CONTACT DERMATITIS:
What’s New, Hot, and Maybe Spicy?

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ANNUAL PROCEDURES IN THE US

- Stent placements ~ 1,000,000
- Total knee arthroplasties ~ 600,000
- Total hip arthroplasties ~ 400,000
- Dental implants ~ 500,000
POTENTIAL ALLERGIES IN METAL IMPLANTS

Metals
Acrylates
Antibiotics
Immunosuppressive Agents
METAL ALLERGY TO IMPLANTED DEVICES

Estimated incidence/prevalence 0 - 5%

Metal allergy higher in patients with failed (vs. well-functioning) implants 60% (vs. 25%)

Malpractice cases related to implants and allegations of inadequate preoperative allergy assessment Increasing

ORTHOPEDIC
Stainless steel
(Nickel, Cobalt, Chromium > Molybdenum)

ENDOVASCULAR
Stainless steel
Cobalt / Chromium
Nitinol (55% Nickel, 45% Titanium)

DENTAL
Vitallium (Cobalt, Chromium, Molybdenum)

GYNECOLOGIC
Copper
Essure® (contains Nickel)

ALLERGY TESTING FOR METAL IMPLANTS

Pre-implant screening

Post-implant testing
69-yr-old man
2010 – right hip replacement (pure titanium)
    with femoral nerve injury requiring brace
2013 – revised replacement with polyurethane head
    (but retaining titanium body)
2014 – pruritic rash on right thigh that evolved into
    generalized eruption
2015 – biopsy of right leg = spongiotic dermatitis
Rash responds to topical triamcinolone

POSITIVE PATCH TESTS
(Chemotechnique allergens)

NACDG 80
Cobalt chloride

Metal series
Titanium nitrite

• Metal allergy is common (up to 20% prevalence)
  Nickel > Cobalt > Chromium
• But titanium allergy is rare
  most commonly associated with
  cardiac pacemakers
  but only 3 cases with orthopedic implants
• 90% of titanium use is not as a metal
  but as titanium oxide powder in:
    sunscreens, cosmetic products,
    pharmaceutical, and foods
POST-IMPLANT CRITERIA

DIAGNOSING METAL ALLERGY

MAJOR
- Chronic dermatitis starting after implantation
- Eruption overlying implant
- (+) Patch test to metal in implant

MINOR
- Eczematous morphology
- Spongiotic histology
- Systemic dermatitis
- (+) Lymphocyte transformation test
- Eruption resistant to treatment

59-yr-old woman

Scheduled for knee replacement

- ? nickel allergy because of reactions to:
  - earrings
  - belt buckles
  - jean snaps
  - eyeglass frames
POSITIVE PATCH TESTS
(Chemotechnique allergens)

NACDG 80
- Cobalt chloride
- Nickel sulfate
- Gold thiosulfate

Metal series
- Copper sulfate
- Gold thiosulfate
- Nickel sulfate
- Palladium chloride
- Sodium tetrachloropalladate
- Stannous chloride

PRE-IMPLANTATION GUIDELINES

Routine patch testing is not recommended, but ought to be considered in patients who report intolerance to metals (like jewelry) since history screens poorly for metal allergy.

For patients who believe they are allergic to a metal, implantation of a device containing the metal is unacceptable without written consent.
PRE-IMPLANTATION GUIDELINES

The implant used should be based on the surgeon’s medical judgement and the patient’s needs, since competing goals may render use of a potentially allergenic alloy unavoidable.

In nickel-allergic patients (other things being equal), pure titanium or oxidized zirconium is the best choice.

REAL / POTENTIAL BENEFITS FROM ALLERGY TESTING FOR METAL IMPLANTS

Identify relevant allergens

PRE-IMPLANT
Provide guidance for selecting the best type of implant

POST-IMPLANT
Provide evidence to adjudicate need for replacing faulty / diseased implants

Yield greater / better real-life knowledge from which sound medical decisions can be made

PRESERVATIVE ALLERGY:

What’s on the upswing?
• 71 year old man has itchy rash on trunk, arms, legs x 2 months, partially resolved by prednisone, but not by topical steroids

• Skin biopsies x 2 = spongiotic dermatitis

Patch Tests

- NACDG-80 (Chemotechnique):
  - Formaldehyde
  - Formaldehyde-releasers
    - Diazolidinyl urea (Germal II)
    - DMDM Hydantoin
    - Imidazolidinyl urea (Germal I)
    - Quaternium-15
  - Non-releasers
    - Iodopropynyl butyl carbamate
    - Paraben mix

- Textile Series (Chemotechnique):
  - Ethyleneurea melamin formaldehyde
  - Melamine formaldehyde
Most Relevant Allergen Sources

- Skin care products
  - Formaldehyde
  - Preservatives (formaldehyde releasers or not)

- Formaldehyde-based fabric finishes
  - Unwashed clothing
  - Some permanent pressings

FORMALDEHYDE & FORMALDEHYDE RELEASERS

- Formaldehyde is ubiquitous and hard to avoid, especially in:
  - skin care products and fabric finishes

- Among preservatives, the formaldehyde releasers are important because they can:
  1. be allergens themselves
  2. release formaldehyde and cause allergies in formaldehyde-allergic patients

- Among formaldehyde releasers, quaternium-15 is the most common allergen

PRESERVATIVE ALLERGENS

<table>
<thead>
<tr>
<th>Preservatives</th>
<th>Non-releasers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzylhemiformal</td>
<td>Choromycin</td>
</tr>
<tr>
<td>Butenol</td>
<td>Copperammonium betaine (trimeamine)</td>
</tr>
<tr>
<td>2-Bromo-3-nitropropionate</td>
<td>Propylparaben/Gentisic Acid</td>
</tr>
<tr>
<td>PPD</td>
<td>Methylchloroisothiazolinone/Methylisothiazolinone (Kathon CG)</td>
</tr>
<tr>
<td>Bioban</td>
<td>Methylbromopropylamine N-oxide/Phenacyl alcohol (Eucryl K400)</td>
</tr>
<tr>
<td>Cocamidopropyl betaine (Amidoamine)</td>
<td>Methyldibromoglutaronitrile</td>
</tr>
<tr>
<td>2-Bromo-3-nitropropan-1-ol</td>
<td>Methyldibromoglutaronitrile/Phenacyl alcohol (Eucryl K400)</td>
</tr>
<tr>
<td>Iodopropynyl butylcarbamate</td>
<td>Methyldibromoglutaronitrile/Methylisothiazolinone (Kathon CG)</td>
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<tr>
<td>Methylparaben</td>
<td>Methyldibromoglutaronitrile/Phenacyl alcohol (Eucryl K400)</td>
</tr>
<tr>
<td>Methylisothiazolinone (Kathon CG)</td>
<td>Thimerosal</td>
</tr>
<tr>
<td>DMDM hydantoin (Glydant)</td>
<td>Thimerosal</td>
</tr>
<tr>
<td>Benzylbenzyl alcohol</td>
<td>Thimerosal</td>
</tr>
<tr>
<td>Methyldibromoglutaronitrile</td>
<td>Thimerosal</td>
</tr>
<tr>
<td>MCI/MI</td>
<td>Thimerosal</td>
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</tbody>
</table>

Most common preservative allergens (MACDG data):
- Formaldehyde > Quaternium-15 > Iodopropynylbutylcarbamate > MIB/PE > MCI/MI
• 45 year old man with recurrent itchy rash x 5 years involving perianal area and scrotum cleared transiently by topical steroids

• Other contactants:
  Blue Star ointment
  Calmoseptine
  Cottonelle wipes
  OTC topical antibiotics

Patch Tests

NACDG (Chemotechnique):

Relevant positives
  Neomycin
  Lauryl glucoside
  ? Methylisothiazolinone
  ? Balsam of Peru (Myroxylon pereirae)
  ? Sesquiterpene lactone

Irrelevant positives
  Disperse blue dye
  Thimerosal

? False negative to Kathon CG
  (Methylchloroisothiazolinone + Methylisothiazolinone)

Preservative Allergens

<table>
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<tr>
<th>Formaldehyde releasers</th>
<th>Non-releasers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzylformaldehyde</td>
<td>Chenoxytol</td>
</tr>
<tr>
<td>Butylhydroxytoluene</td>
<td>Benzylbenzylbutyrate (Brilliant Blue GB)</td>
</tr>
<tr>
<td>2-Bromo-3-nitropropane-1,3-diol</td>
<td>Isodecyl alcohol</td>
</tr>
<tr>
<td>(Bromopal)</td>
<td>Methylparaben</td>
</tr>
<tr>
<td>Diazolidinyl urea (Gemal II)</td>
<td>Methyldibromoglutaronitrile (Kathon CG)</td>
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<td>DMDM hydantoin (Glydant)</td>
<td>Methyldibromo glutaronitrile / Phenoxyethanol (Euxyl K400)</td>
</tr>
<tr>
<td>Imidazolidinone (Gemal I)</td>
<td>Phenoxyethanol / Propylene glycol (Euxyl K400)</td>
</tr>
<tr>
<td>Quaternium-15</td>
<td>Triclophenol</td>
</tr>
<tr>
<td>Triclosan</td>
<td>Triclosan</td>
</tr>
</tbody>
</table>

Most common preservative allergens (NACDG data):
Formaldehyde > Quaternium-15 > Isopropylmyristyl carbamate > MIB/PE > MCI/MI
Methylisothiazolinone (MI)
Methylchloroisothiazolinone (MCI)
MCI/MI (Kathon CG)

• Current patch tests include MCI/MI (not MI alone)

• Because MI concentration in MCI/MI is low, it may miss allergy to MI alone

• These chemicals are a rising cause of allergy to moist wipes, tissue and toilet paper, and potentially hand sanitizers

WHEN STUMPED, THINK SIGNIFICANT OTHER

• Often unrecognized because offending allergen not used by the patient but by a significant other

• Location of eruption corresponds to contact with connubial allergen
• 50 year man with a rash on left nipple that spread to back, chest, fingers, legs, and genitalia

• Skin biopsy = spongiotic dermatitis

Patch Tests
NACDG-80 & Textile Series (Chemootechnique):

- Benzoyl peroxide
- Disperse orange dye
- Methylbromoglutaronitrile
- p-Phenylenediamine (PPD)
Relevant Allergen Sources

- **p-Phenylenediamine**
  Patient does not dye hair, but wife does
  Eruption corresponds to where she lays when they sleep

- **Disperse orange dye**
  In synthetic (not natural) fabrics
  Cross-reacts with PPD

- **Methyldibromoglutaronitrile**
  Preservative in skin care products

51 year old woman has itchy scaly rash around right eye x 1.5 years, treated with topical steroids and tacrolimus with almost no improvement

- Prior patch tests by an allergist were negative
- Does not use cosmetics or hair products because of sensitive skin since childhood
- Erythematous hypopigmented scaly plaques on right upper and lower eyelids

Patch Tests

NACDG-80 (Chemotechnique):
- Cocamidopropyl betaine
- Formaldehyde
- Fragrance mix

Negative to Cosmetic Series (Chemotechnique)

Negative to personal skin care products
<table>
<thead>
<tr>
<th>1st case</th>
<th>2nd case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash location</td>
<td>Chest where wife lays</td>
</tr>
<tr>
<td></td>
<td>One-sidedness (right periorbital)</td>
</tr>
<tr>
<td>Allergen</td>
<td>p-Phenylenediamine</td>
</tr>
<tr>
<td></td>
<td>Fragrance mix</td>
</tr>
<tr>
<td>Source</td>
<td>Wife regularly colors hair with PPD in dye</td>
</tr>
<tr>
<td></td>
<td>Husband regularly uses fragrance</td>
</tr>
<tr>
<td>Best test for relevance is resolution of rash</td>
<td>After patient avoided contact with wife during few days after dying hair</td>
</tr>
</tbody>
</table>

**WILL THE BACK REVEAL WHAT THE LIPS COULD NOT?**

3 Cases of Lip / Perioral Dermatitis

33-yr-old man

Lip swelling for 9 mos
POSITIVE PATCH TESTS
(Chemotechnique allergens)

NACDG 80
- Benzoyl peroxide
- Mercaptobenzothiazole
- Steroid series
  - Negative

RELEVANCE

Patient uses
benzoyl peroxide
wash daily
BENZOYL PEROXIDE

- Both irritant (higher concentrations) and allergen
- First reported as allergen when used for chronic leg ulcers / stasis dermatitis (76% sensitization rate)
- Prior occupational hazard for bakers when used as bleaching agent in flour (banned 50 yrs ago)

BENZOYL PEROXIDE

- Treatment of acne
- Polymerization of acrylates
  Dentures
  Orthopedic implants
  Plastics, Resins, Elastomers
- Manufacture of candles

55 yr-old-woman

Periorbital and perioral rash for 1 yr

Patch test done elsewhere:
  Disperse blue dye
POSITIVE PATCH TESTS
(Chemotechnique allergens)
NACDG 80
  Gold thiosulfate
  Neomycin
Cosmetic series
  Dodecyl gallate
Personal products
  Lipstick

With avoidance of lipstick and gold
and constant use of petrolatum for lips
the rash cleared on the right (but not left) side

Husband used Scope® mouthwash (containing
dodecyl gallate); stopping its use cleared the
perioral (but not periorbital rash)

Husband used gold guitar pick; stopping its use
cleared the periorbital rash
RELEVANCE

• Is patient exposed to patch-test + allergen?
• Does distribution of rash correspond to allergen exposure?
• Does allergen avoidance clear the rash?

68-yr-old man who works in an oil field
Burning perioral rash for 11 mos
worsened by sun exposure
unresponsive to topical steroids
improved by prednisone (4 courses)
cannot tolerate oral cyclosporine (GI upset)

TRUE Test: Negative

Denies: smoking; playing wind instruments;
eating mints

Meds: oral gabapentin, Norco, tamsulosin, zolpidem;
topical fentanyl patch
POSITIVE PATCH TESTS
(Chemotechnique allergens)

NACDG 80
Balsam of Peru (Myroxolon pereirae)

Personal products (including spouse’s)
Negative

BALSAM OF PERU (Myroxolon pereirae)

? FIXED DRUG ERUPTION
• Burning (rather than itching)
• Recurrent “fixed” perioral location
• Resistance to topical steroids
• (Have not performed skin biopsy)
• Patch test (-) to 4/6 Balsam of Peru components
• Drug elimination strategy
PATIENT’S MEDICATIONS

ORAL
Gabapentin
Norco (hydrocodone & acetaminophen)
Tamsulosin
Zolpidem

TOPICAL
Fentanyl patch