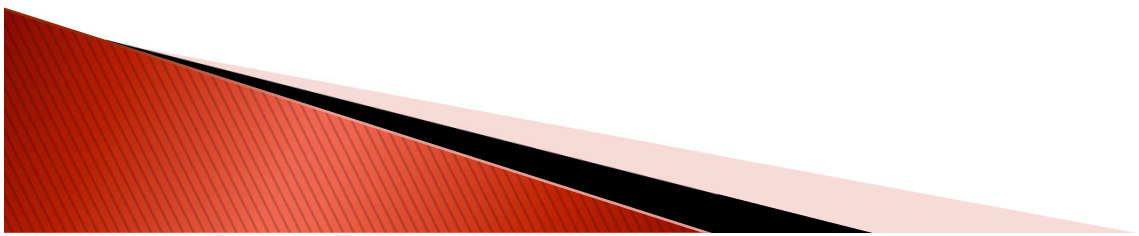


Compound For Acne #4

- Tretinoin 0.1% in Topical Gel
- #30 grams
- Sig: apply to affected area for 3 days then stop for 4 days and repeat cycle on and off for four months

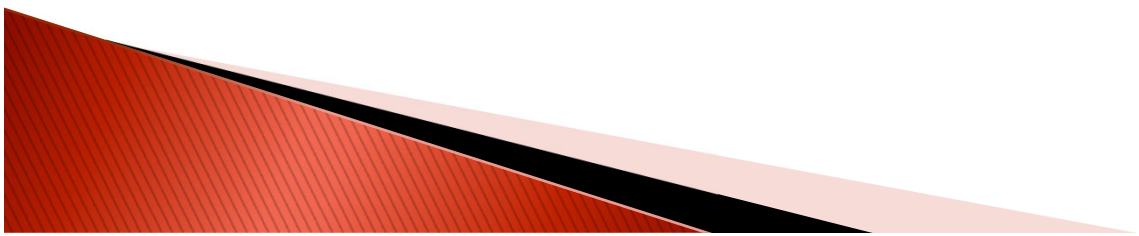
Compound For Acne #5

- Clindamycin 1%/Benzoyl peroxide 3% Topical Gel
- #30 grams
- Sig: apply to affected area qd



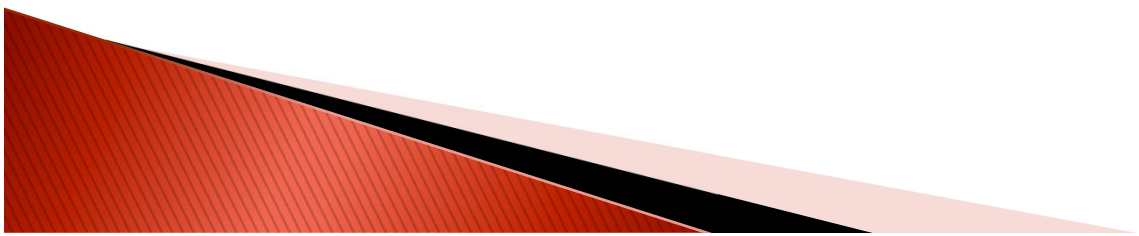
Compound For Acne #6

- Compounded Formula
  - Benzoyl Peroxide 5% as a Topical Spray
  - Sig: spray on affected area qd



Compound For Acne #7

- Compounded Formula
  - Benzoyl Peroxide 10% as a Topical Spray (RheoSpray)
  - Sig: spray on affected area qd



Compound For Acne #8

- Compounded Formula
  - Spironolactone 2.5%/Clindamycin 1%/Tetrahydrocurcuminoids in Topical Cream
  - #15 grams
  - Sig: apply to affected area qd

  - Use only in female patients if using long-term.

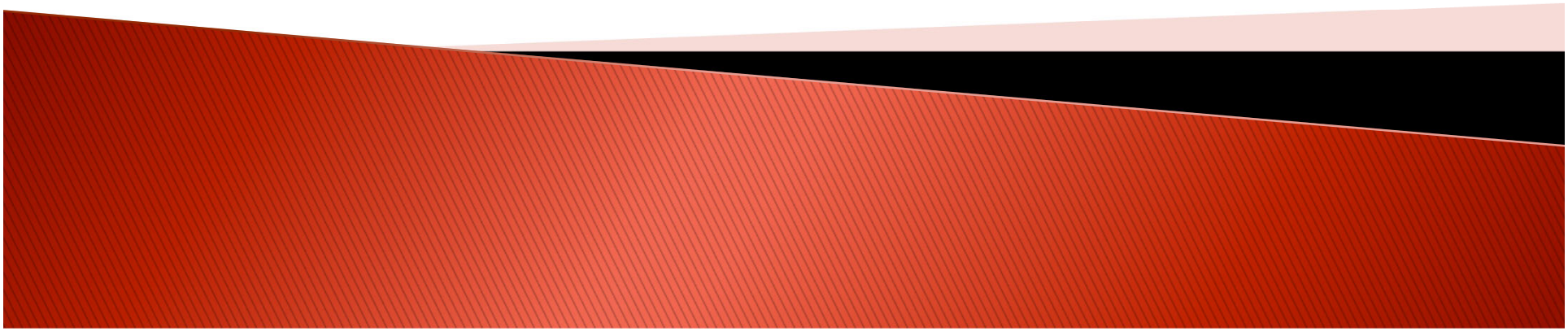
Compound For Acne #9

- Compounded Formula
  - Tretinoin 0.05%/Erythromycin3% in Topical Cream
  - #30 grams
  - Sig: apply to affected area qd

Cleanser For Acne

- Salicylic acid 2%/Aloe vera 1%/Tea tree oil 1% in Topical Foam
- #100 mL
- Sig: apply to the affect area qhs

Atopic Dermatitis/Eczema



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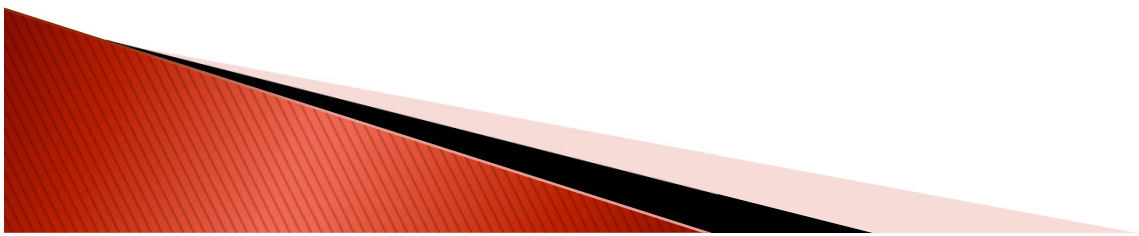
- Murray, M., et al., Atopic Dermatitis (Eczema). In Pizzorno, J., and Murray, M., Textbook of Natural Medicine. St. Louis: Elsevier/Churchill Livingstone, 2013.
- Gaby, A., Eczema. In Nutritional Medicine. Concord, NH: Fritz Perlberg Publishing, 2017.
- Mindell, E., and Smith, P., What You Must Know About Allergy Relief. Garden City Park, NY: Square One Publishers, 2016.

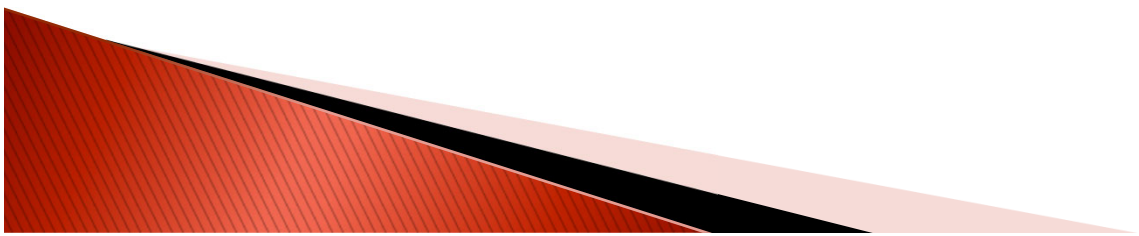
Atopic Dermatitis

- Atopic dermatitis is a pruritic, hereditary skin disorder and is the most common form of eczema.
- The life-time prevalence is 10% to 20% with many cases starting as a baby.
- 20% to 40% of people continue to have atopic dermatitis as adults.
  - Habif, T., Atopic Dermatitis in Clinical Dermatology 5th Ed., St. Louis: Mosby, 2010.



Atopic Dermatitis (Cont.)

- Conventional therapies are effective for some people, but they only suppress the disease and do not fix the etiology.
- The diagnosis requires three major and also three minor features.
- There are 22 minor features which shows that the extent of the atopic dermatitis can be very different from patient to patient.

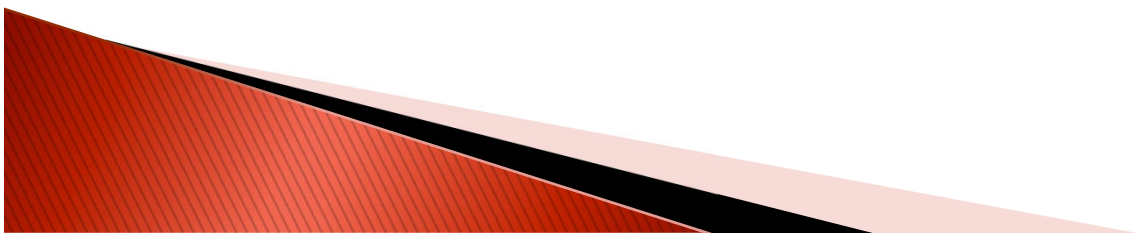


Diagnostic Criteria For Atopic Dermatitis

- Major features
  - Pruritus
  - Typical morphology and distribution
  - Flexual lichenification in adults
  - Facial and extensor involvement in infants and children
  - Chronic or chronically relapsing dermatitis
  - Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis
    - Ibid., Habif.

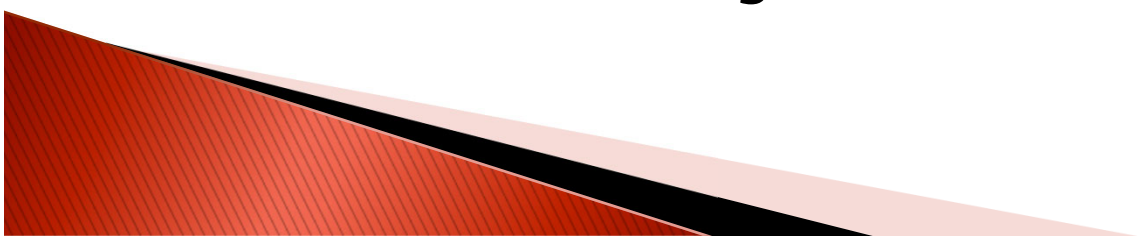
Diagnostic Criteria For Atopic Dermatitis (Cont.)

- Minor features
  - Itch caused by sweating
  - Xerosis
  - Eczema (perifollicular accentuation)
  - Recurrent conjunctivitis
  - Wool intolerance
  - Keratosis pilaris
  - Palmar hyperlinearity
  - Pityriasis alba
  - White dermatographism
  - Susceptibility to cutaneous infection (staph, herpes and other viruses)
  - Nipple dermatitis



Diagnostic Criteria For Atopic Dermatitis (Cont.)

- Minor features (cont.)
  - Dennie–Morgan lines
  - Elevated immunoglubulin E (IgE)
  - Immediate (type I) skin test reactivity
  - Food intolerance
  - Cataracts (anterior–subcapsular)
  - Cheilitis
  - Facial pallor or erythema
  - Hand dermatitis
  - Ichthyosis
  - Keratoconus
  - Orbital darkening

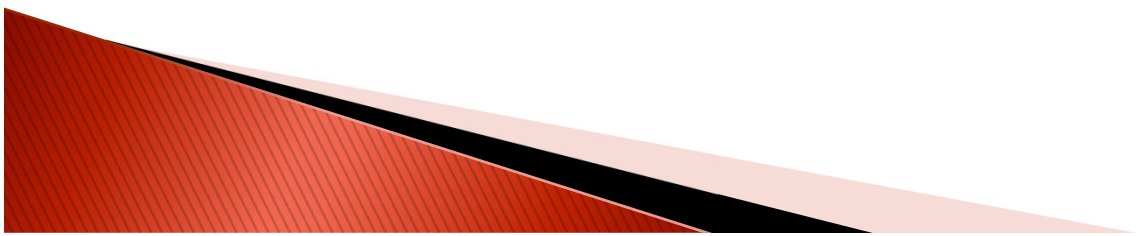


Pathophysiology of Atopic Dermatitis

- The pathophysiology of atopic dermatitis is complex and multifactorial, involving elements of barrier dysfunction, alterations in cell mediated immune responses, IgE mediated hypersensitivity, and environmental factors.
- Loss of function mutations in filaggrin have been implicated in severe atopic dermatitis due to a potential increase in trans-epidermal water loss, pH alterations, and dehydration.
- Other genetic changes have also been identified which may alter the skin's barrier function, resulting in an atopic dermatitis phenotype. The imbalance of Th2 to Th1 cytokines observed in atopic dermatitis can create alterations in the cell mediated immune responses and can promote IgE mediated hypersensitivity, both of which appear to play a role in the development of atopic dermatitis.

Pathophysiology of Atopic Dermatitis (Cont.)

- The role of the environment on the causation of atopic dermatitis and the impact of chemicals such as airborne formaldehyde, harsh detergents, fragrances, and preservatives must also be considered.
- Use of harsh alkaline detergents in skin care products may also unfavorably alter the skin's pH causing downstream changes in enzyme activity and triggering inflammation.
- Environmental pollutants can trigger responses from both the innate and adaptive immune pathways.



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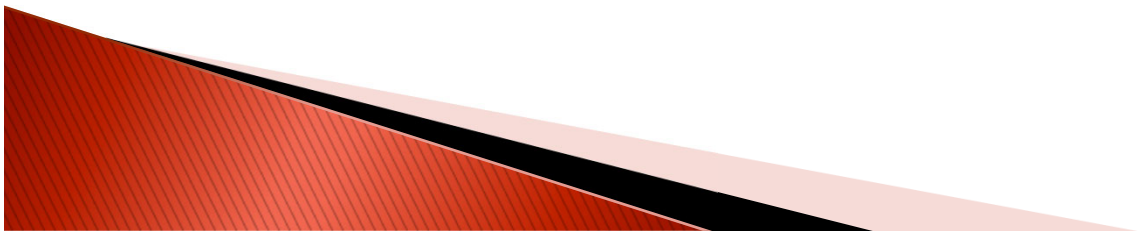
- Yong,-Jun, L., “Thymic stromal lymphopoietin: master switch for allergic inflammation,” JEM 2006; 203:2269-73.

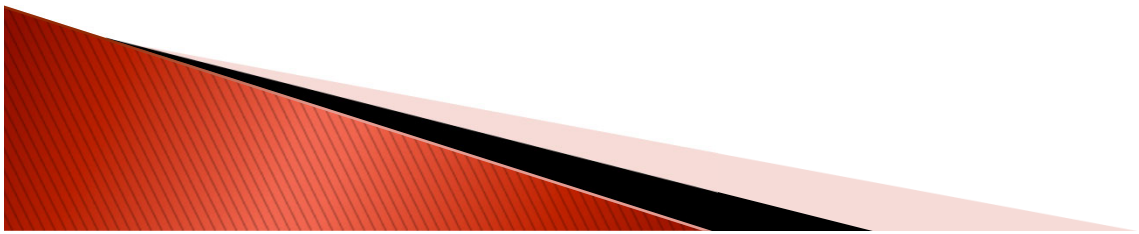
Pathophysiology of Atopic Dermatitis (Cont.)

- TSLP triggers Th2 and is elevated when stimulated by phthalates.
  - Shigeno, T., et al., "Phthalate ester-induced thymic stromal lymphopoietin mediates allergic dermatitis in mice," Immunology 2009; 128(Supp:1):e849-e857.



Pathophysiology of Atopic Dermatitis (Cont.)

- Gastric Helicobacter pylori stimulates epidermal cells to secrete TSLP.
- H. pylori antibody has been shown to be positive in up to 70% of people with atopic dermatitis.
  - Kido, M., et al., "Helicobacter pylori promotes the production of thymic stromal lymphopoietin by gastric epithelial cells and induces dendritic cell-mediated inflammatory Th2 responses," Infect Immun 2010; 78(1):108-14.
- Treating H. pylori has been shown to be helpful in patients with atopic dermatitis.
  - Galadari, I., et al., "The role of Helicobacter pylori in urticaria and atopic dermatitis," Skinmed 2006; 5(4):172-76.

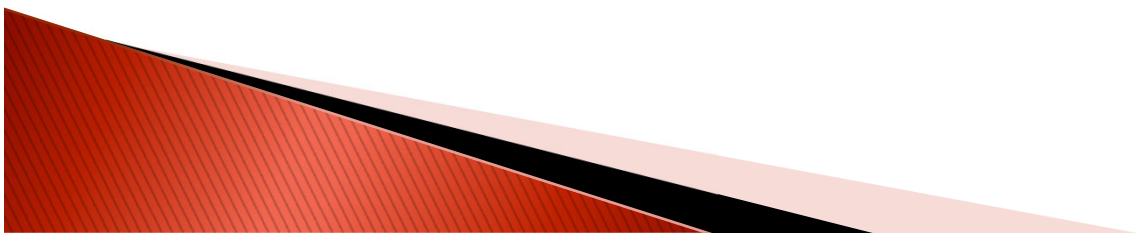


Pathophysiology of Atopic Dermatitis (Cont.)

- If the patient scratches then more damage occurs to the skin due to release of inflammatory cytokines and this further increases the need to itch.
- When the skin barrier is compromised then S. aureus and Candida organisms get into the skin and cause more inflammation.
  - Elias, P., et al., "Abnormal skin barrier in the etiopathogenesis of atopic dermatitis," Curr Opin Allergy Clin Immunol 2009; 9(5):437-46.
  - Ibid., Kaufman.

Pathophysiology of Atopic Dermatitis (Cont.)

- Food allergies have been found to be the cause of atopic dermatitis in 25% to 50% of children.
  - Ibid., Kaufman.
- Common food allergens linked to atopic dermatitis.
  - Eggs
  - Soy
  - Milk
  - Wheat
  - Fish
  - Shellfish
  - Peanuts



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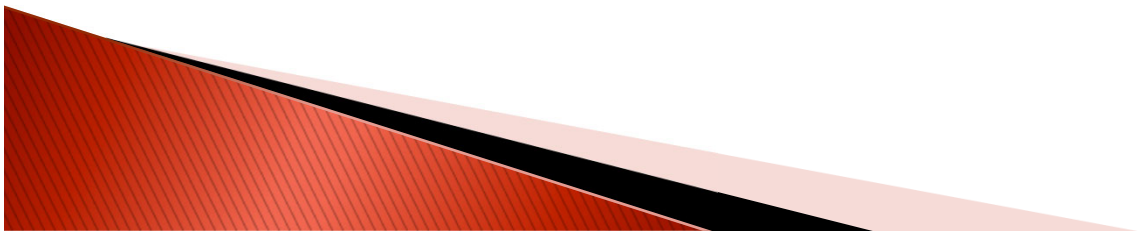
- Ratner, P., et al., “Food allergy and dietary manipulation in atopic eczema,” Ann Allergy 1984; 52: 231.
- Hill, D., et al., “Food allergy in childhood eczema,” Allergol Immunopathol 1980; 8:362.

Pathophysiology of Atopic Dermatitis (Cont.)

- Psychological stress makes the symptoms of atopic dermatitis worse.
  - Chida, Y., et al., "A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis," Psychosom Med 2008; 70:102-16.

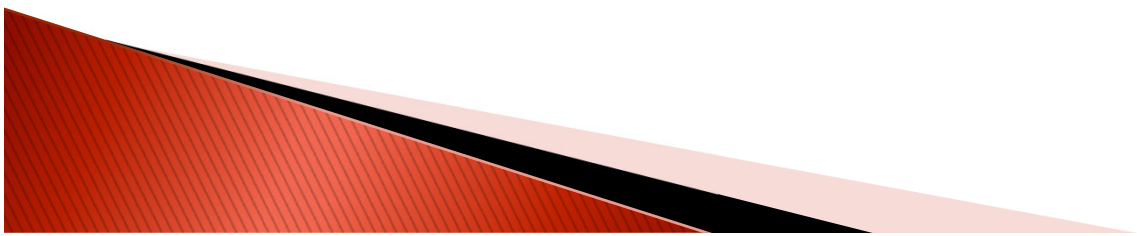


Pathophysiology of Atopic Dermatitis (Cont.)

- An overgrowth of yeast (Candida albicans) in the GI tract has been suggested as a causative factor in allergic diseases including atopic dermatitis.
- High levels of anticandidal antibodies are commonly seen in patients with atopic dermatitis.
  - Ibid., Murray.
- Also the severity of the disease usually correlates with the level of IgE antibodies in relationship to antigens to Candida.

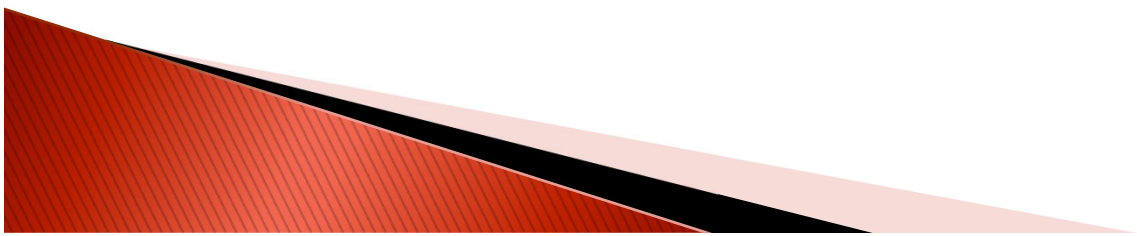
Pathophysiology of Atopic Dermatitis (Cont.)

- Treating the patient with positive candida antibodies with anti-candidal therapies has been shown to be helpful.
  - Savolainen, J., et al., "Candia albicans and atopic dermatitis," Clin Exp Allergy 1993; 23:332-39.
  - Adachi, A., et al., "Role of Candida allergen in atopic dermatitis and efficacy of oral therapy with various antifungal agents," Arerugi 2000; 48(7):719-25.



Pathophysiology of Atopic Dermatitis (Cont.)

- Contact sensitivity to nickel is a cause of eczema.
  - Sometimes the eczema is triggered by ingestion of nickel that occurs naturally in food or leaches food from stainless steel cookware. Improvement or resolution was seen in almost ½ of the individuals in a medical trial.
    - Antico, A., et al., "Chronic allergic-like dermatopathies in nickel-sensitive patients. Results of dietary restrictions and challenge with nickel salts," Allergy Asthma Proc 1999; 20:235-42.

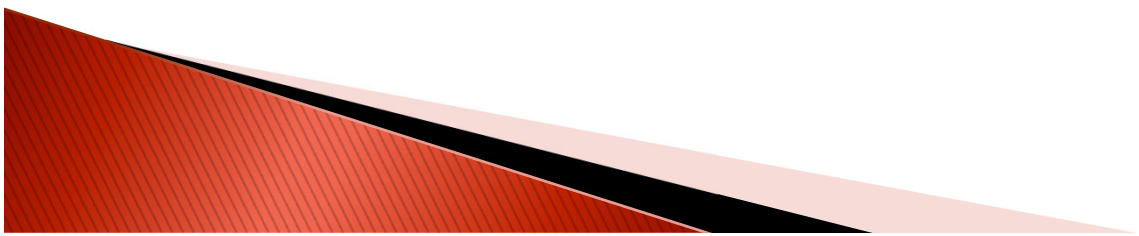


Pathophysiology of Atopic Dermatitis (Cont.)

- Nickel sensitivity (cont.)
  - A study showed that intestinal absorption of nickel may be increased in people with atopic eczema.
    - Hindsen, M., et al., "Nickel levels in serum and urine in five different groups of eczema patients following oral ingestion of nickel," Acta Derm Venereol 1994; 74:176-78.
  - The increase may be due to increased intestinal permeability which is common in patients with eczema.
    - Pike, M., et al., "Increased intestinal permeability in atopic eczema," Jour Invest Dermatol 1986; 86:101-04.

Pathophysiology of Atopic Dermatitis (Cont.)

- Nickel sensitivity (cont.)
  - Patients given cromolyn sodium for allergies decreased both the intestinal permeability and nickel absorption in individuals with dyshidrotic eczema due to a sensitivity to nickel.
    - Pigatto, P., et al., "Disodium cromoglycate versus diet in the treatment and prevention of nickel-positive pompholyx," Contac Dermatitis 1990; 22:27-31.
  - Giving zinc to patients that are nickel sensitive may improve eczema by lowering the reactivity to nickel.
    - Santucci, B., et al., "ZnSO4 treatment of NiSO4-positive patients," Contact Dermatitis 1999; 40:281-82.



Pathophysiology of Atopic Dermatitis (Cont.)

- Study done in Europe involving 10 countries showed that there was a positive association between the intake of trans fats and atopic dermatitis.
  - Weiland, S., et al., "Intake of trans fatty acids and prevalence of childhood asthma and allergies in Europe," Lancet 1999; 353:2040-41.
- Eating trans fats may increase the development of atopic dermatitis since they interfere with the metabolism and use of essential fatty acids.

Conventional Therapies

- Atopic dermatitis management involves early diagnosis, skin barrier function support, mitigation of cutaneous inflammation, and concomitant risk stratification for the development of food allergy, asthma, allergic rhinitis, and environmental allergies.
  - Shaker, M, et al., “The ins and outs of an 'outside-in' view of allergies: atopic dermatitis and allergy prevention,” Curr Opin Pediatr 2018; 30(4):576-81.
  - Weidinger, S., et al., “Atopic dermatitis,” Lancet 2016; 387(10023):1109-22.

Conventional Therapies (Cont.)

- Pharmaceuticals
  - Antimicrobials
    - Mupirocin or bacitracin ointment BID for 7–10 days
    - Cephalexin 250 mg QID for 7 days or
    - Dicloxacillin 250 mg QID for 7 days
  - Antihistamines
    - Oral or doxepin cream 5% compounded applied QID (transdermally may cause sedation if used over large areas)
  - Topical steroids
    - BID for two weeks during acute flare then qd to BID on weekends.
  - Topical immunomodulators
  - Other immunomodulators (cyclosporine)

Conventional Therapies (Cont.)

- Pharmaceuticals (cont.)
  - Antivirals
    - If the case does not resolve, consider a superinfection with herpes virus.
      - For herpes zoster: acyclovir 800 mg five times a day for 7-10 days
      - For varicella-zoster: acyclovir 800 mg QID for 5 days
  - Antifungals
    - Ketoconazole topically or PO 200 mg BID for 10 days
      - Skogh, M., "Atopic eczema unresponsive to evening primrose oil (linoleic and gamma-linolenic acids)," Jour Amer Acad Dermatol 1986; 15:114-15.

Metabolic Therapies

- Autoimmune process
- Lifestyle changes
- Nutrition
- Mind/body/spirit
- Vitamins/minerals
- Essential fatty acids
- Probiotics/5R program
- Pancreatic enzymes
- Botanicals
- Chinese medicine
- Kampo
- Homeopathy
- Treat hypothyroidism if present
- Barrier therapies
- Stress reduction
- Remove allergens
- Breastfeeding
- Decrease cell phone use
- Treat infection
- Compounded therapies

Autoimmune Process

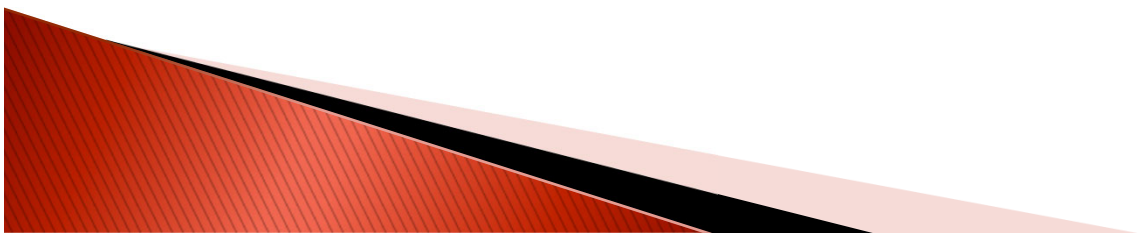
- Three therapies for all autoimmune diseases:
  - Stop all gluten
  - Improve GI health
    - Treat patient if they are infected with Candida or H. pylori.
    - Probiotics
  - LDN
    - Jaros, J., et al., "Low dose naltrexone in dermatology," Jour Drugs Dermatol 2019; 18(3):235-38.
    - Ekelem, C., et al., "Utility of naltrexone treatment for chronic inflammatory dermatologic conditions: A systematic review," JAMA Dermatol 2019; 155(2):229-36.
    - Lee, B., et al., "The uses of naltrexone in dermatologic conditions," Jour Amer Acad Dermatol 2019; 80(6):1746-52.

LDN For Atopic Dermatitis

- LDN is effective for all autoimmune diseases including atopic dermatitis.
- For mild cases
  - Use topical naltrexone to affect immune system: 1% cream base for itching
- For severe cases
  - One 1.5 mg capsule qhs x 7 days
  - Two 1.5 mg capsules qhs x 7 days
  - Three 1.5 mg capsules qhs x 7 days
  - Then 4.5 mg thereafter as a single capsule

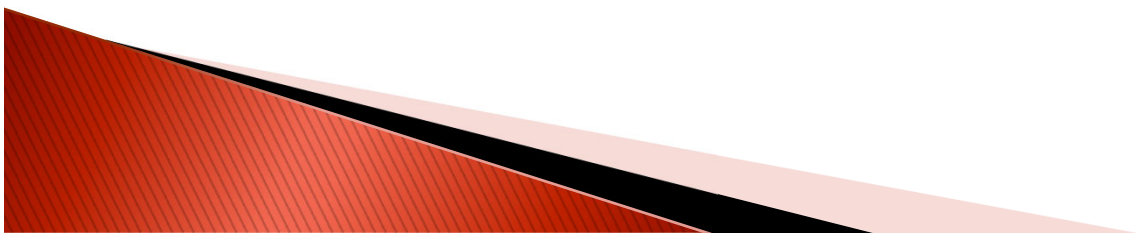
Lifestyle Changes

- Lifestyle changes
  - Moisturizers
  - Hydration
  - Mild soap or soap substitutes
  - Bleach baths
  - Wet dressings
  - Avoidance of allergens
  - Loose-fitting clothes
  - Humidity



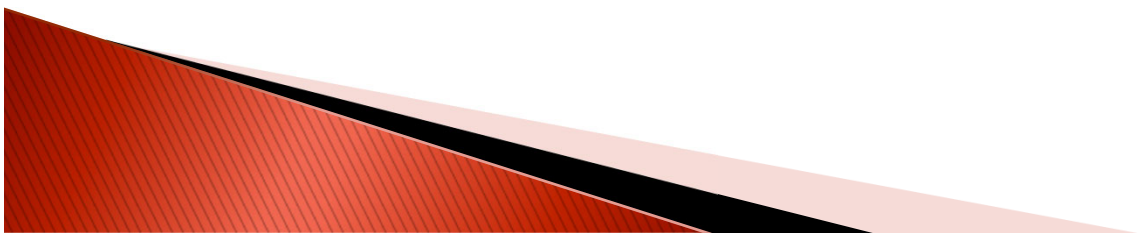
Lifestyle Therapies

- Hydration
  - Rehydration of the stratum corneum reduces the effect of allergens and irritants. It also increases barrier function.
  - Soak in lukewarm bath for 10-20 minutes or take a lukewarm shower.
  - Bath salts can be added to the water after the patient is wet first.
  - If plain water is irritating the add one cup of salt to the water.
    - Ibid. Kaufman.



Lifestyle Therapies (Cont.)

- Mild soap or soap substitutes
  - Use a neutral pH soap
    - Dove
    - Aveeno
    - Basis
  - If the soaps irritate the skin, then use hydrophobic lotions or creams such as Cetaphil. They can be applied without water, rub in until foam is produced and then wipe off with a soft cloth.
    - Ibid., Habif.
    - Ibid., Kaufman.



Lifestyle Therapies (Cont.)

- Many brands of detergents are filled with additives that could aggravate allergy prone skin, possibly triggering eczema.
- Choose brans that are designed hypoallergenic and are free of perfumes, dyes, bleaches, phosphates, enzymes, and fabric softeners such as:
  - All Free and Clear
  - Arm and Hammer Free
  - Seventh Generation
  - Tide Free
  - Woolite Hypo-Allergic

Lifestyle Therapies (Cont.)

- Bleach baths
  - Study used dilute bleach baths combined with nasal application of mupirocin to decrease colonization with S. aureus. Good improvement was seen in areas of the body that were exposed to the bleach baths.
    - Huang, J., et al., "Treatment of Staphylococcus aureus colonization in atopic dermatitis decreases disease severity," Pediatrics 2009; 123:e808-e814.

Lifestyle Therapies (Cont.)

- Moisturizers after bathing
  - After bathing have the patient apply an occlusive ointment over the entire over the whole body to help retain moisture.
    - Petroleum jelly
    - Vegetable oil
    - Aquaphor
  - Application should be within three minutes after bathing.
  - Study showed using virgin coconut oil reduced colonization with S. aureus.
    - Verallo-Rowell, V., et al., "Novel antibacterial and emollient effects of coconut and virgin olive oils in adult atopic dermatitis," Dermatitis 2008; 19:308-15.

Lifestyle Therapies (Cont.)

- Moisturizers after bathing (cont.)
  - Emollients that contain ceramide decrease transepidermal water loss and improves symptoms.
    - EpiCeram
      - Study showed improvement with EpiCeram almost equal to fluticasone cream after 28 days.
        - Sugarman, J., et al.,, "Efficacy of a lipid-based barrier repair formulation in moderate-to-severe pediatric atopic dermatitis," Jour Drugs Dermatol 2009; 8:1106-11.
    - TriCeram

Lifestyle Therapies (Cont.)

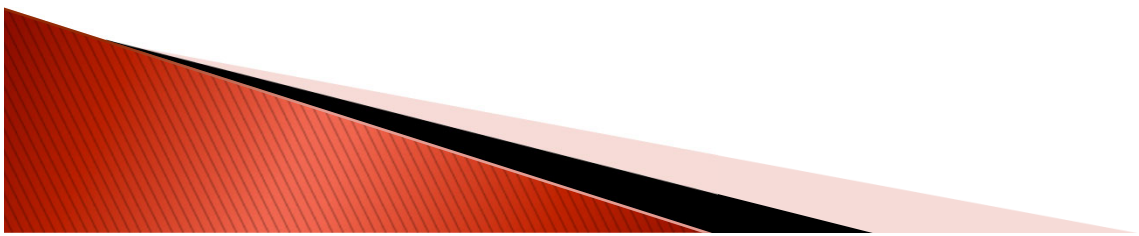
- Moisturizers after bathing (cont.)
  - Urea, alpha-hydroxy acid, and lactic acid products have been typically used for exfoliation and moisturizing.
  - One study compared a 5% urea-containing moisture compared to a 10% urea-containing formula. Both showed almost a 20% improvement over 42 days with BID use.
    - Bissonnette, R., et al., "A double-blind study of tolerance and efficacy of a new urea-containing moisturizer in patients with atopic dermatitis," Jour Cosmet Dermatol 2010; 9:16-21.

Lifestyle Therapies (Cont.)

- Wet dressings are very helpful for skin that is severely affected.
- Apply wet cloth with plain water or Burrow solution to recalcitrant lesions.
- Occasionally rewet dressings.
- Wet dressings also increase the penetration of steroids.
- Burrow solution
  - Dissolve one Domeboro packet or tablet into a pint of lukewarm water.
    - Ibid., Kaufman.

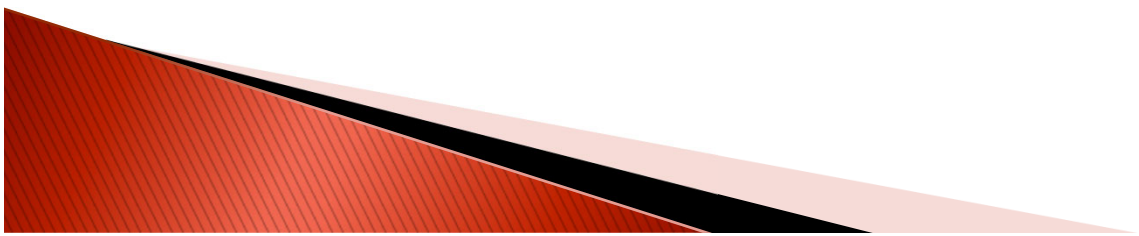
Lifestyle Therapies (Cont.)

- Wet wraps provides a barrier to scratching and also aids in hydration, penetration of medication and emollients.
- Patients also sleep better when they are not scratching.
- After applying medication and emollient, have the patient wrap the area that is affected in warm, wet gauze, or 100% cotton socks with toe part cut off. Add a dry layer over the wet layer and leave on overnight for 5-14 days.
  - Ibid., Murray.



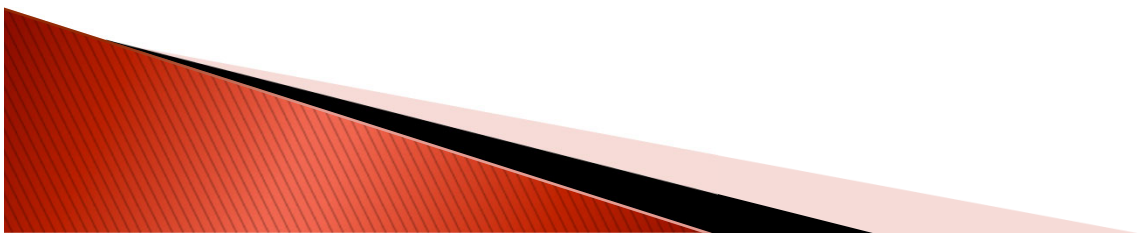
Lifestyle Therapies (Cont.)

- Ceramide-containing emollients can be used to decrease water loss trans-epidermally.
  - CeraVe
  - Nature Pure's Hippophae-Ceramide Cream
  - Hippophae Oil (sea buckthorn)
  - Ceramides
  - Squalane
  - Olive oil
  - Beeswax
  - Extracts of St. John's wort
  - Ginkgo biloba
  - Calendula
  - Chamomile
    - Ibid., Murray.



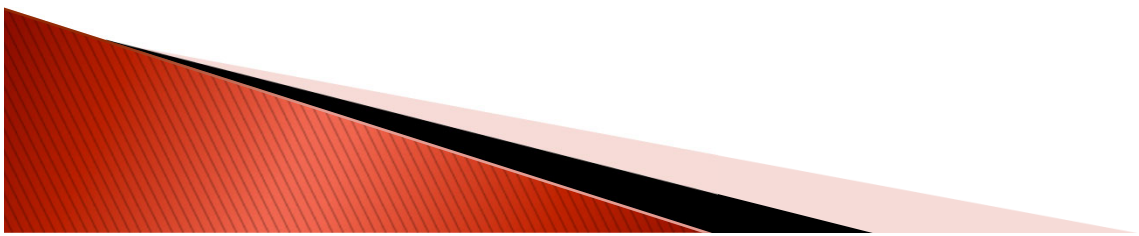
Lifestyle Therapies (Cont.)

- Avoid allergens
- Loose fitting clothing
  - Have the patient wear loose fitting clothing that is made of natural fibers such as cotton or silk.
  - Avoid wool
  - Have the patient wash new clothing before wear to remove chemicals
  - Use liquid detergents without fabric softeners or brighteners
  - Rinse clothes an extra cycle when washing



Lifestyle Therapies (Cont.)

- Humidity
  - Controlled temperature and humidity decreases triggers for atopic dermatitis such as cold, dry air, and heat.
  - In the winder humidify the air to 30% to 40% humidity.
  - Air conditioning in the summer decreases sweating which can be a trigger and it also helps prevent the growth of mold.
    - Ibid., Kaufman.

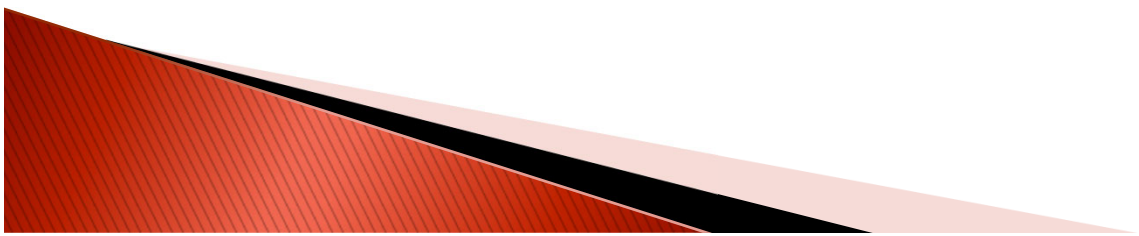


Nutrition

- Breast feeding or use of hydrolyzed formulas may be helpful.
- Allergy elimination diet
  - Food allergies affect 10% to 40% of children that have atopic dermatitis.
    - Ibid., Rakel.
  - The gold standard for diagnosing allergy is a placebo-controlled double-blind oral food challenge. History and IgE testing. Prick tests may not be accurate.
    - Bath-Hextall, F., et al., "Dietary exclusions for established atopic eczema," Cochrane Database Syst Rev 2008; CD005203.

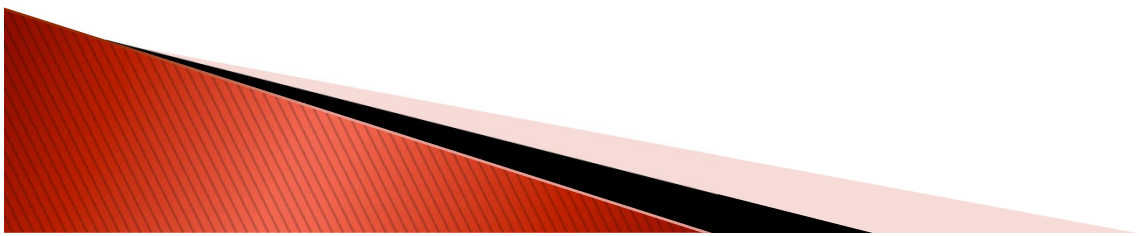
Nutrition (Cont.)

- Oolong tea
  - Study showed 63% of patients that drank Oolong tea TID, made from five tea bags had significant improvement that was objective.
  - The response lasted for 6 months in over 50% of the patients involved in the study.
  - The polyphenols contained in the tea have an anti-allergy effect.
    - Uehara, M., et al., "A trial of oolong tea in the management of recalcitrant atopic dermatitis," Arch Dermatol 2001; 137:42-3.



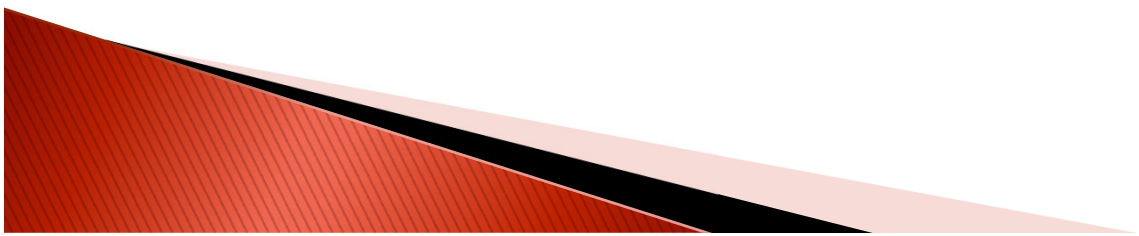
Mind/Body/Spirit Therapy

- Stress reduction decreases symptoms.
- Some patients may benefit from massage, biofeedback or hypnosis.
  - Weber, M., et al., "Improvement of pruritus and quality of life of children with atopic dermatitis and their families after joining support groups," Jour Eur Acad Dermatol Venereol 2008; 22:992-97.



Vitamins/Minerals

- Some nutrients may be effective to treat eczema.
  - Zhu, Z., et al., "Assessment of the effectiveness of vitamin supplement in treating eczema: A systematic review and meta-analysis," Evid Based Complement Alternat Med 2019; 2019:6956034.
  - Vitamin D and vitamin E used together was found to be more effective than separate usage.
    - Javanbakht, M., et al., "Randomized controlled trial using vitamins E and D supplementation in atopic dermatitis," Jour Dermatol Treat 2011; 22:144-50.

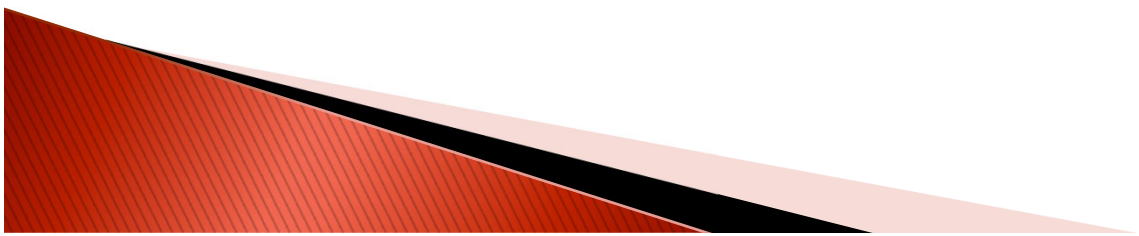


Vitamins/Minerals (Cont.)

- Vitamin E alone
  - One study which was single-blind look at almost 100 patients. They were given either 400 IU vitamin E or placebo for eight months.
  - 60% of the treated group had significant improvement compared to 2% of the placebo group with also reductions in serum Ig3 levels.
    - Tsoureli-Nikita, E., et al., "Evaluation of dietary intake of vitamin E in the treatment of atopic dermatitis: a study of the clinical course and evaluation of the immunoglobulin E serum levels," Inter Jour Dermatol 2002; 41:146-50.

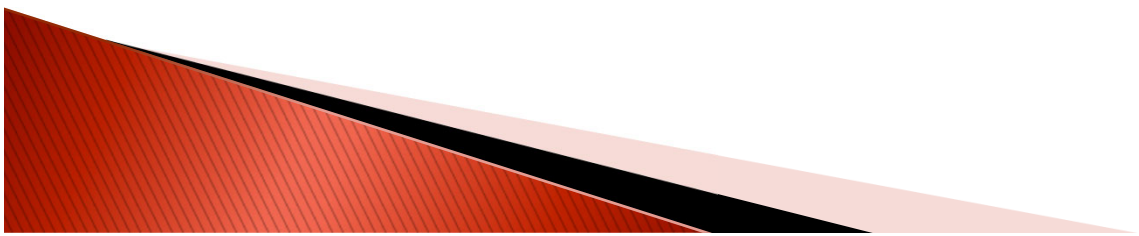
Vitamins/Minerals (Cont.)

- Zinc
  - Some cases of eczema may be due to zinc deficiency.
  - Zinc supplementation is effective in patients that are zinc deficient.
  - If zinc is supplemented long-term then also give copper.
  - Study suggested that zinc + fatty acid supplementation may be better than either alone.
    - Horrobin, D., et al., "Zinc, essential fatty acids, and prostaglandins," Arch Dermatol 1979; 115:641-42.



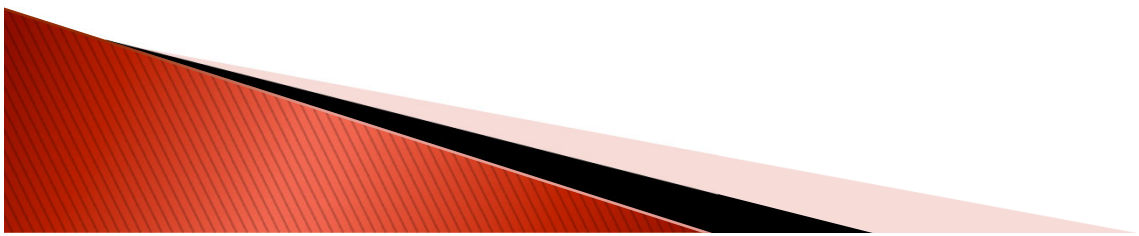
Vitamins/Minerals (Cont.)

- Zinc (cont.)
  - Zinc plays a central role in skin integrity via barrier and immune mechanisms and may also be relevant in the pathogenesis of atopic dermatitis.
  - This study concluded that low serum, hair and erythrocyte zinc levels are associated with atopic dermatitis.
    - Gray, N., et al., "Zinc and atopic dermatitis: a systematic review and meta-analysis," Jour Eur Acad Dermatol Venereol 2019; 33(6):1042-50.



Vitamins/Minerals (Cont.)

- Vitamin B12 cream
  - Trial revealed that vitamin B12 cream 0.07% compounded applied BID was affective in both children and adults with eczema.
    - Januchowski, R., "Evaluation of topical vitamin B12 for the treatment of childhood eczema," Jour Altern Complement Med 2009; 15:387-89.

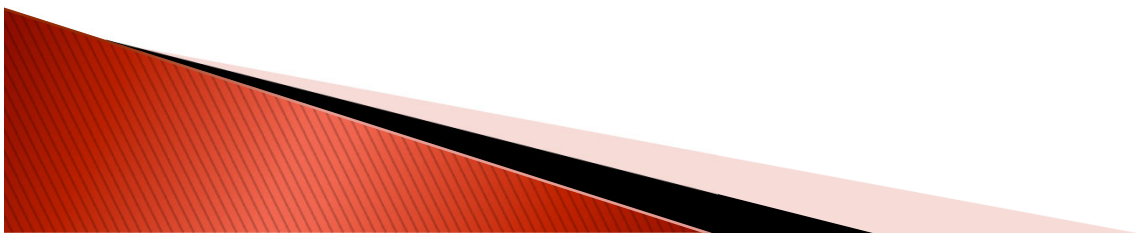


Vitamins/Minerals (Cont.)

- Vitamin D
  - Maintaining a vitamin D serum concentration within normal levels is warranted in atopic dermatitis was shown to be important in this study.
    - Kechichian E., Ezzedine K. Vitamin D and the skin: an update for dermatologists. American Journal of Clinical Dermatology. 2018;19(2):223-235.
  - This meta-analysis showed that serum vitamin D level was lower in the atopic dermatitis patients and vitamin D supplementation could be a new therapeutic option for this disease.
    - Kim, M., et al., "Vitamin D status and efficacy of vitamin D supplementation in atopic dermatitis: A systematic review and meta-analysis," Nutrients 2016; 8(12):789.

Vitamins/Minerals (Cont.)

- Selenium was not found to be effective.
  - Studies showed that patients with atopic dermatitis had low levels of selenium in their blood and reduced activity of glutathione peroxidase.
  - But no improvement was seen in supplementing with 600 micrograms qd of selenium for 3 months.
    - Hinks, L., et al., "Trace element status in eczema and psoriasis," Clin Exp Dermatol 1987; 12:93–7.
    - Fairris, G., et al., "The effect on atopic dermatitis of supplementation with selenium and vitamin E," Acta Derm Venereol 1989; 69:359–62.



Essential Fatty Acids

- A study in patients with atopic dermatitis showed abnormalities in fatty acid metabolism.
- The mean concentration in plasma phospholipids of the omega-6-fatty acid, linoleic acid were found to be high. The concentrations of all of the breakdown products including gamma-linolenic acid (GLA) were decreased.
- Furthermore, the mean concentration of the essential omega-3-fatty acid, alpha-linolenic acid (ALA) was high, but all of its metabolites were lower.
- These same abnormalities were seen in adipose tissue.
  - Wright, S., et al., "Adipose tissue essential fatty acid composition in patients with atopic eczema," Eur Jour Clin Nutr 1991; 45:501-55.

Essential Fatty Acids (Cont.)

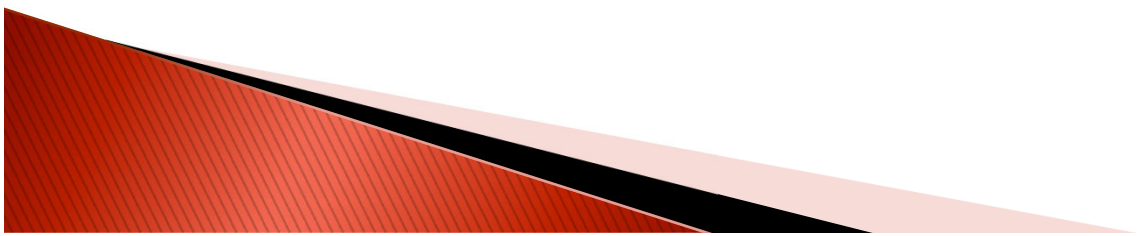
- The above findings suggest that patients with atopic dermatitis have a reduced activity of the enzyme delta-6-desaturase which is needed for the conversion of linoleic acid to GLA and of ALA to EPA.
  - Ibid., Gaby.
- Also, individuals with atopic dermatitis have a decreased ability to incorporate linoleic acid or other fatty acids into cell membranes.
  - Oliwiecki, S., et al., "Levels of essential and other fatty acids in plasma and red cell phospholipids from normal controls and patients with atopic eczema," Acta Derm Vernereol 1990; 71:224-28.

Essential Fatty Acids (Cont.)

- EPA/DHA and GLA have all been shown to be beneficial.
- Also instruct the patient to avoid trans-fatty acids.
  - Bukutu, C., et al., "Complementary, holistic, and integrative medicine: atopic dermatitis," Pediatr Rev 2007; 28:e87-e94.
  - Koch, C., et al., "Docosahexaenoic acid (DHA) supplementation in atopic eczema: a randomized, double-blinded, controlled trial," Brit Jour Dermatol 2008; 158:786-92.
  - Steward, J., et al., "Treatment of severe and moderately severe atopic dermatitis with evening primrose oil (Epogam): a multi-centre study," Jour Nutr Med 1991; 2:9-15.

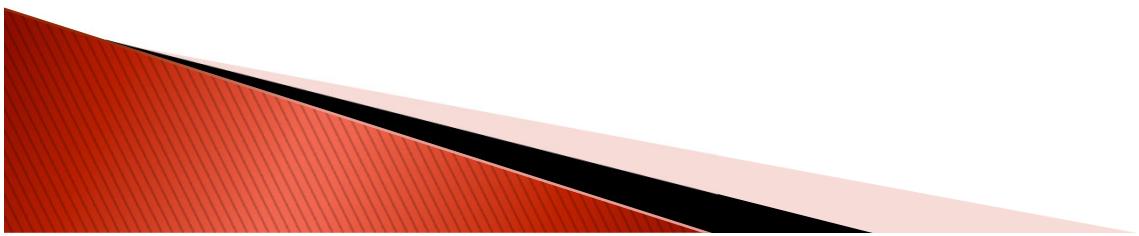
Essential Fatty Acids (Cont.)

- Another study showed that undershirts that were coated in borage oil decreased redness, itching, and epidermal water loss.
  - Kanehara, S., et al., "Clinical effects of undershirts coated with borage oil on children with atopic dermatitis: a double-blind, placebo-controlled clinical trial," Jour Dermatol 2007; 34:811-15.



Essential Fatty Acids (Cont.)

- Dosages in adults
  - EPA/DHA: 2-4 grams qd
  - GLA as borage oil: 500 mg-1,000 mg qd
  - GLA as evening primrose oil:1-2 grams qd
  - Sunflower oil: 5 grams qd
    - Callaway, J., et al., "Efficacy of dietary hempseed oil in patients with atopic dermatitis," Jour Dermatol Treat 2005; 16:87-94.
    - Fiocchi, A., et al., "The efficacy and safety of gamma-linolenic acid in the treatment of infantile atopic dermatitis," Jour Int Med Res 1994; 22:24-32.



Botanicals

- Licorice (Glycyrrhiza glabra) has been shown to be beneficial.
- Double-blind studies have shown that licorice in combination with other botanicals in a Chinese herbal formulation were therapeutic in adults.
  - Atherton, D., et al., "Treatment of atopic eczema with traditional Chinese medicinal plants," Pediatr Dermatol 1992; 9:373-75.
  - Sheehan, M., et al., "Efficacy of traditional Chinese herbal therapy in adult atopic dermatitis," Lancet 1992; 340:13-7.

Botanicals (Cont.)

- Similarly positive results were found in a double-blind study in children.
  - Sheehan, M., et al., "A controlled trial of traditional Chinese medicinal plants in widespread non – exudative atopic eczema," Brit Jour Dermatol 1992; 126:179-84.

Botanicals (Cont.)

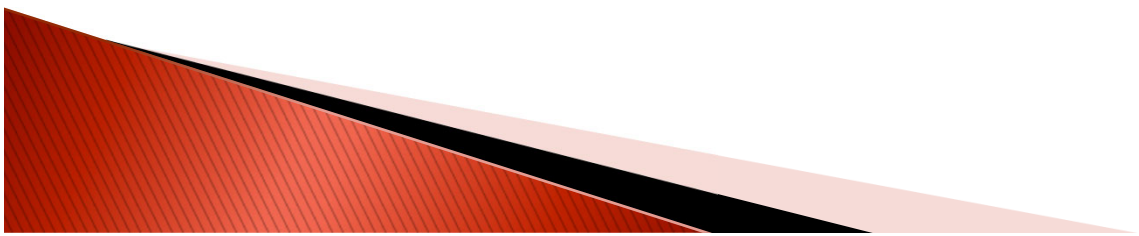
- The formula in addition to licorice contains
  - Ledebouriealla seseloides
  - Potentilla chinensis
  - Clematis chinensis
  - Clematis armandi
  - Rehmania glutinosa
  - Paeonia lactiflora
  - Lophatherum gracile
  - Dictammus dasycarpus
  - Tribulus terrestris
  - Schizonepeta tenuifolia
    - Ibid., Murray.

Botanicals (Cont.)

- Licorice is a major player in the effectiveness of the Chinese herbal formula, consequently even using licorice alone may be beneficial.
- Licorice can be used transdermally or PO.
- Studies have shown that glycyrrhetinic acid had a similar effect as topical HC in the treatment of eczema, contact and allergic dermatitis, and also psoriasis with most of the participants having excellent results.
  - Evans, F., "The rational use of glycyrrhetinic acid in dermatology," Brit Jour Clin Pract 1958; 12:269-74.
  - Ibid., Murray.

Traditional Chinese Medicine

- Cochrane Review revealed that a five-herb concoction was effective in children.
  - Hon, K., et al., "Efficacy and tolerability of a Chinese herbal medicine concoction for treatment of atopic dermatitis: a randomized, double-blind, placebo-controlled study," Brit Jour Dermatol 2007; 157:357-63.



Traditional Japanese Medicine (Kampo)

- A case report using Kampo showed excellent results.
  - Chino, A., et al., "A case of atopic dermatitis successfully treated with Juzentaihoto (Kampo)," Altern Ther Health Med 2010; 16:62-4.
- Trial of Shiunko which is an herbal mixture used in Kampo lowered bacterial counts in some of the subjects.
  - Higaki, S., et al., "Efficacy of Shiunko for the treatment of atopic dermatitis," Jour Int Med Res 1999; 27:143-47.
- Another study using Kampo showed a positive effect in many of the patients.
  - Kobayashi, H., et al., "Diet and Japanese herbal medicine for recalcitrant atopic dermatitis: efficacy and safety," Drugs Exp Clin Res 2004; 30:197-202.

Homeopathy

- One study of children that used a homeopathic cream of Oregon grape root (M. aquifolium), pansy (Viola tricolor hortensis), and gotu kola (Centella asiatica) was very beneficial.
  - Abeck, D., et al., “Behandlung des atopischen Ekzems bei Kindern mit einer pflanzlichen Heilsalbe: Ergebnisse einer offenen Studie mit Ekzevowen derma,” Akt Dermatol 2005; 31:523-26.

Hypothyroidism

- Medical trial showed that hypothyroid patients with eczema: their symptoms improved when their hypothyroidism was treated.
  - Barnes, B., “Thyroid therapy in dermatology,” Cutis 1971; 8:581-83.

Stress Reduction

- Studies have shown that patients with atopic dermatitis are more anxious, hostile, and have more neurosis than matched controls.
  - Jordan, J., et al., "Emotions and the skin: the conditioning of scratch responses in cases of atopic dermatitis," Brit Jour Dermatol 1972; 86:574-85.
- One study showed that psychotherapies were helpful allowing the patient to use less steroids for up to two years.
  - Hanifin, J., et al., Guidelines of care for atopic dermatitis, developed in accordance with the American Academy of Dermatology (AAD)/American Academy of Dermatology Association, "Administration Regulations for Evidence-Based Clinical Practice Guidelines," Jour Amer Acad Dermatol 2004; 50:391-404.

Remove Allergens

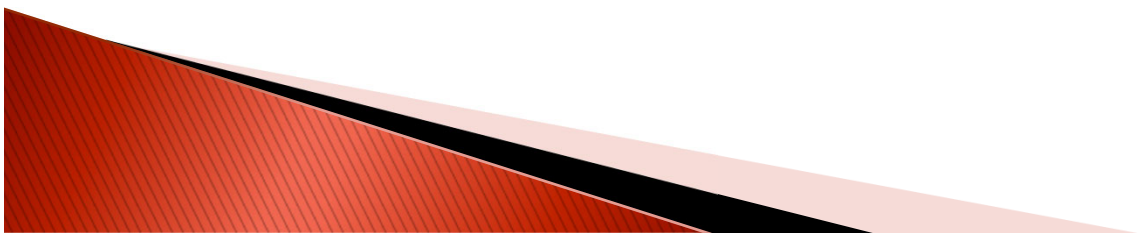
- Immunotherapy has been shown to be useful in patients with dust mite sensitization.
  - Cadario, G., et al., "Sublingual immunotherapy efficacy in patients with atopic dermatitis and house dust mites sensitivity: a prospective pilot study," Curr Med Res Opin 2007; 23(10):2503-06.
- Remove as many environmental allergens as possible.
- Have the patient do an allergy elimination diet and remove all food allergens from their diet.

Breastfeeding

- In observation studies on babies that are at high risk for eczema (family history of atopy): the babies that were breastfed had a had less a rate of eczema than babies that were not breastfeed.
  - Chandra, R., “Prospective studies of the effect of breast feeding on incidence of infection and allergy,” Acta Paediatr Sacnd 1979; 68:691-94.
  - Moore, W., et al., “Infant feeding and subsequent risk of atopic eczema,” Arch Dis Child 1985; 60:722-26.

Breastfeeding (Cont.)

- Breastfeeding for more than six months provided more protection than shorter time frames.
  - Saarinen, U., et al., "Breastfeeding as prophylaxis against atopic disease: prospective follow-up study until 17 years old," Lancet 1995; 346:1065-69.

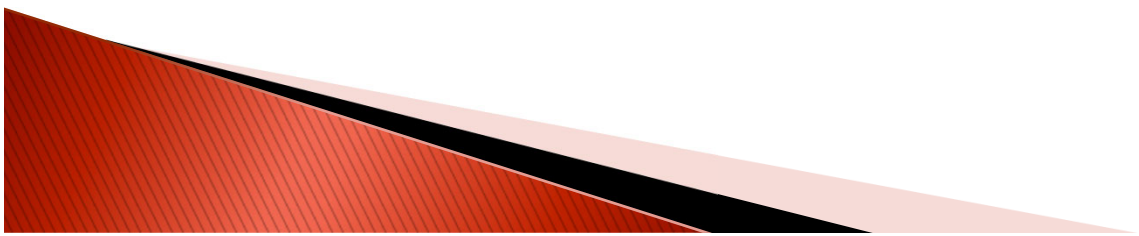


Breastfeeding (Cont.)

- The diet of the nursing mother is also important. Mother's that avoided eating eggs, cow's milk and fish during the first 3 months of breastfeeding, their children had lower rates of eczema.
  - Hattevig, G., et al., "Effect of maternal avoidance of eggs, cow's milk and fish during lactation upon allergic manifestations in infants," Clin Exp Allergy 1988; 19:27-32.
  - Sigurs, N., et al., "Maternal avoidance of eggs, cow's mil, and fish during lactation: effect on allergic manifestations, skin-prink tests, and specific IgE antibodies in children at age 4 years," Pediatrics 1992; 89:735-39.

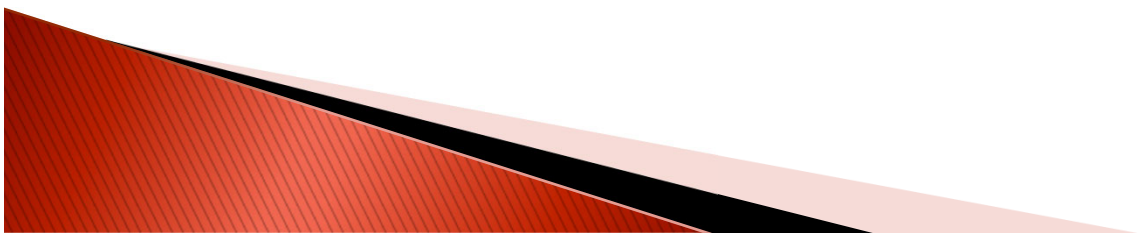
Breastfeeding (Cont.)

- In a double-blind trial, mothers that took fish oil during pregnancy and used while breastfeeding saw a lower rate of eczema in their children.
  - Furuhjelm, C., et al., "Fish oil supplementation in pregnancy and lactation may decrease the risk of infant allergy," Acta Paediatr 2009; 98:1461-67.



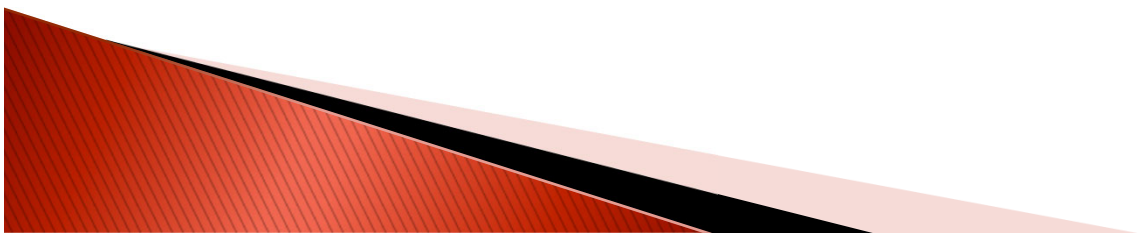
Cellphone Use

- One study showed that with cell phone use for an hour continuously, there was an increase in allergic response to dust and pollen in adult patients with eczema.
  - Kimata, H., “Enhancement of allergic skin wheal responses by microwave radiation from mobile phones in patients with atopic eczema/dermatitis syndrome,” Int Arch Allergy Immunol 2002; 129:348-50.



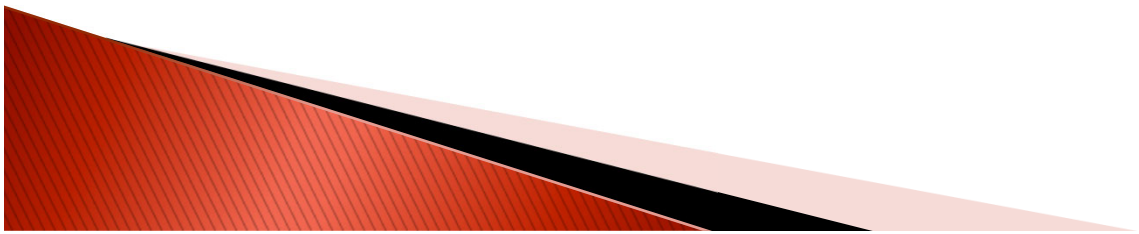
Treat Infections

- Treat patient if they are infected with Candida or H. pylori.



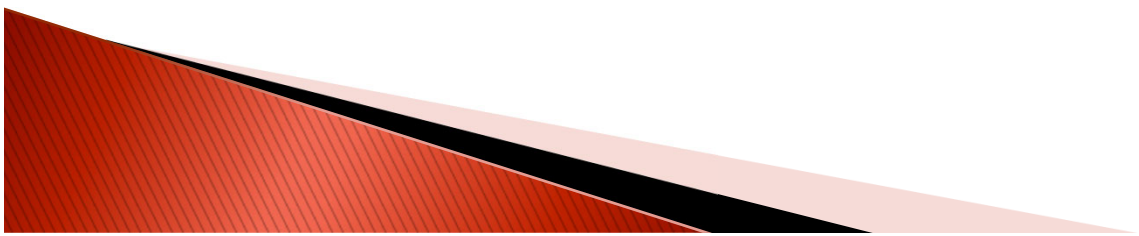
Compound Formula For Atopic Dermatitis/Eczema #1

- Compounded Formula
  - Tacrolimus 0.1%/Ketotifen 0.05% in Topical Cream #90 grams
  - Sig: apply to affected area BID



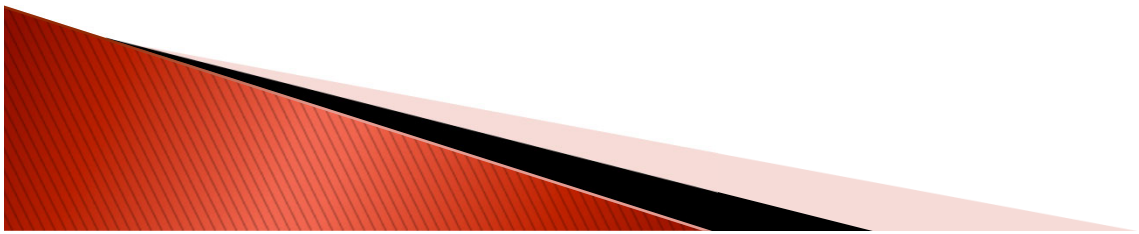
Compound Formula For Atopic Dermatitis/Eczema #2

- Compounded Formula
  - Ketotifen 0.05%/Cyanocobalamin 0.07% in Topical Cream
  - #90 grams
  - Sig: apply to affected area BID



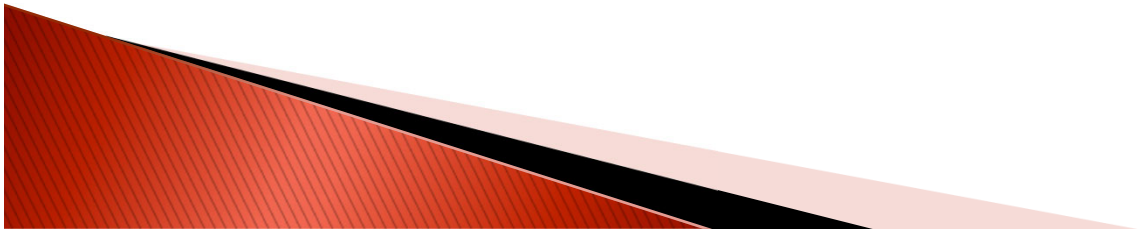
Compound Formula For Atopic Dermatitis/Eczema #3

- Compounded Formula
  - Fluocinolone Acetonide 0.01%/Ketotifen 0.05% Topical Cream
  - #90 grams
  - Sig: apply to affected area BID



Compound Formula For Atopic Dermatitis/Eczema #4

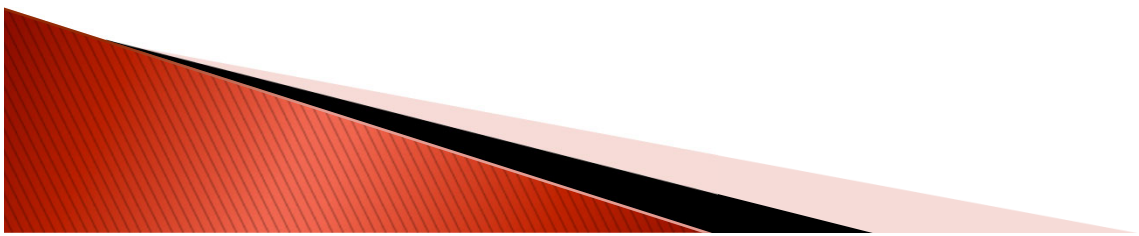
- Formula
  - Naltrexone HCL 1% in Topical Cream
  - #60 grams
  - Sig: apply to affected area BID



The Gut Skin Connection

Gut Skin Connection: Pathophysiology of Atopic Dermatitis

- Gastric Helicobacter pylori stimulates epidermal cells to secrete TSLP.
- H. pylori antibody has been shown to be positive in up to 70% of people with atopic dermatitis.
  - Kido, M., et al., "Helicobacter pylori promotes the production of thymic stromal lymphopoietin by gastric epithelial cells and induces dendritic cell-mediated inflammatory Th2 responses," Infect Immun 2010; 78(1):108-14.
- Treating H. pylori has been shown to be helpful in patients with atopic dermatitis.
  - Galadari, I., et al., "The role of Helicobacter pylori in urticaria and atopic dermatitis," Skinmed 2006; 5(4):172-76.

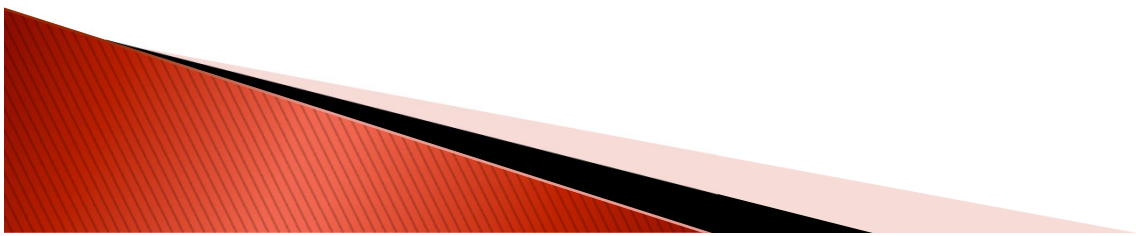


Gut Skin Connection (Cont.)

- A study found that supplementing with HCL in patients that have low levels may be helpful.
  - Ayres, S., “Gastric secretion in psoriasis, eczema and dermatitis herpetiformis,” Arch Dermatol Syph 1929; 20:854-59.

Gut Skin Connection: Probiotics

- A healthy GI tract is very important for all patients especially those with atopic dermatitis.
- Study showed that probiotics and prebiotics are important in preventing food allergies and eczema.
  - Kuitunen, M., "Probiotics and prebiotics in preventing food allergy and eczema," Curr Opin Allergy Clin Immunol 2013; 13(3):280-86.



Gut Skin Connection: Probiotics (Cont.)

- Studies have shown that Lactobacillus rhamnosus strain GG alone or with Lactobacillus reuteri given to infants with atopic dermatitis and cow's milk allergy revealed a decrease in symptoms.
  - Isolauri, E., et al., "Probiotics in the management of atopic eczema," Clin Exp Allergy 2000; 30:1604-10.
  - Majamaa, H., et al., "Probiotics: a novel approach in the management of food allergy," Jour Allergy Clin Immunol 1997; 99:179-85.
  - Rosenfeldt, V., et al., "Effect of probiotic Lactobacillus strains in children with atopic dermatitis," Jour Allergy Clin Immunol 2003; 111:389-95.

Gut Skin Connection: Pancreatic Enzymes

- In a case report, a patient with eczema her entire life was treated with pancreatic enzymes and had complete resolution of her skin manifestations.
  - McCann, M., “Pancreatic enzyme supplement for treatment of multiple food allergies,” Ann Allergy 1993; 71:269.

Conclusion

- As you have seen for these skin conditions, there are many etiologies and a great deal of research on both conventional and metabolic therapies.
- The newest medical trials are starting to focus on the gut-skin connection.