Contact Dermatitis

Definitions

- Contact Dermatitis
  - Reactions due to contact of an agent with the skin
  - Inflammation of the skin with spongiosis or intercellular edema
  - Results from interaction of chemical & skin
- Nonimmunologic vs. Immunologic
- Many chemicals may act as ***both*** irritants and allergens
- Irritant Contact Dermatitis (ICD)
  - 80% of contact dermatitis
- Allergic Contact Dermatitis (ACD)
  - 20% of contact dermatitis

Definitions

- Irritant Contact Dermatitis
  - Nonimmunologic/nonspecific
  - Variation in susceptibility
  - Most irritants produce delayed or cumulative rxns
  - Some rxns may be **necrotic** or **ulcerative**
  - An irritant is a substance that causes direct damage to skin without sensitization

Definitions

- Allergic Contact Dermatitis
  - Immunologic
  - ***Requires sensitization*** and occurs only in genetically determined subset of population
  - Classic delayed hypersensitivity (Type IV)
  - Mediated by immune cells rather than Abs
  - Occurs in 2 phases
    - Sensitization
    - Elicitation

Clinical Presentation

- May be difficult to distinguish between ICD and ACD, especially late
- Potent irritants may cause severe necrosis and "chemical burns" with ulceration
- Strong irritants--burning, stinging, vesicles
- Irritants and allergens may produce an acute, subacute, or chronic eczematous presentation
- Presentation relates to:
  - Chemical
  - Individual
  - Exposure
  - Environment

Immunology--Hypersensitivities

- Type I
  - Anaphylactic
- Type II
  - Cytotoxic
- Type III
  - Immune complex
- Type IV
  - Delayed hypersensitivity
  - T-cells

Immunology

- T-cells predominate in ACD and ICD (and most inflammatory dzs)
- CD4 cells
  - Th1
    - IL-2, IFN-γ, TNF-β
    - Mediate delayed hypersensitivity
    - IFN-γ inhibits Th2 activation
  - Th2
    - IL-4, IL-5, IL-6, IL-10
    - Help B cells produce antibodies
- CD8 cells
  - Suppressor/cytotoxic cells

Immunology

- ACD
  - Inflammatory cascade induced by exposure to an antigen capable of reacting with sensitized T-cells
- ICD
  - Inflammatory cascade induced by exposure to a chemical irritant or toxin capable of damaging keratinocytes, endothelium, or s. corneum
- End result--inflammation
  - Redness
  - Swelling
  - Heat
  - Pain

ICD Pathophysiology

- ICD
  - Irritant is a substance that causes direct damage to skin without prior sensitization
  - Membrane damage-->phospholipase activation-->release of arachidonic acid-->synthesis of eicosanoids
  - Second messenger systems activated
  - T-cells are activated by IL-1, GMCSF, and eicosanoids
  - Eicosanoids also lead to vasodilation, increased vascular permeability directly and indirectly through mast cell activation

ACD Pathophysiology

- Sensitization
  - Allergens are usually: low molecular weight, highly reactive, and lipid soluble
  - Unprocessed allergen is a hapten
  - Hapten penetrates epidermis and taken up by Langerhans' cells by pinocytosis
  - Hapten chemically altered in cell via lysosomal or cytosolic enzymes
  - Hapten conjugated to HLA-DR-->this complex expressed on Langerhans' cell surface

ACD Pathophysiology

- Sensitization
  - Langerhans' cells (LC) exposed to allergens-->keratinocytes secrete cytokines-->activates Langerhans' cells-->**stimulates T cells**
  - Antigen presented to **CD4** (maybe also CD8) T cells via the **T-cell receptor-CD3 complex**
  - Presence or absence of certain T cell subsets is **genetically predetermined**
  - LCs migrate to lymph nodes>interaction with CD4 cells
  - LCs secrete **IL-1**-->stimulates T cells to secrete **IL-2** and express **IL-2 receptors--**>T cell proliferation of cells capable of responding to the antigen
  - NOW you're sensitized!!!

ACD Pathophysiology

- Elicitation
  - Reexposure
  - LC takes up hapten and presents to primed T cell either in skin or lymph node-->activation
  - LCs secrete IL-1-->T cells produce IL-2 and IL-2Rs-->T cell proliferation and expansion **WITHIN THE SKIN**!
  - T cells also secrete **IFN-γ**-->activates keratinocyte-->expression of **ICAM-1** (WBC interaction) and **HLA-DR** and production of **IL-1**, **IL-6**, and **GMCSF**

ACD Pathophysiology

- Elicitation
  - Cytokines and eicosanoids are produced-->activation of mast cells and macrophages
  - All these process lead to vascular dilation and increased permeability
  - INFLAMMATION!

ACD Pathophysiology

- Suppressor T cells may also be generated on exposure to antigen
- Balance between sensitization and suppression results in disease or no disease on reexposure
- Atopes have a decreased capacity to be sensitized to common allergens
  - **Atopes mount a Th2** response to allergens
  - **ACD is a Th1 response**
  - Atopes more likely to develop ICD (barrier)

Clinical Features

- ACD
  - Well-demarcated pruritic eczematous eruption
  - Acute--blistering and weeping
  - Chronic--lichenified and scaly, fissured
  - Rash usually delayed by 1-2 days of exposure, maybe a week
  - Allergy may develop after years of contact
  - Distribution, distribution, distribution

Clinical Features

- ACD Common Misconceptions/Pearls
  - Allergy is not dose-dependent
  - May not be bilateral (e.g. both hands for glove dermatitis)
  - May be patchy
  - May affect the palms and soles
  - Most severely affected site may be different from the primary site of exposure
  - Allergy not cost-dependent
  - Certain sites are more susceptible to allergens--eyelids, genitals

Clinical Features

- ICD--multiple types
  - Acute ICD
  - Acute Delayed ICD
  - Irritant Reaction ICD
  - Cumulative ICD
  - Asteatotic Deramatitis
  - Traumatic ICD
  - Pustular and Acneiform ICD
  - Non-erythematous ICD
  - Subjective or Sensory ICD
  - Airborne ICD
  - Frictional ICD

Clinical Features

- Acute ICD
  - Burning, stinging, soreness
  - Erythema
  - Edema
  - Bullae
  - Possibly Necrosis
  - Usually due to potent irritants--acids, alkalis

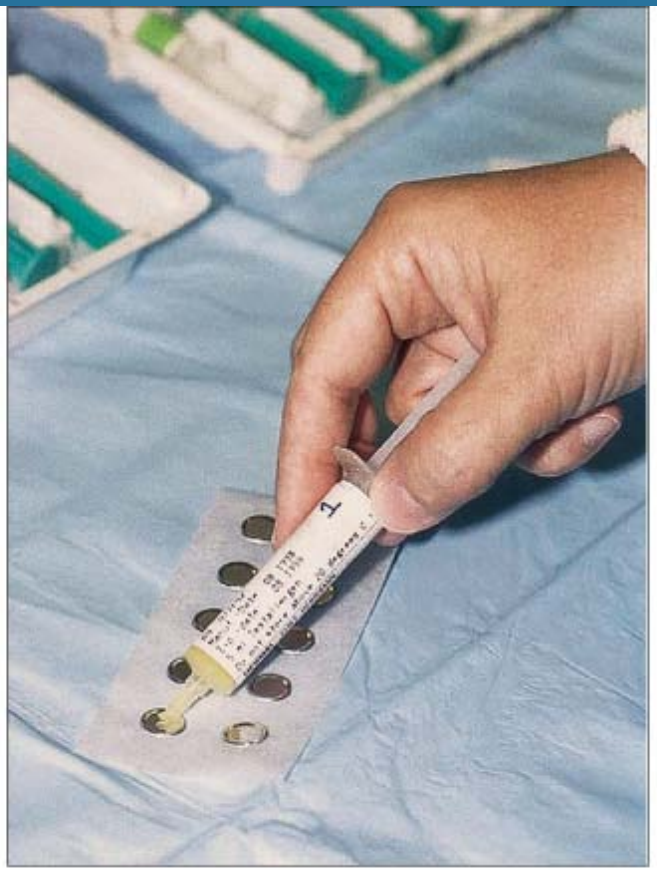
Patch Testing

- Should be done more often
- All patients should be tested to a standard series
- T.R.U.E. test system--antigens dispensed in polymer base
  - 23 or 24 antigens
- Finn Chamber System--small syringes and dropper bottles attached with Scanpor tape
  - 20 antigens

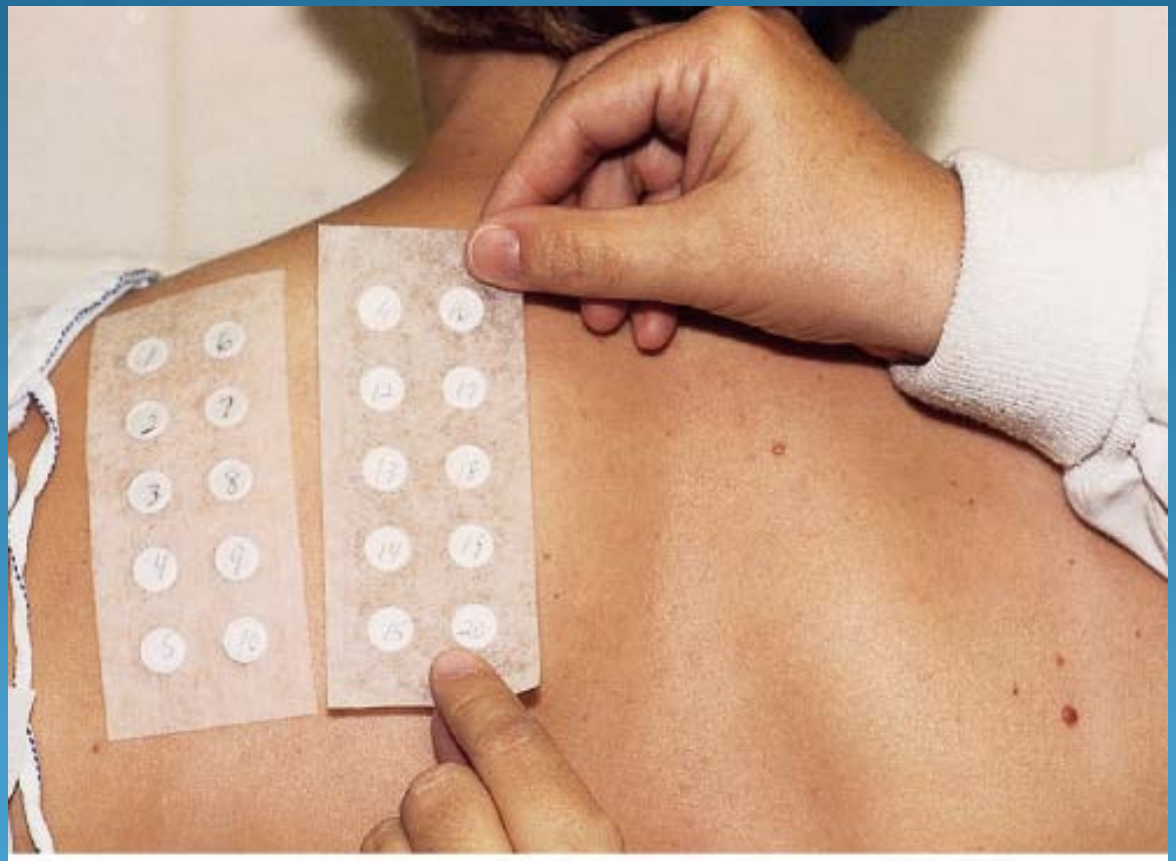
What does T.R.U.E. Test stand for?

- Thin-layer Rapid Use Epicutaneous Test

Finn Chamber



Finn Chamber/Scanpor® Tape



Patch Testing

- Don't patch test when dermatitis is acute/severe
- Don't test if on systemic steroids or at least 1 week after d/c
- Remove patch test in 2 days and read and then read again 3-7 days after initial application
- May not shower or bathe, keep back dry
- Shave hairy backs--day of application
- Don't do patch testing on patients with immediate, urticarial type of disease

Patch Testing

Table 15.2 International Grading System for patch tests.

INTERNATIONAL GRADING SYSTEM FOR PATCH TESTS	
+/–	Doubtful reaction, faint macular erythema
+	Weak, non-vesicular reaction with erythema, infiltration and papules
++	Strong, vesicular reaction with erythema, infiltration and papules
+++	Spreading bullous reaction
–	Negative reaction
IR	Irritant reaction

Irritants

- Acids
  - Epidermal damage via protein denaturation and cytotoxicity
  - Hydrofluoric acid and sulfuric acid cause most severe burns
  - Erythema, vesication, and necrosis
- Alkalis
  - Often cause more severe and painful rxns
  - Degrade lipids
  - Saponification of fatty acids results in deeper penetration of alkalis
- Metal salts
- Solvents

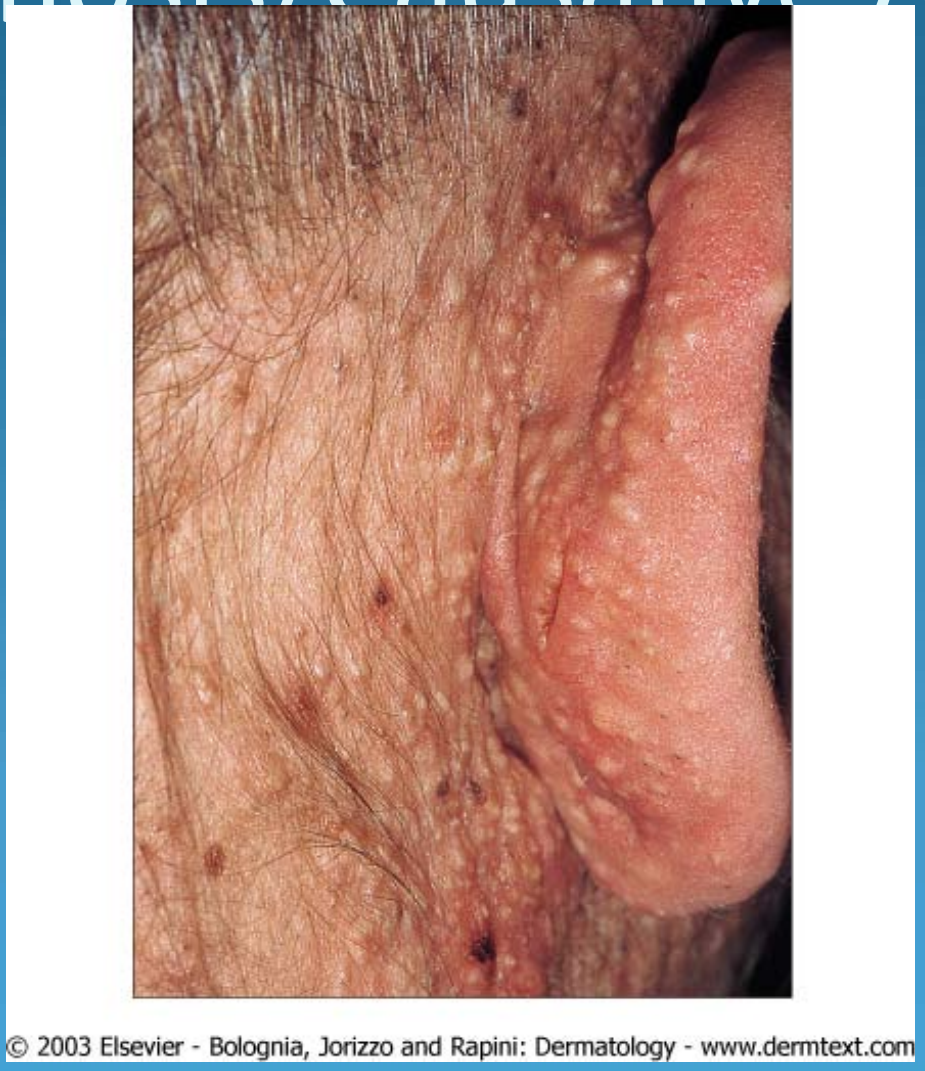
Irritants

- Alcohols
- Detergents and Cleansers
- Disinfectants
- Plastics
- Food
- Water (the universal solvent)
- Fabric/man-made vitreous fibers
- Plants

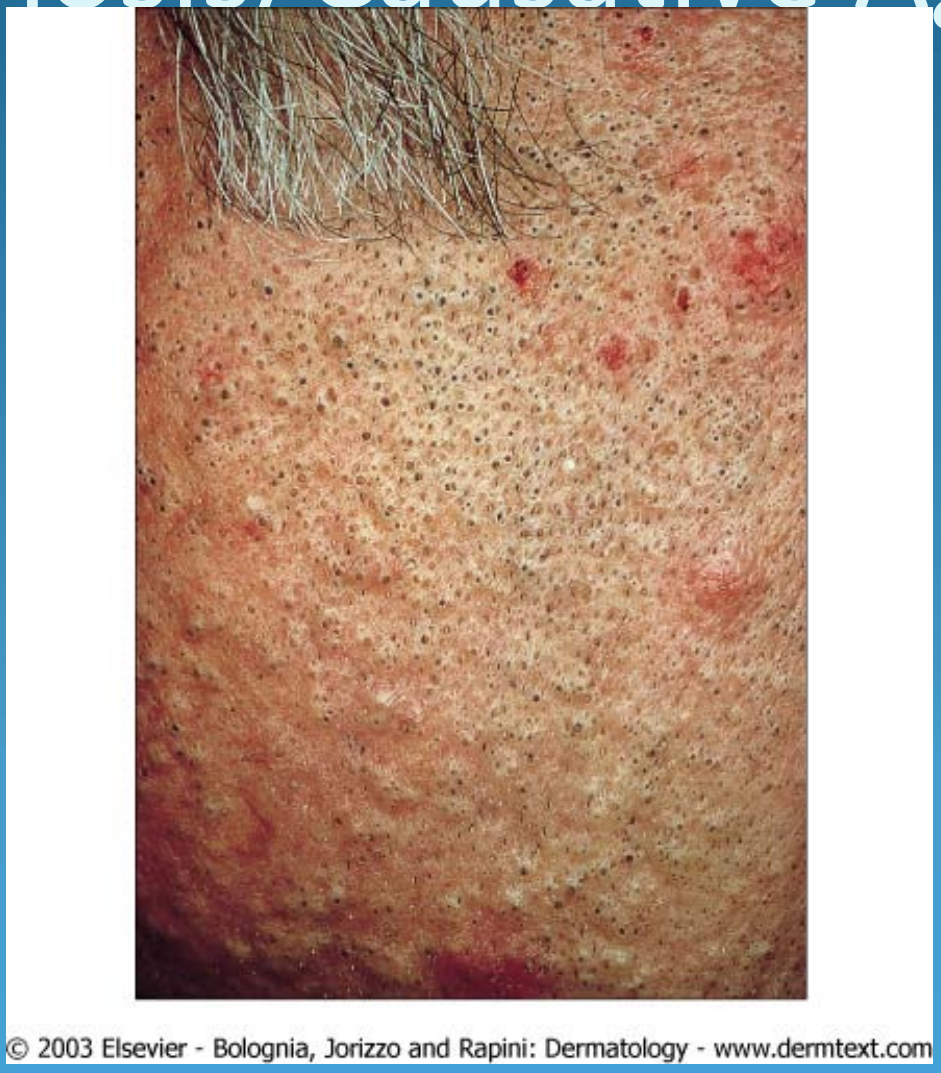
Contact Urticaria

- Pruritus wheal and flare
- Develops within 60 minutes of exposure, resolves 24 hrs
- Protein content of latex rubber is responsible
- Occurs more often in atopes, spina bifida patients or those who have undergone multiple surgeries/catheterizations

Diagnosis/Causative Agent?



Diagnosis/Causative Agent?



Chloracne

- Open and closed comedones
- Uninflamed nodules and cysts
- Exposure to halogenated polycyclic hydrocarbons such as polychlorinated dibenzodioxins (PCDDs)--fungicides, insecticides, herbicides, and wood preservatives
- Classically Agent Orange
- 2,3,7,8-tetrachlorodibenzo-*p*-dioxin

Name/Allergen?

Poison Ivy

- Urushiol (Oleoresin)
- Family Anacardiaceae
  - Poison Ivy/Oak/Sumac
  - Mango peel
  - Cashew nut shells
  - Rengas tree
  - Indian marking tree nut
  - Brazilian pepper tree
  - Japanese lacquer tree
  - Ginkgo biloba tree (not Anacardiaceae)

Poison Ivy

- Family **Anacardiaceae**
- Genus ***Toxicodendron*** -- poison ivy/oak/sumac
- *Toxicodendron radicans* -- Common or Eastern Poison Ivy
- Historically called ***Rhus* dermatitis**
- *Rhus* is the largest genus in the family Anacardiaceae but doesn't contain the allergeneic plants
- Allergeneic plants-->*Toxicodendron*

Poison Ivy

- Urushiol self-melanizes on exposure to oxygen
- “Black-spot test” -- crush plant between folds of white paper
  - Urushiol turns dark brown in 10 minutes and black by 24 hours
  - Urushiol is self-melanizing on exposure to oxygen

Poison Ivy

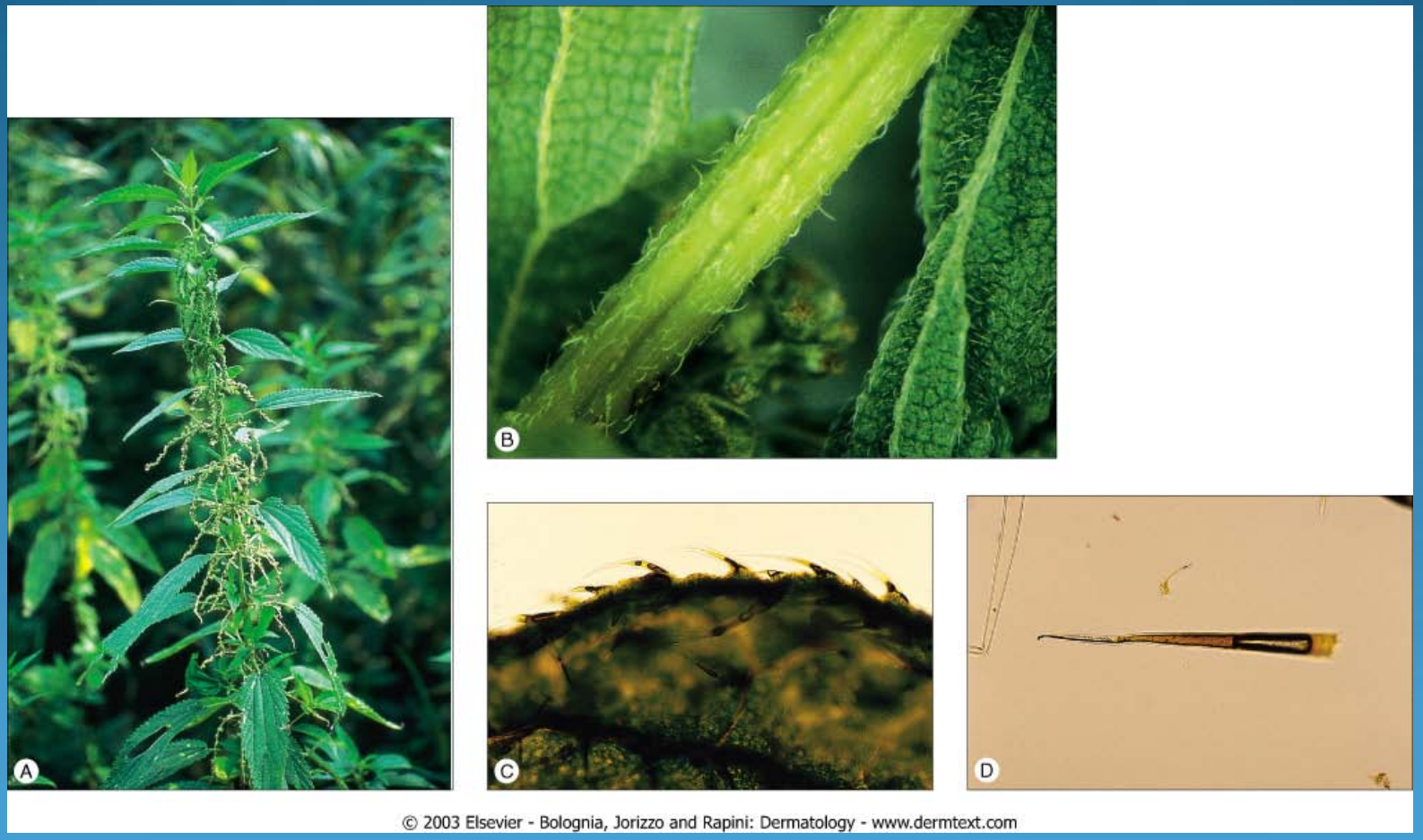
Name/Allergen?

Poison Sumac/Urushiol

Name/Allergen?

Poison Oak/Urushiol

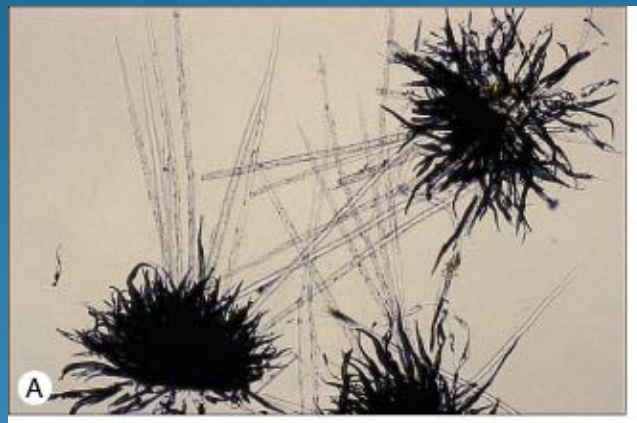
Name?



Stinging Nettle (*Urtica dioica*)

- Toxin-mediated (non-immunologic) contact urticaria
- Sharp hairs (**trichromes**) contain **histamine, serotonin, and acetylcholine**

Name?



Mechanical Irritant Dermatitis

- Small spines--**Glochids**--act like little fish hooks embedded in skin
- Prickly pear (***Opuntia spp***.) common cause
- **Sabra dermatitis**
  - Names for dermatitis developed by harvesters of the Sabra fig (Indian fig)
- Side effect of mechanical irritant dermatitis--inoculation of organisms

Mechanical Irritant Dermatitis

- *M. kansasii*
- Blackberries
- *Sporothrix schenckii*
- Rose thorns, sphagnum moss, grasses
- *M. marinum*
- Cactus spines
- *M. ulcerans*
- Spiky tropical vegetation
- *S. aureus* and *C. tetani*
- Spines and thorns

Name/Diagnosis?

Chemical Irritant Dermatitis

- **Calcium oxalate--*Dieffenbachia picta*** (Araceae)--Dumb cane
- Bulb dermatitis--daffodils contain calcium oxalate
- Hunan Hand Syndrome?
- Capsaicin
- Buttercups?
- Ranunculin
- Spurges (euphorbiaceae) contain irritant phorbol esters in latex

This leads to?

This leads to?

This leads to?

And this?

Phytophotodermatitis

- Phototoxic reaction
- Erythema (with or without blistering)
- Delayed hyperpigmentation
- Non-immunologic/Phototoxic
- UVA light + topical or oral contact with photosensitizer -- **furocoumarins** (**psoralens**)
- Limes, celery, rue most common causes

Phytophotodermatitis

- Plants of family **Apiaceae** (formerly **Umbelliferae**) most common cause
  - Hogweed -- *Heracleum sphondylium*
  - False Bishop's weed
  - Angelica/Wild Angelica
  - Cow parsley
  - Wild chervil
  - Celery
  - Fennel
  - Parsnip
  - Cow parsnip
  - Parsley

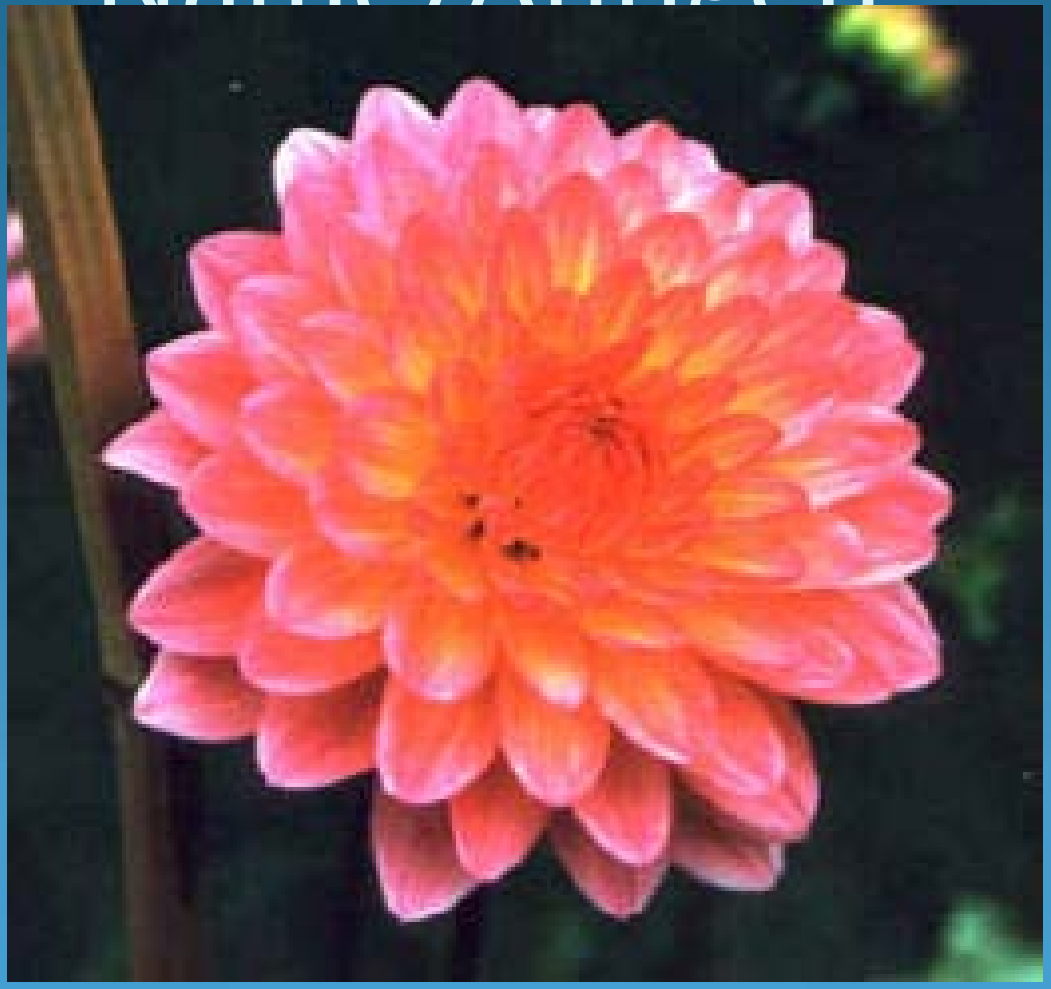
Phytophotodermatitis

- Rutaceae
  - Limes
  - Orange
  - Lemon
  - Grapefruit
  - Gas plant/Burning Bush
  - Rue
  - Blister plant
- Moraceae -- mulberry
- Fabaceae (Leguminosae)
- St. John's Wort

Phytophotodermatitis

- Berlock dermatitis -- **bergamot oil** (perfumes or tan promoters)
- Strimmer™ dermatitis
  - Red, irregular macules and papules -- like buckshot on chest
  - Hogweed (*Heracleum sphondylium*)
  - Giant Hogweed (*Heracleum mantegazzianum*)
  - Cow parsley (*Anthriscus sylvestris*)

Name/Antigen?



Hint: It's a Dahlia

Name/Antigen?

Name/Antigen?

Asteraceae (Compositae)

- **Sesquiterpene lactone**
- Over 200 allergenic members of Asteraceae
- Daisy
- Chrysanthemum
- Artichoke
- Feverfew
- Liverwort
- Dandelion
- Sunflower
- Chicory
- Lettuce
- *Parthenium hysterophorus* -- "Scourge of India"

Name/Antigen?

Alstroemeria spp.

- Peruvian lily
- **Tuliposide A** -- a glycoside
- Acid hydrolysis converts to **tulipalin A** -- the allergen
- Allergen passes through vinyl gloves

Name/Antigen?

Garlic/Radish

- Diallyl disulfide
- Alliaceae family
- Irritant and allergen

Primrose

Allergen -- Primin

Croton Plant (Spurge Family)

- Irritant
  - Phorbol esters

Castor Bean

- Allergen
  - Ricin
- Clinical
  - Anaphylaxis

Sesame Oil

- Allergen
  - Sesamine

What commonly prescribed topical medication is found in rubber?

- Hydroquinone

Mustard, radish

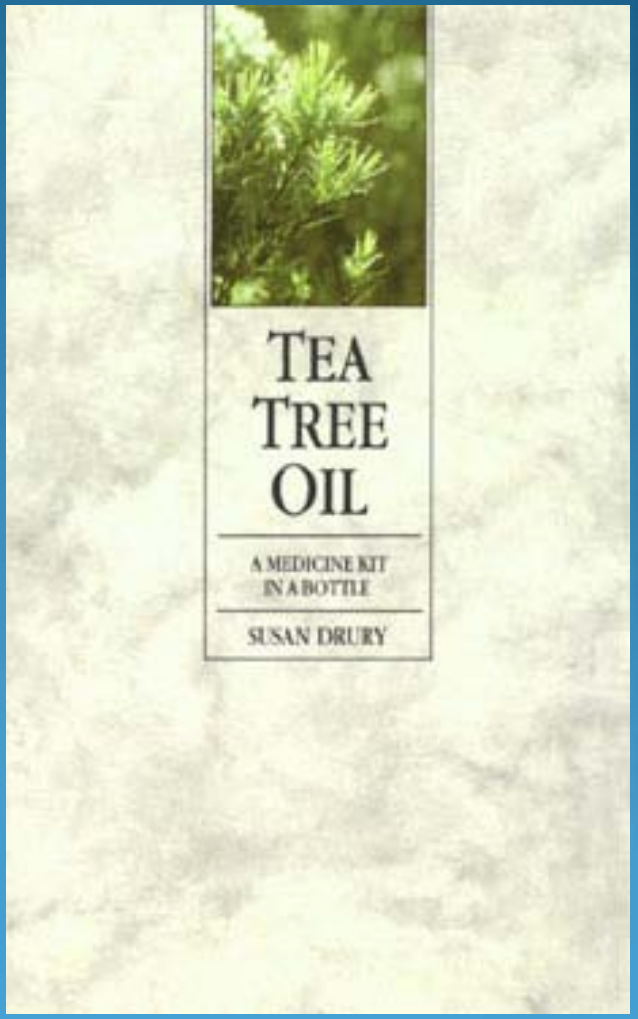
- Allergen
  - Allyl isothiocyanate

Lichen

- Allergen
  - D-usnic acid
  - Evenic acid
  - Atronorin

Allergen?

- Melaleuca plant
- D-limonene



Allergen?

- Mercaptobenzothiazole is present in spandex

Pine tree

- Allergen
  - Colophony

What cross-reacts with latex?

- Banana, Avocado, Chestnut, Kiwi, Passion Fruit
- **Banana, Avocado, Chestnut have highest association**
- Other foods include papaya, tomatoes, melon, potato, carrot, celery, apple, and the list goes on and on.
- Just remember BACK uP!

Colophony

- Aka rosin or abeitic acid
- Athletic grips
- Cosmetics (mascara, rouge, eye shadow)
- Chewing gum
- Pine products
- Medications (wart remover, hemorrhoid creams)
- Paper and paper products
- Printing inks
- Varnishes
- Adhesives
- Dental cements and impression pastes
- Glue tackifiers (shoes)

What?

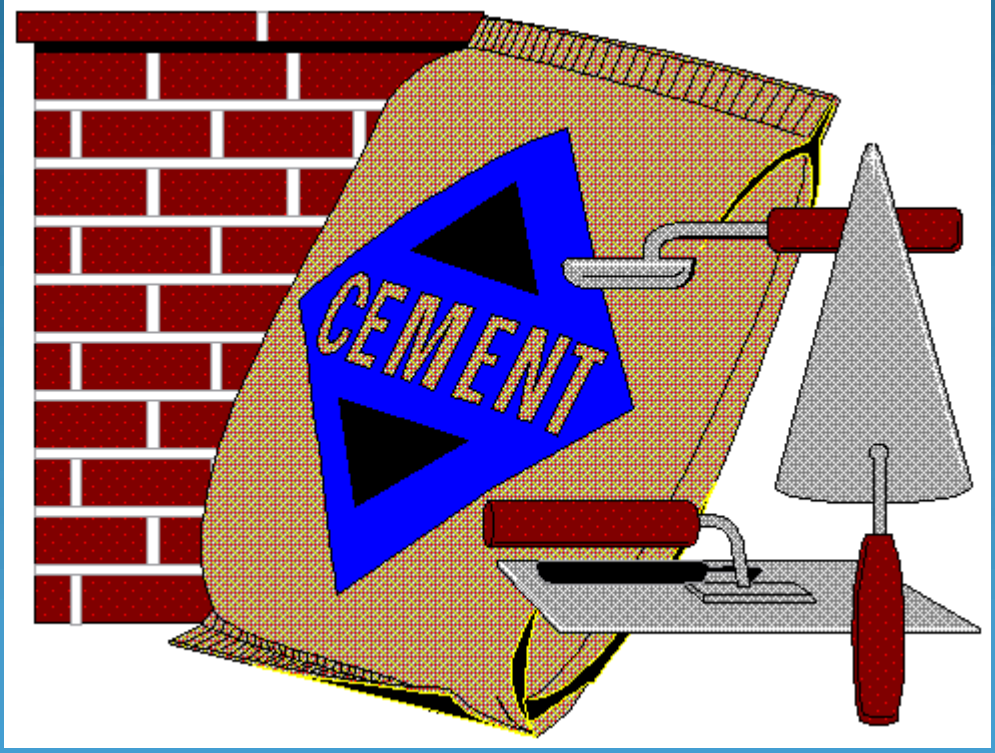
Nickel Dermatitis

- Most common allergen
- What test might you use in clinic?
- Dimethylglyoxime test is a test for nickel content -- turns pink
- Cross-reacts with?
- ***Cobalt and chromate***

Cobalt

- Combined with other metals in hard alloys
- Cobalt is sometimes synthetically combined with nickel and chromium and is also found in association with these metals in nature
- **80% of individuals who are sensitive to cobalt are sensitive to nickel or chromate or both**
- This is a cosensitivity, not a cross-sensitivity
- In men, this is usually chromate--b/c of the presence of **chromate and cobalt in cement**
- Sensitization to nickel or chromate (or both), with active dermatitis, predisposes to cobalt sensitivity

Allergen?



Chromate

- Potassium dichromate
- Leather
- Ceramics
- Cement
- Green tattoos
- Engraving and printing chemicals, paints and inks, wood preservatives, and photographic developing chemicals

Allergen?

Spearmint

- Carvone
- Family Lamiaceae

Allergen?

Peppermint

- Menthol
- Family Lamiaceae

Glycerol Thioglycolate

- Hairdressers and clients
- Acid permanents

Allergen in Permanent Hair Dye?

- *p*-Phenylenediamine (**PPD**)
- Also Henna tattoos
- Rubber
- Plastics
- PPD cross-reacts with?
- **Azo- and aniline dyes, ester anesthetics, PABA, sulfonamides**

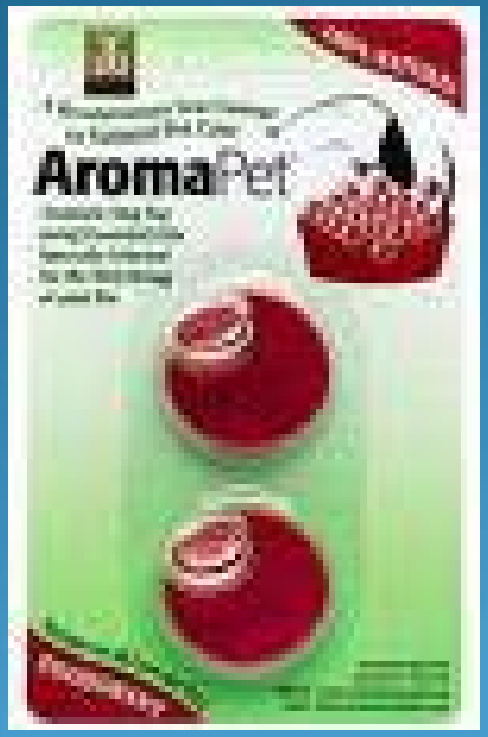
Henna tattoo

Allergen?

Ammonium persulfate

Often used to “boost” peroxide hair bleaches

Allergen?



Components of Fragrance Mix I

- Geraniol
- Cinnamic aldehyde (Cinnamaldehyde)
- Cinnamyl alcohol
- Hydroxycitronellal
- A-Amylcinnamaldehyde
- Isoeugenol
- Eugenol
- Oak moss

Cross-Reactions with Fragrance Mix

- Balsam of Peru
- Cassia oil
- Cinnamon
- Cloves
- Citronella candles
- Ethylene bassylate
- Tiger balm

Fragrance Mix Controversy

- Many believe that Fragrance Mix I (with 8 antigens) was missing a significant number of patients sensitive to fragrance
- Many perfumes contain 100 or more substances and the search continues for a more “appropriate” antigen panel

Fragrance Mix II

- ***Hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyral®)***
- Citral
- Citronellol
- Farnesol
- Coumarin
- α-hexyl-cinnamic aldehyde

Tattoo Pigments

- Chromium
- Green
- Mercury or Cinnabar
- Red
- Cobalt
- Blue
- Cadmium
- **Yellow**
- Iron oxide
- Brown

Tattoo Pigments

- Zinc oxide
- White
- Carbon
- Blue-Black
- Gold
- Lilac
- Manganese
- Purple
- Ferric hydrate
- Ochre

- What is the allergen in vaccines (e.g. hepatitis), contact lens solution, antitoxins, liquid soap?

- **Thimerosal**
- **Piroxicam** cross-reactivity (photosensitivity)
- **Mercury** cross-reactivity due to mercurial component, previously thought to be due to the thiosalicylate portion.

Allergen?


INSTANT
Krazy
GLUE
ALL
PURPOSE
• NOW BONDS BETTER ON PLASTIC, METAL, WOOD, RUBBER, GLASS, CERAMIC
• STAY FRESH CONTAINER
• ONE DROP APPLICATION
WARNING: EYE IRRITANT
SUPER DUPER
SUPER GLUE
BETTER VALUE

- **Ethyl Cyanoacrylate**

- What is the other name for Euxyl K 400?

- ***Methyldibromoglutaronitrile=Euxyl K 400***
- Preservative found in many creams, cosmetics, shampoos, lotions, etc.
- Other names
- Merquat 2200
- Tektamer 38

What is the other name for Euxyl K100?

- ***Euxyl K100 = Kathon CG = Methylchloroisothiazolinone***

Allergen and Common Location of Dermatitis?

Nail Polish

- **Tosylamide/formaldehyde resin**
- Formerly known as toluenesulfonamide/formaldehyde resin
- **Eyelid dermatitis** is common
- Also on face and neck and periungually

Most common sensitizing topical antibiotic?

- Neomycin
- Neomycin and bacitracin sensitivity frequently occur concurrently in the same patient.

Which allergen, found in rubber, becomes antigenic when washed in bleach?

- Zinc dibenzylthiocarbamate

Corticosteroids

- Cross-reactivity occurs within a group but may occur among groups especially between B and D
- 3 good screening panels
- **Tixocortol pivalate -- A (most HCs)**
- **Budesonide -- B (TAC) {and D}**
- **Hydrocortisone-17-butyrate -- D (Clobetasol)**

Table 15.6 Corticosteroid classes and patch test concentrations. *Available without prescription in the US. †Suggested screening agents. In petrolatum unless stated otherwise. Eth, Ethanol; Pet, petrolatum; parentheses contain other, suggested concentrations or vehicles.

CORTICOSTEROID CLASSES AND PATCH TEST CONCENTRATIONS	
Drug	**Concentration (%)**
Class A: Hydrocortisone and tixocortol type	
Cortisone	
Cortisone acetate	25
Hydrocortisone*†	2.5 Eth (1, 2, 5, 10, 25, Eth or Pet)
Hydrocortisone acetate*	25
Methylprednisolone	
Methylprednisolone acetate	10
Prednisolone	5 (10)
Prednisolone acetate	5
Tixocortol pivalate†	1
Class B: Triamcinolone acetonide type	
Triamcinolone acetonide†	0.5 (1,5)
Triamcinolone alcohol	
Halcinonide	1
Flucinonide	1
Flucinolone acetonide†	0.5 (0.05, 1, 5, 10)
Desonide	0.05
Budesonide†	0.1
Amcinonide	0.5
Class C: Betamethasone type	
Betamethasone	
Betamethasone–disodium phosphate	1
Dexamethasone	
Dexamethasone–disodium phosphate	1
Fluocortolone	
Class D: Hydrocortisone-17-butyrate and clobetasone-17-butyrate type	
Hydrocortisone butyrate†	1 Eth (0.1 Eth)
Hydrocortisone valerate	
Clobetasone butyrate	0.5
Clobetasol propionate	0.5 (0.05 Eth)
Betamethasone valerate	5 (10) (0.1, 1 Eth)
Betamethasone dipropionate	5
Fluocortolone hexanoate	1
Fluocortolone pivalate	1
Prednicarbate	

What are the three most common causes of cosmetic ACD?

1. Fragrance
2. Preservatives
3. PPD

- Parabens are the most common preservative **USED** in cosmetics, but don't commonly cause ACD

Preservatives

- Parabens
- Formaldehyde
- Formaldehyde releasing (FRPs)
- Methychloroisothiazolinone
- Para-tertiary butyl phenol
- Thimerosal
- Sorbic acid
- Benzophenones
- Butylated hydroxyanisole & hydroxytoluene
- Chloroxylenol
- Phenoxyethanol
- Parachlorometacresol
- Iodine compounds

Formaldehyde Releasers

- Quaternium-15=Dowisil 200
  - Acts against yeast, molds, bacteria, and pseudomonas
  - ***Most common* cause of preservative induced ACD**
  - Shampoos, hair conditioners, make-up, moisturizing lotions, liquid soaps bath gels, sunscreens, shaving products, mascara
- Imidazolidinyl urea
  - Antibacterial
  - **Safe for use in formaldehyde sensitive pts**
- Diazolidinyl urea
  - Antibacterial
  - More potent sensitizer than imidazolidinyl
- Bronopol
  - Broad spectrum
  - Degraded to formaldehyde over time
- Dimethyloldimethyl (DMDM) hydantoin
  - Highly water soluble
  - Cross reacts with formaldehyde sensitive pts
  - Shampoos and skin moisterizers
- MDM hydantoin
- Hydantoin
- Glutaraldehyde
  - **Cold sterilizer**, embalming, X-ray film solution
  - Dental workers

Formaldehyde Releasers

- DMHP
- Formaldehyde solution
- p-Formaldehyde
- Tris (hydroxymethyl) nitromethane
- 5-bromo-5-nitro-1,3-dioxane
- 2-bromo-2-nitropropane-1,3-diol

Rubber Dermatitis

- Accelerators -- used in vulcanization (treatment to give strength, elasticity, and resistance to solvents)
  - Tetramethylthiuram disulfide
  - Mercaptobenzothiazole
  - Diphenylguanidine
  - **Mercaptobenzothiazole most common cause of shoe allergy**
  - **Thiuram most common cause of glove allergy**

Rubber Dermatitis

- Antioxidants
  - Used to preserve rubber
  - Phenyl-alpha-naphthylamine (amine type)
  - Hydroquinone
  - N-Isopropyl-N-phenyl-paraphenylenediamine (IPPD)
  - Propyl p-paraphenylenediamine
    - Tires
    - Heavy-duty rubber goods
    - Boots
    - Elastic underwear

Allergen?

Thiuram Mix

- Includes 4 chemicals
- In rubber, prevents degradation
- Found in latex, condoms, adhesives, pesticides, medications like Antabuse, diaphragms, repellents, fungicides

- With what does ethylenediamine cross-react?

Ethylenediamine

- Aminophylline=Theophylline + ethylenediamine
- Hydroxyzine: multiple piperazine-based antihistamines
- Ethylenediamine is a stabilizer in medicated creams
- Present in generic nystatin creams
- Mycolog II cream does not have ethylenediamine

- What irritant/allergen is used as a surfactant in shampoos and cosmetics?

- **Cocamidopropyl betaine**
- One of the most commonly used surfactants
- Contact lens solution
- Antiseptics
- Shampoos