

ALLERGIC CONTACT DERMATITIS

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Disclosures

- ▣ I do intend to discuss an unapproved/investigative use of a commercial product/device in my presentation – Dormer comprehensive patch testing.
 - T.R.U.E Test™
 - ▣ is approved by FDA.

- ▣ “I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.”

Learning Objectives

- ▣ Have an understanding of the pathophysiology and visual appearance of allergic contact dermatitis
- ▣ How to approach a patient with allergic contact dermatitis
 - evaluation and testing
- ▣ Understand the top allergens in the population
- ▣ Approach for the treatment of the allergic contact dermatitis

Dermatitis

▣ Dermatitis:

- A condition of the skin in which it becomes red, swollen, and sore, sometimes with small blisters, resulting from direct irritation of the skin by an external agent.

▣ Types:

- Stasis dermatitis.
- Allergic contact dermatitis.
- Atopic dermatitis.
- Irritant contact dermatitis.
- Neurodermatitis.
- Perioral dermatitis.
- Seborrheic dermatitis.
- Ect.....

▣ Today's Talk:

- **Irritant Contact Dermatitis (ICD)**
 - ▣ most common at about 80% of cases
- **Allergic Contact Dermatitis (ACD)**
 - ▣ about 19% of cases
- **Contact Urticaria (CU)**
 - ▣ 1%

Allergic vs Irritant Contact Dermatitis

ALLERGIC

- ▣ Less common (20%)
- ▣ Type IV hypersensitivity
- ▣ Requires lipophilic, low molecular weight haptens
- ▣ Requires prior sensitization
- ▣ Concentration *independent*
- ▣ Diagnosed with history and physical; *possible patch testing needed*

IRRITANT

- ▣ Most common (80%)
- ▣ **Non-immunogenic**
- ▣ Damage usually noted to keratinocytes of the skin
- ▣ No prior sensitization required
- ▣ Concentration dependent
- ▣ Diagnosed with history and physical

Hypersensitivity Reactions

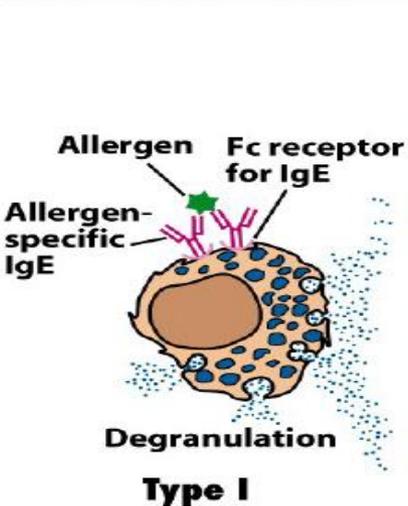
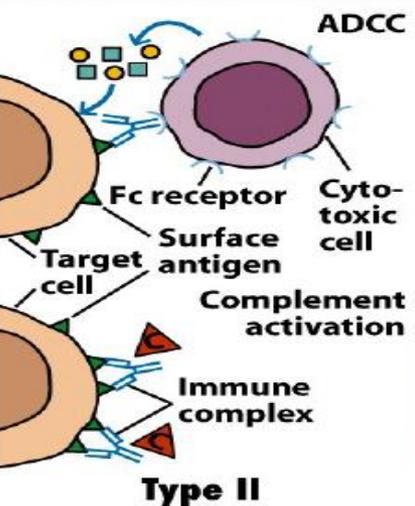
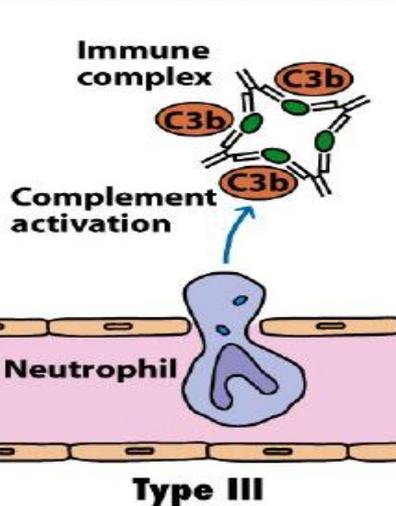
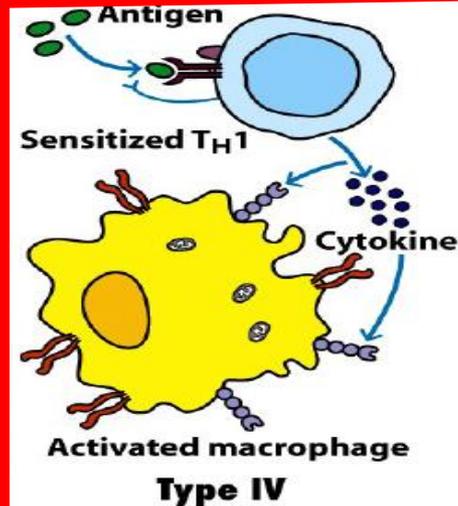
 <p>Type I</p>	 <p>Type II</p>	 <p>Type III</p>	 <p>Type IV</p>
<p>IgE-Mediated Hypersensitivity</p>	<p>IgG- or IgM-Mediated Cytotoxic Hypersensitivity</p>	<p>Immune Complex-Mediated Hypersensitivity</p>	<p>Cell-Mediated Hypersensitivity</p>
<p>Ag induces cross-linking of IgE bound to mast cells and basophils with release of vasoactive mediators.</p>	<p>Ab directed against cell surface antigens mediates cell destruction via complement activation or ADCC.</p>	<p>Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils.</p>	<p>Sensitized T_H1 cells shown above release cytokines that activate macrophages or T_C cells that mediate direct cellular damage. T_H2 cells and CTLs mediate similar responses.</p>
<p>Typical manifestations include systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema.</p>	<p>Typical manifestations include blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia.</p>	<p>Typical manifestations include localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus.</p>	<p>Typical manifestations include contact dermatitis, tubercular lesions, and graft rejection.</p>

Figure 15-1
 Kuby IMMUNOLOGY, Sixth Edition
 © 2007 W. H. Freeman and Company

Clinical Features

ALLERGIC

- ▣ Macular erythema, indurations, papules, vesicles, bullae and/or excoriations
- ▣ May occur locally, spread beyond area of exposure
- ▣ Tends to itch
- ▣ Latency is 72-120 hrs up to weeks
- ▣ Resolution in 1-2 weeks

IRRITANT

- ▣ Generally scaly, erythematous background
- ▣ Most often limited to exposed areas
- ▣ Tends to burn or be painful
- ▣ Latency usually within 48hrs
- ▣ Often resolves in 96hrs.

•Allergic Contact Dermatitis – 20%



•Irritant Contact Dermatitis – 80%



How Prevalent is Contact Dermatitis?

- Allergen exposure is influenced by climate, occupation, cultural habits and regulations.
 - The prevalence of contact allergy against specific allergens **differs among countries** as a result in changes and developments in surrounding environments and societies.
- According to a 2005 report in the United States, estimates of prevalence range from 5% to 50%, depending on population and defining criteria.
- Contact dermatitis is associated with more than 9 million physician office visits and as many as 10% of all dermatology clinic visits.
- Treating contact dermatitis costs approximately \$1.4 billion annually, with significant losses (~\$500 million) attributed to missed workdays and low productivity.
- The annual population incidence of occupational contact dermatitis ranges from an estimated 5.7 to 101 cases per 100,000 workers per year.

Each Case Needs to be
Examined From the
Patients Lifestyle or
Work

Irritants Encountered in Various Occupations

- Agriculture workers/gardeners
 - Fertilizers, pesticides, diesel, plants
- Artists
 - **Solvents**, clay, plaster
- Automotive
 - **Solvents**, oils, cleaners
- Bakers
 - Flour, DETERGENTS
- Bartenders/Cooks
 - DETERGENTS, wet works
- Bookbinders/Library
 - **Solvents**, glues
- Butchers
 - DETERGENTS, wastes
- Cleaners
 - DETERGENTS, **solvents**
- Construction workers
 - Cement
- Dentists
 - DETERGENTS, cleaners
- Floor-layers/tile workers
 - **Solvents**
- Electricians
 - Fluxes
- Florists
 - Manure, fertilizers
- Hairdressers
 - Wave solutions, shampoos, bleaching agents
- Hospital workers
 - DETERGENTS, disinfectants, foods
- Homemakers
 - DETERGENTS, cleaners

Kids?

Pediatric Population

- ▣ Personal hygiene products
- ▣ Electronics
- ▣ Coins/Keys
- ▣ Medications
- ▣ Family members
- ▣ Toys



Toys

▣ Nickel and cobalt release from children's toys purchased in Denmark and the United States.

Jensen P, Hamann D, Hamann CR, Jellesen MS, Jacob SE, Thyssen JP.

▣ BACKGROUND:

Nickel is the most common allergen detected by patch testing in children. There is an increasing number of cases in children who have not had exposure to piercing. Although the clinical relevance of nickel patch test reactions in children is sometimes uncertain, continued vigilance to identify new sources of nickel exposure in this age group is important. Recent case reports have described allergic nickel contact dermatitis in children following exposure to toys, but the magnitude of this problem is unknown.

▣ OBJECTIVE:

The aim of this study was to evaluate nickel and cobalt release from children's toys.

▣ METHODS:

We purchased **212 toys** in 18 different retail and online stores in the United States and Denmark. Nickel and cobalt release was tested using the dimethylglyoxime and cobalt screening spot tests.

▣ RESULTS:

A total of **73 toys (34.4%) released nickel**, and none released cobalt.

▣ CONCLUSIONS:

Toys are a commonly overlooked source of nickel exposure and sensitization. Therefore, dermatologists, allergists, and pediatricians should consider the role of toys in their evaluation of children with dermatitis, and the parents of children with positive nickel patch test reactions should be told that toys may release nickel and be a potential chemical source in the manifestation of allergic contact dermatitis.

What we Test. How we Test.

History is Key

- ▣ Look for clues
 - Where did the dermatitis begin
 - What sites were involved
 - Consider allergens known to be associated with sites vs full patching – **making the testing fit the diagnosis**
 - ▣ Eye lids, Hands face, ect
- ▣ Document current active dermatitis
- ▣ Use modern devices to help
 - cell phone pictures

History is Key Cont

- ▣ Skin in ACD is different than “normal” skin



- ▣ Physical Exam
 - New vs chronic dermatitis
 - **Geographic/Location clues**

Exposed Area Locations

- ▣ Face and Hands
 - Highest exposed areas
 - ▣ **Hands – 48%** most common reactions site
 - Airborne
 - ▣ Methylisothiazolinone (MIT), fragrances, Bronopol
 - Connubial dermatitis
 - ▣ PPD, nail polish, fragrances

- ▣ Feet
 - Para-tertiary butylphenol (PTBP) formaldehyde – glue, rubbers, leather agents (chromate)

Case

- ▣ History
 - Where did this happen
 - When did this happen
- ▣ Acute vs chronic
 - Acute contact dermatitis
 - ▣ wet, oozing lesions
 - Chronic
 - ▣ Lichenified, dark
- ▣ Where is it located



Sports – Acetophenone azine

□ Acetophenone azine: a new allergen responsible for severe contact dermatitis from **shin pads**.

Raison-Peyron N, Bergendorff O, Bourrain JL, Bruze M.

□ BACKGROUND:

Contact dermatitis resulting from the use of shin pads is usually caused by rubber components, dyes, benzoyl peroxide, or formaldehyde resins.

□ OBJECTIVES:

To investigate and identify a new allergen in shin pads that was responsible for severe contact dermatitis in a young football player.

□ METHODS:

High-performance liquid chromatography (HPLC) of samples of shin pads was performed. The boy was patch tested with pieces of shin pads and with acetophenone azine, a chemical substance identified by HPLC in the foam of the shin pads.

□ RESULTS:

HPLC identified acetophenone azine at concentrations of approximately 20 µg/g of shin pad samples. Patch tests gave strongly positive reactions to pieces of shin pads and to acetophenone azine down to 0.001% in acetone, whereas acetophenone and hydrazine sulfate were both negative. Twenty controls were negative for acetophenone azine 0.01% in acetone.

□ CONCLUSIONS:

Acetophenone azine is a new, **strong allergen of shin pads**, and more generally of other sport equipment based on ethylene vinyl acetate. It may be used as a **biocide**, but this has to be confirmed. Further investigations are needed to understand factors such as exposure, cross-reaction patterns, metabolism, and the optimal patch test preparation.

□ FIX: put duct tape or barrier between shin guard and the skin.



Specific Location

- ▣ Peri-oral
 - Food additives, fragrances, preservatives, detergents
- ▣ Peri-umbilical/wasteline
 - Ni/Co, Chromates
- ▣ Eyelid
 - Fragrances, methylisothiazolinone (MI)
 - ▣ Even in younger children
- ▣ Vulva
 - Fragrances (majantol - tampons), colophony, MI (adhesives)
- ▣ Back of thighs
 - Chairs in summer, toilet seat and cleaners used on them
- ▣ Hands
 - Modeling clay, play gels
 - Plasticine – MI

Mystery Case?

- ▣ 21yo female - college student.
- ▣ Very itchy, only one side - R
- ▣ Going on for about 2mo
- ▣ Have done OTC cream that helps with itching but rash never goes away
- ▣ Went on Spring break and went away



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Asymmetrical Distribution

- ▣ One cheek
 - nickel from phone
 - case from phone (rubber)
- ▣ One hand
 - computer mouse (rubber)
 - rubber on phones
- ▣ One wrist
 - computer keys – gaming keyboards
- ▣ One palm & Fingers
 - wipes (Fragrance and preservatives)

Cosmetics

- ▣ Facial cosmetics dermatitis
 - Bilateral
 - Patchy
- ▣ Eyelid
 - Absolute thinnest skin on body
 - Most affected site of ACD = **nail varnish/acrylics**
- ▣ Neck
 - “run-off” pattern
 - Cosmetics applied to face, scalp and hair often affect the neck
- ▣ Lips
 - Contact dermatitis – primary **fragrance**

History is Key cont

▣ Patient's Environment

- Home
- Work
- School/Daycare
- Afterschool/work actives
- Sports
- Self hygiene products

- Family hygiene products
 - ▣ **Connubial – Moms and Grandmothers love to kiss**
- Medications



Patch Testing

SECONDAY TO HISTORY ALWAYS!!!

Patch Testing

- ▣ Patch Testing
 - Practical
 - Scientific
 - Objective

- ▣ Dormer Testing Kit



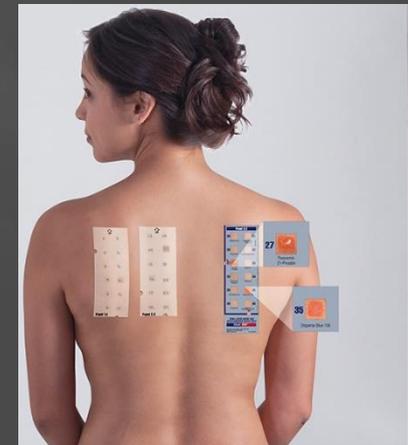
Patch Test

- Standardized test kits
 - T.R.U.E. Test™
 - Dormer



- Kits for specific exposures are available:
 - hairdresser, metal workers, antibiotics, photo allergens, ect.

- Personal items
- Allergens from the cosmetic industry
- Industrial allergens



T.R.U.E vs Dormer Comprehensive

▣ Dormer Comprehensive chamber

- Pro
 - ▣ Unlimited allergens
 - ▣ Specific to Patient
- Con
 - ▣ Difficult for Patient
 - ▣ Difficult to obtain
 - ▣ Not FDA indicated
 - ▣ Requires training and staff

▣ T.R.U.E Test™

- Pro
 - ▣ Widely available
 - ▣ FDA indicated
 - ▣ Comes with patient support
 - ▣ No specific staff needed
- Cons
 - ▣ Only 36 allergens
 - ▣ Difficult for patient

Patch Chambers

Chamber	Distributor	Chamber Shape	Panel Tape	Open Design	Moisture Resistant	Preset Filter Paper	Coated Chamber	Chamber Sizes	Loose Chambers Available	Cover Included	Covers Sold Separately	Works with patchTransport
Finn	 SmartPractice	Round	Scanpor	✗	✗	✗	✗	8mm	✓	✗	✓	With Cover
		Round	Scanpor	✗	✗	✗	✗	12mm	✓	✗	✗	✗
		Round	Scanpor	✗	✗	✗	✗	18mm	✓	✗	✗	✗
Finn PP	 SmartPractice	Round	Scanpor	✗	✗	✗	✓	8mm	✓	✗	✓	With Cover
		Round	Scanpor	✗	✗	✗	✓	12mm	✓	✗	✗	✗
		Round	Scanpor	✗	✗	✗	✓	18mm	✓	✗	✗	✗
Finn Aqua	 SmartPractice	Round	Polyurethane	✓	✓	✗	✓	8mm	✗	✗	✓	✓
allergEAZE CLEAR	 SmartPractice	Square	Polyurethane	✓	✓	✓	✗	8mm	✗	✗	✓	✓
allergEAZE	 SmartPractice	Square	Non Woven	✓	✗	✓	✗	8mm	✗	✗	✗	✓
Hill Top	Hill Top	Square	Durapore	✗	✗	✓	✗	19mm	✗	✗	✗	✗
Hill Top	Hill Top	Square	Durapore	✗	✗	✓	✗	25mm	✗	✗	✗	✗
IQ Ultra	Dormer	Square	Non Woven	✗	✗	✓	✗	8mm	✗	✓	✓	✗
Van der Bend	Not in US	Square	Non Woven	✓	✗	✓	✗	8mm	✗	✗	✗	✗
Curatest	Not in US	Round	Non Woven	✓	✗	✓	Patch	8mm	✗	✗	✗	✗
Curatest F	Not in US	Round	Polyurethane	✓	✓	✓	Patch	8mm	✗	✗	✗	✗

The Value of the T.R.U.E. Test

	Marks et al NACDG 1998	Referral Centers. Saripelli et al 2003	Derm Private Practice 2006	Allergy Practices 2011
Clinically relevant allergens by T.R.U.E.	54.1%	25%	31.7%	56.9%
Missed positives by T.R.U.E. allergens alone	12.4%	22.4%	24%	12.5%
Additional allergen identified with supplemental testing	34.4%	52.1%	24%	25.6%

Marks et al. NACDG JAAD. 1998; 38: 911-918

J Am Acad Derm. 2003;49:65-9

Milltello G et al. Dermatitis. 2006 17;2:77-84.

Camacho-Haitti M; Axelrod, et al. Multi-center, Retrospective Review of Patch testing for Contact Dermatitis in Allergy. Annals of Allergy, Asthma and Immunology 2011; 107; 487-92.

Indications for Patch Testing

- ▣ Confirm diagnosis of ACD
- ▣ Identify triggers
- ▣ Determine cause of an occupational dermatitis
- ▣ Demonstrate absence of a sensitivity to a specific substance
- ▣ Include or exclude the diagnosis of ACD for medical-legal cases
- ▣ Identify potential health hazards

When is Patch Testing Right

- ▣ Is the patient right to go through with testing
 - Another plausible diagnosis
 - Pt/Parent who refuses to avoid all possible agents
 - Hx of testing before
 - On chronic systemic steroids
 - Great deal of UV exposure
 - Poor historian
 - Erythrodermic
 - ▣ Treatment first then test
- ▣ Are the allergens right for the patient
 - Increase efficacy with increase index of suspicion
 - Use of patients own products as adjuvant

Contraindications to Patch Testing

- ▣ Generalized acute or severe dermatitis
- ▣ Oral corticosteroid use
- ▣ Topical steroids use
- ▣ Immunocompromised patients
 - HIV patients still show very sensitive reactions despite having abnormal T-cell levels
- ▣ Sun Burn
 - Dysfunctional Langerhans cells

Patch Test Readings

- ▣ Two (maybe three) readings
 - ▣ Pre-first office discharge – contact urticarial (that 1%)
 - 1st reading – 48hrs post application
 - 2nd reading – can vary 3, 4 or 7d after application.
- ▣ Single reading
 - 3-4 days after application
- ▣ 1st vs 2nd readings
 - 2nd reading helps distinguish irritant vs allergic reactions
 - 30% of negative testing at 48hrs may show positive results at full reading

Delayed Patch Test Readings after 5 Days

- ▣ Metals
 - Gold
 - Potassium dichromate
 - Nickel
 - Cobalt

- ▣ Topical Antibiotics
 - Neomycin
 - Bacitracin

- ▣ Topical Corticosteroids

Pearls

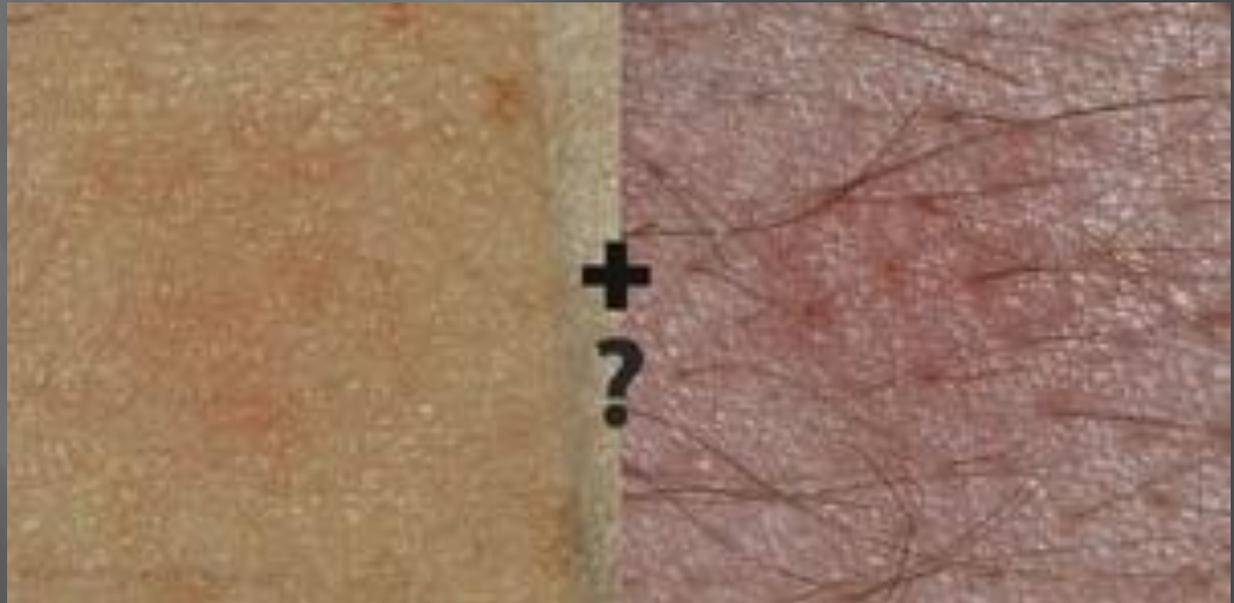
- ▣ Streamlining
 - Handouts
 - ▣ pre-questionnaire
 - ▣ Pre-FAQ consult
 - ▣ Pre-consult instruction sheet
 - Instructional videos
 - Test their own products + standards

- Make sure they throw away sensitizers and add the items to their “allergy” list.

Patch Test Interpretation

Patch Test Interpretation - 0

- ▣ **Doubtful reaction**
 - Faint macular
 - No infiltration
 - Homogenous erythema



Patch Test Interpretation -

1+

- ▣ **Weak positive reaction**
 - Erythema
 - Infiltration
 - Papules

- ▣ Can always clarify by retesting or use of personal agent
 - See if the reactions appear the same

- ▣ History will be key



Patch Test Interpretation - 2+

- ▣ **Strong positive reaction**
 - Discrete vesicles
 - Erythema
 - Infiltration
 - Papules



Patch Test Interpretation - 3+

- ▣ **Extreme positive reaction**
 - Coalescing vesicles
 - Bullous or ulcerative reaction



Patch Test Interpretation - IR

- ▣ **IR Irritant reaction**
 - Discrete patchy erythema



Causes of False Positive Reactions

- ▣ Use of irritant substances
 - Sharply demarcated
 - Confined to disk or patch area
 - Shiny with blisters
 - Burning or painful. Less of an itch
 - Decreased severity between readings



- ▣ Pustular patch reactions
 - Common in atopic patients
 - Nickel, copper sulfates, arsenic trioxide and mercuric chloride testings
 - Minimal pruritis by patient



Causes of Negative Reactions

- ▣ Insufficient reproduction of original conditions
 - Shoes and clothing
 - ▣ No Sweating or friction
 - Topical medications
 - ▣ Inadequate penetration
- ▣ Failure to test the true antigen
- ▣ Low concentration
 - Threshold of material is too low - irritant
- ▣ Improper testing technique
 - Poor contact
- ▣ Failure to perform delayed readings
- ▣ Need for photo patch testing
- ▣ Failure to remember or use of steroids into the testing period

Sensitizing Agents

Top Agents in Literature Review

- 2008 was the first published studies done in the United States with regards to patients and contact dermatitis
 - Prior to that we had patch studies in healthy people along with **European studies**
 - These were the most common allergens according to literature.

Allergen	Number Citations		Allergen	Number Citations
Nickel	289		MCI/MI	18
Cobalt	98		Q15	16
Formaldehyde	81		Budesonide	16
Balsam Peru	64		Tixocortol	13
Neomycin	64		Carba	12
Chromate	56		Propylene Glycol	11
Colophony	33		Disperse Dye	9
Compositae	25		Fragrance Mix 2	8
Lanolin	20		Cocamidopropyl betaine	5

The International Top 10-Sensitizations

	NACDG 2001-4 (2008)	US-Upenn Pediatric Study (2008)
Nickel	28.3%	17.5%
Fragrance Mix I	5.1%	6.3%
Cobalt	17.8%	8.8%
Thimerosal	15.4%	12.5%
Myroxylon pereirae (BoP)	3.9%	11.3%
Chromium	3.6%	5%
Neomycin	8%	11.3%
Lanolin	3.6%	1.3%
Thiuram	1.8%	1.3%
Papa-phenylenediamine (PPD)	2.1%	5%

NACDG – North American Contact Derm Group. Based out of US and Canadian clinics.
Midwest bias to Caucasian patients.

Jacob SE, et al. Clinically relevant patch test reactions in children – a US based study. Ped Derm. 2008. Sept-Oct25(5), 520-7.
 Zug KA, et al. Contact allergy children referred for patch testing. NACDG Data 2001-2004. Arch Dermatology 2008, Oct.

Neomycin

- ▣ Neomycin is an **antibiotic**, unrelated to penicillin, which is used externally to treat burns, wounds and infected skin conditions, as well as, eye ear and nose infections.
- ▣ It can also be encountered in root canal and some other dental treatments.
- ▣ What else is Neomycin called?
 - *Biosol*
 - *Fradiomycin*
 - *Framycetin*
 - *Mycifradin sulphate*
 - *Myacyne*
 - *Mycifradin*
 - *Neloate*
 - *Neodecyltin*
 - *Neomas*
 - *Neomin*
 - *Neomycin undecylenate*
 - *Neomixr 325 and neomixr AG 325*
 - *Nivemycin*
 - *Pimavecort*
 - *Sofra-Tulle*
 - *Soframycin*
 - *Vonamycin Powder V*

Neomycin

- ▣ Cross reacts with paromomycin, butirosin, framycetin, tobramycin, kanamycin and gentamicin
- ▣ Concomitant sensitizations:
 - neomycin and bacitracin
- ▣ Risk: stasis dermatitis, leg ulcers, anogenital dermatitis and otitis externa

Thiuram Mix

- ▣ These various chemicals can be found in a broad range of **rubber-based** products, such as gloves, elastic bands, condoms, balloons and kitchen utensils.
- ▣ They may also be found in adhesives, animal repellent, cosmetic applicators, disinfectants, medical devices, clothing, soap and swimwear.
- ▣ Additionally, in tires, tubes, hoses, conveyor belts, electric cords, earphones and some agricultural products such as fungicides

Thiuram Mix

The chemicals in Thiuram Mix are:

- ▣ Diepentamethylenethiuram disulfide
 - Used as an accelerator and vulcanizing agent for latex (gloves) and butyl rubber.

- ▣ Tetraethylthiuram disulfide
 - Used as an accelerator, activator, stabilizer and vulcanizing agent for various rubber products. Also used as a fungicide, seed disinfectant and alcohol deterrent.

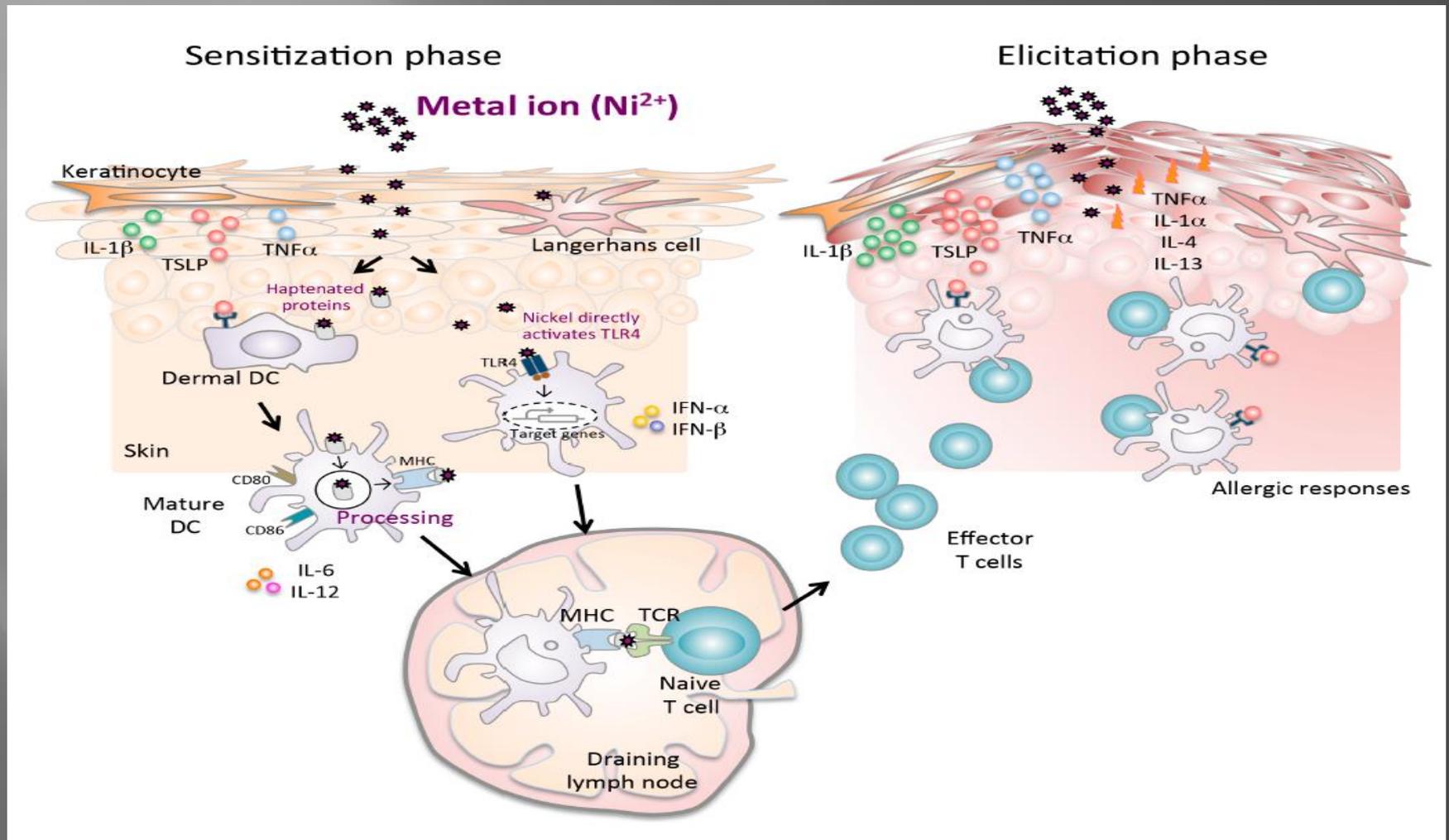
- ▣ Tetramethylthiuram disulfide
 - Used as a rubber accelerator and vulcanizer. Works as a fungicide, disinfectant for seed, bacteriostat in soap, animal repellent, etc.

- ▣ Tetramethylthiuram monosulfide
 - An accelerator and activator for natural rubber nitrile-butadiene and butyl rubber.

Nickel Sulfate Hexahydrate

- ▣ This chemical has numerous household and industrial applications.
- ▣ It is found in coins, jewelry, eyeglasses, utensils, metal buttons, keys, paper clips, enamel dyes, pigment for paint and wallpaper and electrical wiring.
- ▣ It is also used as a fuel additive.
- ▣ What else is Nickel Sulfate Hexahydrate called?
 - *Blue salt*
 - *Carbonyl nickel powder*
 - *Nickel*
 - *Nickel (II) Sulfate Hexahydrate*
 - *Nickel monosulfate hexahydrate*
 - *Nickel sulfate hexahydrate*
 - *Sulfuric acid, nickel (2+) salt, hexahydrate*
 - *Single nickel salt*

Pathophysiology: Nickel Sensitization



Nickel

- ▣ 10% of the population is sensitized
 - Increasing
- ▣ Cellphones are a new source of allergy



Metal Implant “allergy”

- ▣ Often suspected but rarely documented
- ▣ 5% of orthopedic implants and up to 25% of patients with preoperative metal sensitivity may develop cutaneous allergic reactions upon re-exposure
- ▣ Clinical manifestations
 - Cutaneous
 - ▣ Localized
 - ▣ Generalized – most eczematous
 - Urticaria and vasculitis has been reported
 - Implant Failure

Biomedical Devices

- ▣ Orthopedic implants
 - Very low to no Nickel content in devices
 - Report of dermatitis to biomedical devices can lead to
 - ▣ Consultation request of allergy or dermatology
 - ▣ Increased health care cost
 - ▣ Medial legal pitfalls
 - Metal disk that is sent from ortho has only a minor value
 - ▣ Need to investigate the **metal salts and ions** that develop when inside the body
 - ▣ Studies done with the disks that are sent are notorious for giving **FALSE NEGITIVES**
 - Should **never** be tested **alone**

Biomedical Devices

- ▣ Endovascular stenting
 - Retrospective study of coronary in-stent restenosis 6mo post stainless steel stent placement & patients 2mo after angioplasty
 - ▣ 11/131 (8%)
 - 7 to nickel
 - 4 to molybdenum
 - ▣ Clinical history was not positive for reactions in the past
 - ▣ All 11 patients with a positive patch test to metals showed higher restenosis rate compared to their peers
 - ▣ **Conclusion: suggest that metals – particularly to nickel – can play a relevant role in inflammation and fibroproliferatory restenosis**
 - Prospective study 174 stented patients
 - ▣ 109 initial placement and 65 in-stent restenosis
 - ▣ Patients with **recurrent** of in-stent restenosis had significantly higher patch test to medals: Ni and Mn.
 - Highest odds ratio: 5.41 with Ni positives

Biomedical Devices

▣ Conclusions

- Most reactions to endovascular, ortho, dental metal implants are based on case reports and small cohorts
 - Approximately 5% developed eczematous reactions with metallic implants
 - Proven cases seem to show the following metals as primary triggers:
 - Ni
 - Co
 - Cr
 - Cu – GYN devices
- Need for patch testing is controversial at this time
 - **Poorly reliable in PREDICTING reactions**
- Consider patch testing referral
 - **Preimplantation has a history of metal reactions** or sensitivity
 - **Post** implantation having cutaneous eruptions months to years after implantation
- A negative patch test is reassuring for absence of delayed sensation
- **A positive patch testing does not prove relevance**

Nickel in the Diet

- ▣ Evidence supports the contribution of dietary nickel dermatitis as **vesicular hand eczema**
- ▣ Meta-analysis of systemic contact dermatitis following oral exposure to nickel estimated that:
 - 1% of nickel allergic patients would have systemic reaction to nickel content in normal diet
 - 10% would react to a 0.55-0.89mg dosage of nickel
 - Approximately 50% would flare after 2.5mg of nickel
- ▣ Rare to use a low nickel diet unless patient wishes to in the midst of uncontrollable dermatitis with a positive nickel patch

Nickel in the Diet

Nickel concentration		
>50mcg	Soy bean - 1 cup (895 mcg) Cocoa - 1T (147 mcg) Cashew - 18 nuts (143 mcg)	Figs - 5 (85 mcg) Lentils - ½ cup (61 mcg) Raspberry (56 mcg)
20-50mcg	Vegetables canned - ½ cup (40mcg) Lobster - 3oz (30mcg) Frozen Peas - ½ cup (27mcg)	Asparagus - 6 (25mcg) Oat Flakes - 2/3 cup (25mcg) Pistachios - 47 nuts (23mcg)
<20mcg	Strawberries - 7 (9mcg) Bread wheat - 1 slice (5mcg) Poultry - 3.5oz (5mcg) Carrots - 8 sticks (5mcg) Apple - 1 medium (5mcg)	Cheese - 1.5oz (3mcg) Yogurt - 1cup (3mcg) Mineral water - 8oz (3mcg) Mushroom raw - ½ cup (2mcg) Corn Flakes - 1 cup (2mcg)

Cobalt (II) Chloride-Hexahydrate

- ▣ Cobalt is a silver-gray, magnetic, brittle metal which is used to produce **blue colors** in pottery, glass, porcelain and enamel and is also combined with other metals to make metal alloys.
- ▣ The most common source of exposure is nickel-plated objects which most always contain cobalt.
- ▣ A positive reaction to cobalt therefore often accompanies nickel sensitivity.
- ▣ What else is Cobalt (II) Chloride-Hexahydrate called?
 - *Cobalt Dichloride Hexahydrate*
 - *Cobalt Blue*
 - *Cobaltous*
 - *Cobaltous chloride, hexahydrate*
 - *Chloride Hexahydrate*

Fragrance

- ▣ Over 2800 fragrance ingredients in database of Research Institute for Fragrance Materials, Inc.
 - 100 are known allergens
- ▣ Fragrance are complex substance containing hundreds of different chemicals
- ▣ One of the most common causes of ACD from cosmetics

Fragrance Mix I

The chemicals in **Fragrance Mix I** are:

- ▣ **Amyl Cinnamal**
 - A raw material in the production of perfumes.

- ▣ **Cinnamyl Alcohol**
 - A component found in perfumed cosmetic products and deodorants.

- ▣ **Cinnamal**
 - A common ingredient in perfumes for household products like deodorizers, detergents and soap. Flavor in toothpaste, sweets, ice cream, soft drinks, chewing gums, and cakes.

- ▣ **Eugeno**
 - Used as fragrance in perfumery as substitute for oil of Cloves. Dental analgesic in impression materials and periodontal packing. Used in the production of Vanillin. Also used as insect attractant.

Fragrance Mix I

The chemicals in **Fragrance Mix I** are:

- ▣ **Geraniol**
 - As fragrance in perfumery. As insect attractant.

- ▣ **Hydroxycitronellal**
 - A fragrance used in various perfumes, antiseptics, insecticides and household products.

- ▣ **Isoeugenol**
 - A fragrance used in perfumery, over-the-counter medicines, dental materials and foods. Also used in the production of Vanillin flavor. Found in oils of nutmeg, ylang-ylang, etc.

- ▣ **Oakmoss Absolute**
 - An extract of oak moss for use as fragrance in many perfume mixtures, after-shave lotions, etc. The raw material for this product is made from a hexane extraction of the moss giving a concrete, then the absolute is obtained by extracting the concrete with ethanol. The moss used is *Evernia Prunastri*.

Fragrance

- ▣ “Unscented”
 - Erroneously suggest a product does not contain fragrance
 - In fact – a masking fragrance is actually present
 - ▣ “2 for 1 special”

- ▣ “Fragrance-free” products
 - Typically free of classic fragrance ingredients
 - Generally acceptable for the allergic patient

- ▣ “Fragrance-free with botanical extracts” contain products for improving odor characteristics

Fragrance Panels

Fragrance Mix I	Balsam of Peru (myroxylon pereirae)	Fragrance Mix II
Cinnamic alcohol 1%	Cinnamic acid	Coumarin 2.5%
Cinnamic aldehyde 1%	Benzoyl Cinnamate	Hydroxyisohexyl 3-cyclohexene carboxyaldehyde (Lyral) 2.5%
Alpha-amy cinnamaldehyde 1%	Benzoyl Benzoate	Citronellol 0.5%
Hydroxycitronellal 1%	Benzoic acid	Farnesol 2.5%
Gerniol 1%	Vanillin	Citral 1%
Isoeugenol 1%	Nerodilol	Alpha-Hexyl cinnamic aldehyde
Eugenol 1%		
Oak moss 1%		

Fragrance Panels Mix

- ❑ Low specificity of the test
 - Strong irritant potentials, need to treat weak positives with caution
 - Need to show strong positive to call it a true positive for avoidance
- ❑ Consider retesting with mild positives to increase probability of the test
- ❑ Standard fragrance mix
 - Fragrance mix I and Balsam of Peru – 60-70% of all ACD reactions
- ❑ With patients that do have a history positive case with fragrance products, 35% had positive reactions to fragrance mix II and negative to fragrance mix I.

Fragrance

- ▣ Leave on fragrances
 - Induced dermatitis at normally utilized concentrations

- ▣ Concentration of fragrance left on fabric by laundering was VERY LOW and the majority of the time below threshold induction levels
 - **Its not the laundry detergent!**

Myroxylon pereirae resin (Balsam of Peru)

- ▣ Balsam of Peru is an aromatic liquid mainly used for flavoring in food and drink, fragrance in perfumes and as an ingredient in medicinal products.
- ▣ It can be found in perfumes, deodorants, after shave lotions, cosmetics baby powders, sunscreens, shampoos and conditioners, artificially baked goods, soft drinks, aperitifs, ointments, wound spray, lozenges, surgical dressings, toothpaste and mouthwash
- ▣ What else is Myroxylon pereirae resin called?
 - *Balsam of Peru*
 - *Balsamum peruvianum*
 - *Balsams, Peru*
 - *Balsam Peru oil*
 - *Black balsam*
 - *China oil*
 - *Honduras balsam*
 - *Indian balsam*
 - *Myroxylon pereirae klotzsch resin*
 - *Myrospermum pereira balsam*
 - *Myroxylon pereirae klotzsch oil.*
 - *Oil balsam peru*
 - *Peruvian balsam*
 - *Peru balsam*
 - *Peru balsam oil*
 - *Surinam balsam*
 - *Toluijera pereira balsam*

Fragrance – BoP Diet

- ▣ 50% of patients with a positive patch test to Balsam of Peru (BoP) had significant reduction to their dermatitis with a BoP reduced diet

- ▣ Foods to avoid in a BoP diet
 - Citrus fruits
 - Flavoring agents
 - Pastries, candy, chewing gum
 - Spices
 - Cinnamon, cloves, vanilla, curry, allspice, ginger, anise
 - Tea and tobacco
 - Chocolate
 - Cough lozenges
 - Ice cream
 - Cola, spiced soft drinks (Dr. Pepper)
 - Tomatoes

Fragrance

- ▣ Cosmetic companies are not legally responsible for putting what the makeup of their fragrance on labels due to it being proprietary

- ▣ Other fragrance sensitizers
 - Lyral
 - Jasmine
 - Lavender
 - Sandalwood
 - Tea tree oil
 - Ylang ylang oil
 - Lemongrass oil
 - Narcissus
 - ect

Thimerosal

- ▣ This compound is used as an ophthalmic **preservative**, a topical antibacterial and a topical veterinary antibacterial and antifungal agent.
- ▣ Mercury biased
- ▣ It can be found in contact lens solutions and cosmetic products like eye makeup. Further research may identify additional product or industrial usages of this chemical.
- ▣ What else is THIMEROSAL called?
 - *Elcide*
 - *Ethylmercurithiosalicylic acid sodium salt*
 - *Mercurothiolate*
 - *Merfamin*
 - *Merseptyl*
 - *Merthiolate*
 - *Mertorgan*
 - *Merzonin*
 - *Merzonin sodium*
 - *Nosemack*
 - *SET*
 - *Sodium ethylmercuric thiosalicylate*
 - *Thiomersalate*

Amerchol L 101 (Lanolin)

- ▣ Amerchol is an **emollient** and an emulsifier used in medicated ointments, furniture polish, waxes, textiles and inks.
- ▣ It can also be found in hair products, lipsticks, moisturizers, furs, cutting oils, leather and paper.
- ▣ What else is Amerchol L 101 called?
 - *Lanolin alcohol*
 - *Wool alcohol*

4-Phenylenediamine base (PPD)

▣ This chemical is used in the manufacture of rubber, as a reagent in **hair dyes**, lithography, photocopying, oils, greases, gasoline, rubbers and plastics.

- ▣ What else is 4-Phenylenediamine base called?
 - 1,4-Diaminobenzene
 - 1,4-Benzenediamine
 - 1,4-Phenylenediamine
 - 4-Aminoaniline
 - benzofur d
 - C.I. 76060
 - C.I. developer 13
 - C.I. oxidation base 10
 - developer 13
 - durafur black
 - Developer 12
 - Developer PF
 - fouramine d
 - fourrine d;
 - fourrine i
 - fur black r
 - fur brown 41866
 - furro d
 - fur yellow
 - Futramine D
 - Fur Black 41866
 - Mako h
 - Orsin
 - oxidation base 10
 - pelagol dr
 - pelagol grey d
 - Pelagol D
 - PPD
 - Peltol D
 - Phenylhydrazine
 - p-Aminoaniline
 - p-benzenediamine
 - p-Diaminobenzene
 - p-Phenylene diamine
 - Phenylenediamine base
 - Renal PF
 - Rodol D
 - Santoflex ic
 - Tertral D
 - Ursol D

PPD

- ▣ Very sensitizing
- ▣ One of the most potent sensitizers on the panels
- ▣ Very strong binder to the skin – can cause blistering reactions and scarring.

PPD



- ▣ Hair dye
 - Used to give a black or brown color
- ▣ PPD is found in higher concentrations in hena-balck than most hair dye
 - Natural hena is more orange
- ▣ Reactions are reported in 5.3% of the population who have never used hair dye before
 - Usually picked up as people become older and hair starts to gray
 - Has been seen in a pediatric population due to hair dye being used

PPD

- ▣ Prevention
 - OTC open kits sold and if used properly can show sensitization before full hair dye is done
- ▣ New hair dyes contains FD & C and D&C dyes
 - Appear to have limited cross reactivity with PPD
 - ▣ Elumen Hair Color



Black Henna Tattoos – PPD allergy



Sensitization to PPD from tattoos is most likely
lifelong

Improving since FDA has been more vocal about this

Cosmetic Preservatives

▣ Formaldehyde

- Formaldehyde
- **Quarternium 15**
- Diazolidinyl urea
 - ▣ Germall II
- Imidazolidinyl urea
 - ▣ Germall
- Bromonitropropane
 - ▣ Bronopol
- DMDM Hydantoin
 - ▣ Glydant

▣ Non-Formaldehyde

- Methyldibromoglutaronitrile
 - ▣ Euxyl K400
- MCI/MI
- **Parabens**
- Chloroxylenol
- iodopropynylbutylcarbamate

Formaldehyde

- ▣ This compound is widely used in a multitude of industrial applications.
- ▣ It is often used as a **preservative**, disinfectant and antiseptic and can be found in common household products such as pesticide, adhesives, hair products cosmetics, paints and polishes.
- ▣ What else is Formaldehyde called?:
 - BFV
 - Fannoform
 - Formalin
 - Formalin 40
 - Formalith
 - Formic aldehyde
 - Formol
 - FYDE
 - HCHO
 - HOCH
 - Karsan
 - Lysoform
 - Methan 21
 - Melamine-Formaldehyde Resin
 - Methylene glycol
 - Methylene oxide
 - Methyl aldehyde
 - Methanal
 - Morbicid
 - Oxomethane
 - Oxomethylene
 - Oxymethylene
 - Superlysoform
 - Veracur

Formaldehyde

- ▣ Most common potential source of exposure
 - Cosmetics
 - ▣ Rarely listed on ingredient label
 - ▣ Direct use is forbidden in some countries – Europe
 - ▣ Contains formaldehyde releasers
 - Permanent press textiles
 - ▣ Increased strength, prevents shrinking, resists wrinkling of the clothing fibers
- ▣ Formaldehyde ≠ Formaldehyde Resin

Formaldehyde in Textile Resin

- ▣ Even exposure once a month is enough to cause a rash. “Dress clothes” worn on weekends or special occasions maintain the dermatitis
 - Each wash cycle removes the resin but might always maintain a small amount.

Quarternium 15

- ▣ One of the most common cosmetic preservatives
- ▣ Most sensitization is from a formaldehyde allergy

Acrylates

- ▣ Adhesives, paint, printing inks, solvents
- ▣ Soft contact lenses

- ▣ Artificial nails

- Fingertip dermatitis and parathesia
- Periungunal and eye lid dermatitis

- ▣ Bone cement and ortho implants

- ▣ Dental resin

- Painful and burning stomatitis

Treatment

Was Patch Testing Useful?

- ▣ Did we get
 1. A positive reaction and rash that gets worse
 - ▣ Confirms reaction
 2. A positive reaction that doesn't mean anything
 - ▣ Not consistent with what the history is telling
 3. A negative reaction
 4. A rash that is worse but get a negative patch test
 - ▣ Consider retesting and expanding
 - ▣ Exposure to agent while outside of office

Treatment of Contact Dermatitis

- ▣ **Identify and avoid contact** with allergens and irritants
 - Give exposure list – synonyms and sources
- ▣ Alternative and substitutions of possible
 - Cover nickel plated objects
 - Wash formaldehyde containing garments
 - Gloves and barriers
 - Avoidance
- ▣ Not treatments; Supportive care:
 - Antihistamines
 - Topical and oral steroids
 - Steroid sparing agents – cyclosporine, ect
 - UV light therapy

Treatment of Contact Dermatitis

- ▣ Acute contact dermatitis – wet, oozing lesions
 - Aluminum sulfate and calcium acetate (Domeboro) in clean absorbent cloth 20-30min as a compress 2-3x per day
 - Oatmeal baths (aveeno) in extensive areas
 - Oral corticosteroids if severe
 - Fluorinated steroids for 1-2wk duration only

- ▣ Chronic contact dermatitis
 - Emollients to decrease itching
 - Low to medium strength topical steroids
 - Antihistamines to help with itching
 - UV light
 - Cyclosporine
 - Topical calcineurin inhibitors

Corticosteroids

STRUCTURAL GROUPS OF CORTICOSTEROIDS

Cross reactivity based on 2 immune recognition sites-
C 6/9 & C16/17 substitutions

Class A (Hydrocortisone & Tixocortol pivalate: has C17 or C21 short chain ester)

Hydrocortisone, -acetate, Tixocortol, Prednisone, Prednisolone, -acetate, Cloprednol, Cortisone, -acetate, Fludrocortisone, Methylprednisolone-acetate

Class B (Acetonides: has C16 C17 cis-ketal or -diol additions)

Triamcinolone acetonide, -alcohol, Budesonide, Desonide, Fluocinonide, Fluocinolone acetonide, Amcinonide, Halcinonide

Class C (non-esterified Betamethasone; C16 methyl group)

Betamethasone sodium phosphate, Dexamethasone, Dexamethasone sodium phosphate, Fluocortolone

Class D1 (C16 methyl group & halogenated B ring)

Clobetasone 17-butyrate, -17-propionate, Betamethasone-valerate, -dipropionate, Aclometasone dipropionate, Fluocortone caproate, -pivalate, mometasone furoate

Class D2 (labile esters w/o C16 methyl nor B ring halogen substitution)

Hydrocortisone 17-butyrate, -17-valerate, -17-aceponate, -17-buteprate, methylprednisolone aceponate

Corticosteroids

- ▣ Increase detection probably due to
 - Greater awareness
 - Expanding market for steroids
 - Improved testing

- ▣ Suspect
 - In stasis ulcers and chronic eczema
 - When dermatitis fails to respond
 - When dermatitis worsens with treatment

Shampoos

- ▣ Products with the lowest chance of a reaction with atopics
 - AFM safe choice hair and body shampoo
 - Free and Clear shampoo



Contact Allergen Management Program (CAMP)

- ▣ Databases
 - Topical Skin care product database
- ▣ American Contact Dermatitis Society
 - Need to be accepted in to the society via letter of reference

Shotgun Approach

P.E.A.S. – Pre-Emptive Avoidance Strategy

- ▣ 30% show improvement
- ▣ Idiopathic Response
 - Nickel
 - Balsam of Peru/Fragrances
 - Formaldehyde
 - Cocamidopropyl betaine (CAPB)
 - Propylene Glycol
 - Methylisothiazolinone (MI)

Empiric Treatment – LoCAL Skin Diet

- ▣ LoCAL
 - Low contact allergen
- ▣ Eliminates most of the common allergens
 - Fragrance
 - Formaldehyde releasing preservatives
 - MCI/MI
 - MDG/PE
 - Lanoin
 - CAPB
 - Benzophenone-3
- ▣ Cover girl fragrance free liquid makeup
- ▣ Clinique blushing blush power
- ▣ Clinique soft press eye shadow
- ▣ Max factor vivid impact lip liner
- ▣ Almay hypoallergenic roll-on antiperspirant/ deodorant
- ▣ Cerave moisturizing lotion
- ▣ Cetaphil gentle skin cleanser
- ▣ Free & Clear shampoo
- ▣ Free & Clear hair spray

Thank you

Questions

- ▣ Contact dermatitis is what class of hypersensitivity reaction:
- ▣ 1. I
- ▣ 2. II
- ▣ 3. III
- ▣ 4. IV
- ▣ 5. V

Questions

- ▣ **True** or false:
- ▣ Metal disk that is sent from orthopedic doctors or companies has only a minor value in testing for biomedical implants?

Questions

- ▣ The ultimate treatment for contact dermatitis is:
- ▣ 1. Continued contact to sensitize the patient
- ▣ 2. Identification via skin prick testing and avoidance
- ▣ 3. Identification via patch testing only and avoidance
- ▣ 4. Using history along with possible patch testing to identify and avoid the triggering substance
- ▣ 5. Using topical steroid cream to resolve the rash

Questions

- ▣ True or **False**:
- ▣ There are many more cases of contact dermatitis than there are of irritant dermatitis.

Questions

- ▣ Which of the following is true regarding 4-Phenylenediamine base (PPD)
- ▣ 1. It is a very strong sensitizing agent
- ▣ 2. This can be used in tattoos resulting in scarring
- ▣ 3. The major place this item is found in is hair dye
- ▣ 4. You do not need to have prior contact with PPD in order to have a reaction
- ▣ **5. All the above**