New Insights on Hidden Food Allergies

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Learning Objectives

Upon completion of this learning activity, participants should be able to:

• Investigate food allergy even though the subject was not aware of exposure to food by ingestion, touch, or smell.

• Use a thorough history-taking as an important guide in searching for the culprit food allergen.
Common Food Exposure

Gastrointestinal

Skin

Respiratory
Hidden Food Allergies

OUTLINE

A. Food allergen in another tolerated food
B. Non-food allergen in a tolerated food
C. Food allergen in medical products
D. Transfer of food allergen or of food-sIgE
Food Allergen in Another Food

External contaminant (intentional or accidental)
- Food industry
- Restaurants
- Homes
- Other

Intrinsic contaminant
- Maternal food in breastmilk
- Bovine milk protein in beef
- Fruit seeds in juice
ALLERGY INFORMATION: CONTAINS MILK AND SOY INGREDIENTS.
McDonald’s French Fries Contain Possible Allergens Wheat, Milk

By DAVID P. HAMILTON

McDonald’s Corp. said its french fries contain “wheat and milk ingredients” that might cause problems for diners sensitive to these substances.

McDonald’s previously had described its fries as free of substances that can cause allergic or other medical reactions in sensitive people. The Oak Brook, Ill., fast-food giant said the change in its ingredient disclosures followed its decision to conform to new federal food-labeling rules, and doesn’t reflect any change in the ingredients of its fries or the way they are prepared.

Some people with food-sensitivity conditions previously considered McDonald’s fries safe based on information supplied by the company. For instance, some individuals with celiac disease—an autoimmune condition triggered by gluten, a protein found in wheat, rye and barley—worried in an online forum that perhaps McDonald’s fries have always contained gluten, despite the company’s assertions to the contrary.

Cathy Kapica, McDonald’s director of global nutrition, said the company’s fries include a “natural flavoring” made, in part, from extracts of wheat and dairy products. Dr. Kapica said those extracts are processed in ways designed to remove wheat and dairy pro-
delicious dessert with absolutely no dairy products.

Smooth. Creamy. Yet, no cream or dairy products of any kind. With only half the calories of rich ice creams.

Also in Strawberry, Raspberry, Mandarin and Pineapple.

Dole® Fruit Sorbet. Look for it next to the other fine frozen desserts in your store.
Food-derived substances

**Dextran:** Partially hydrolyzed corn or potato starch.

**Dextrin:** Hydrolysate of starch (from corn, wheat, rice, or tapioca) by heat or hydrochloric acid.

**Dextrose:** Powdered corn starch.

**Maltodextrin:** Starch from corn, wheat, potato, or rice.

**Pregelatinized starch:** Starch from corn, wheat, potato, or tapioca.

**Sodium starch glycolate:** Starch from potato, corn, wheat, or rice.
Milk-allergic children may react to beef
(Werfel et al: JACI 1997; 99:293)

- 20% (5/25) of milk-allergic subjects have beef allergy.
- 72% (8/11) of beef-sensitive subjects are milk-sensitive.
- The offending proteins are usually heat-stable

Eggwhite in processed meat
(Leduc et al: Allergy 1999; 54:564)

Eggwhite allergens were detected in processed meats; raw & pasteurized.
Allergy to fruit seeds

Non-food Allergen in a Tolerated Food

- Additives & Spices
- Medication
- Natural rubber latex
- House dust mite
- Parasite
Ingredients: Enriched Wheat Flour (Wheat Flour, Niacin, Reduced Iron, Thiamine Mononitrate, Riboflavin and Folic Acid), Partially Hydrogenated Soybean Oil, Cheddar Cheese (Pasteurized Milk, Cheese Cultures, Salt, Enzymes), Salt, Sugar, Yeast Extract, Citric Acid, Sodium Bicarbonate, Whey, Corn Syrup, Paprika, Monosodium Glutamate, Turmeric, Lactic Acid, Spices, Onion Powder, Garlic Powder, Artificial Colors (FD&C Yellow #5 & #6).

Allergen Alert: Manufactured in a plant that processes peanuts, nuts, and sesame seeds.
INGREDIENTS: SUGAR, CORN SYRUP, MODIFIED FOOD STARCH, CONTAINS 2% OR LESS OF THE FOLLOWING: ORANGE JUICE CONCENTRATE, GRAPE JUICE CONCENTRATE, PEACH CONCENTRATE, BLUEBERRY PUREE, STRAWBERRY PUREE, RASPBERRY PUREE, BANANA PUREE, LEMON PUREE, COCOA POWDER, PEANUT FLOUR, PEANUTS, HYDROGENATED CANOLA AND COTTONSEED OILS, CHOCOLATE LIQUOR, COCOA BUTTER, PURE VANILLA, COCONUT, STRAWBERRY POWDER, CREAM, NONFAT MILK, SOY LECITHIN (AN EMULSIFIER), CONCENTRATED APPLE JUICE, CONCENTRATED PEAR JUICE, CONCENTRATED PINEAPPLE JUICE, CONCENTRATED PEACH JUICE, CONCENTRATED PASSIONFRUIT JUICE, APRICOT PUREE, PAPAYA PUREE, GUM ACACIA, GUM GHATTI, GLYCEROL ESTER OF WOOD ROSIN, SODIUM BENZOATE (PRESERVATIVE), CITRIC ACID, SODIUM CITRATE, MALIC ACID, NATURAL AND ARTIFICIAL FLAVORS, COFFEE, COLOR ADDED (RED #40 LAKE, YELLOW #6 LAKE, YELLOW #5 LAKE, BLUE #2 LAKE, YELLOW #5, RED #40, YELLOW #6, BLUE #1 LAKE, BLUE #1), TAPIOCA DEXTRIN, BEESWAX, CARNAUBA WAX, CONFECTIONER'S GLAZE, SALT.
Recurrent urt/angio, particularly after eating ice cream
Anisakis simplex

- A nematode infests sea mammals. Various species of seafood act as intermediate hosts for the larvae.
- High infestation in Japan & Spain.
- Larvae protein is heat-stable & may cause systemic allergy.
Food Allergens in Medical Products

- Oral medications
- Injectables
- Dermatologic topical
- Nasal drops
- Respiratory inhalers
- Suppositories
- Dental preparations
## Most common inactive ingredients (foods & non-food) incorporated in solid oral medications

*(Beker et al. Sci Transl Med 11:6753, 2019)*

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Classification</th>
<th>Percentage occurrence in medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose</td>
<td>Food</td>
<td>44.82%</td>
</tr>
<tr>
<td>Corn starch</td>
<td>Food</td>
<td>36.54%</td>
</tr>
<tr>
<td>PEG</td>
<td>Polymer</td>
<td>36.03%</td>
</tr>
<tr>
<td>Povidone</td>
<td>Polymer</td>
<td>35.80%</td>
</tr>
<tr>
<td>Carboxymethylcellulose</td>
<td>Other</td>
<td>21.38%</td>
</tr>
<tr>
<td>Gelatin</td>
<td>Food</td>
<td>16.93%</td>
</tr>
<tr>
<td>Brilliant blue</td>
<td>Dye</td>
<td>14.47%</td>
</tr>
<tr>
<td>Sunset yellow FCF</td>
<td>Dye</td>
<td>12.27%</td>
</tr>
<tr>
<td>Allura red</td>
<td>Dye</td>
<td>11.20%</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>Other</td>
<td>11.14%</td>
</tr>
<tr>
<td>Indigo carmine</td>
<td>Dye</td>
<td>10.63%</td>
</tr>
</tbody>
</table>
Allergic reactions in 7 infants to food proteins in topical agents

<table>
<thead>
<tr>
<th>Case</th>
<th>Diagnosis</th>
<th>Product</th>
<th>Reaction</th>
<th>Positive ST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two infants</td>
<td>AD</td>
<td>Wheat Starch for bath</td>
<td>Immediate rash</td>
<td>SPT to wheat</td>
</tr>
<tr>
<td>Infant</td>
<td>AD + CMA</td>
<td>Emollient Cream w oat</td>
<td>Exacerbated AD</td>
<td>APT emollient cream</td>
</tr>
<tr>
<td>Infant</td>
<td>AD + CMA</td>
<td>Gum Balm (Lactis proteinum)</td>
<td>Contact urticaria</td>
<td>SPT cow milk</td>
</tr>
<tr>
<td>Infant</td>
<td>AD + CMA</td>
<td>Saugella Soap w milk</td>
<td>Gen. contact urticaria</td>
<td>SPT soap &amp; cow milk</td>
</tr>
<tr>
<td>Infant</td>
<td>AD</td>
<td>Topical Decongestiant W peanut oil</td>
<td>Rash on AD</td>
<td>SPT peanut</td>
</tr>
<tr>
<td>Infant</td>
<td>AD + egg allergy</td>
<td>Shampoo w egg</td>
<td>Persistent facial AD</td>
<td>SPT egg</td>
</tr>
</tbody>
</table>

### Allergic reactions in 4 women to food proteins in topical agents

<table>
<thead>
<tr>
<th>Case</th>
<th>Diagnosis</th>
<th>Product</th>
<th>Reaction</th>
<th>Positive ST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woman</td>
<td>Exercise-induced Anx to wheat</td>
<td>Shower gel <em>(Triticum vulgare)</em></td>
<td>Generalized erythema</td>
<td>SPT to wheat</td>
</tr>
<tr>
<td>Woman</td>
<td>Allergy to wheat</td>
<td>Shampoo <em>(Wheat protein)</em></td>
<td>Contact eczema</td>
<td>SPT wheat &amp; shampoo</td>
</tr>
<tr>
<td>Woman</td>
<td>Allergy to wheat</td>
<td>Mascara <em>(Wheat protein)</em></td>
<td>Facial angioedema &amp; gen. urticaria</td>
<td>SPT to wheat &amp; mascara</td>
</tr>
<tr>
<td>Woman</td>
<td>Allergy to sesame</td>
<td>Foundation cream <em>(sesame oil)</em></td>
<td>Contact urticaria</td>
<td>SPT to foundation cream &amp; sesame</td>
</tr>
</tbody>
</table>

• 276 skincare products’ labels were reviewed for the presence of common foods.
• 39% of the products listed at least one food allergen.
• A total of 156 allergens were recorded:
  41.7% almonds, 22.4% wheat, 15.4% soy, 10.3% oat, 8.3% sesame, 1.3% milk, and 0.6% peanut.
Food allergens in skincare products for children in Lithuania

(Adomaite et al: Contact Dermatitis 83:271, 2020)
<table>
<thead>
<tr>
<th>Food</th>
<th>Implicated medication formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gelatin</td>
<td>Avid, Benadryl Liqui-Gels, Benadryl Allergy Nighttime, Claritin Liqui-Gels, Claritin Reditabs, Hydroxyzine pamoate cap (Sandoz, Teva), Sinequan cap, Vistaril cap</td>
</tr>
<tr>
<td>Lactose</td>
<td>Atarax tab, Claritin tab, Claritin-D tab, Claritin Reditabs, Phenergan tab, Zyrtec tab, Zyrtec-D tab, Xyzal tab</td>
</tr>
<tr>
<td>Starch (corn, potato, rice, or wheat)</td>
<td>Allegra tab, Atarax tab, Avid cap, Allegra-D tab, Benadryl, Clarinex tab, Clarinex Reditabs, Claritin tab, Claritin-D tab, Chlor-Trimeton tab, Sinequan cap, Sudafed PE Sinus &amp; Allergy, Vistaril tab</td>
</tr>
<tr>
<td>Cinnamon</td>
<td>Benadryl Liquid Elixir</td>
</tr>
<tr>
<td>Cocoa butter</td>
<td>Phenergan Rectal Suppository</td>
</tr>
</tbody>
</table>
Milk allergy through a particular injectable corticosteroid
(Eda et al: Allergol Intl 2009; 58:137)
(Savvatianos et al: Allergy 2011: 66:983)

- Some milk-allergic children reacted to Solu-Medrol 40 mg/ml
- SPT was positive to Solu-Medrol 40 mg/ml but negative to multiple injectable corticosteroid preparations, including Solu-Medrol 125 mg/ml which was well tolerated.
- Solu-Medrol 40 mg/ml contained lactose (& has β-lactoglobulin).
# Lactose-containing asthma medications

(Source: Manufacturer’s website)

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Active ingredients</th>
<th>Lactose content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advair Diskus</td>
<td>Fluticasone/salmeterol</td>
<td>12.5 mg/blister</td>
</tr>
<tr>
<td>Asmanex Twisthaler</td>
<td>Mometasone</td>
<td>Small amounts</td>
</tr>
<tr>
<td>Flovent Diskus</td>
<td>Fluticasone</td>
<td>12.5 mg/blister</td>
</tr>
<tr>
<td>Pulmicort Flexhaler</td>
<td>Budesonide</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Serevent Diskus</td>
<td>Salmeterol</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Foradil</td>
<td>Formoterol</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Solu-Medrol</td>
<td>Methylprednisolone/succinate 40 mg</td>
<td>25 mg/vial 1ml</td>
</tr>
<tr>
<td>injectable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accolate tablet</td>
<td>Zafirlukast</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Singulair tablet</td>
<td>Montelukast 10 mg</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Deltasone tablet</td>
<td>Prednisone</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Millipred tablet</td>
<td>Prednisolone</td>
<td>Not indicated</td>
</tr>
</tbody>
</table>
Anaphylaxis to egg lysozyme in nasal drops

Allergy to egg lysozyme in vaginal suppositories

Anaphylaxis to BSA during artificial insemination with the husband’s semen
(Wuthrich et al: Allergy 1995;50:179)

Patients allergic to egg or soybean may react to lecithin in propofol
(Murphy et al: Anesth Analg 2011; 113:140)
Food proteins in vaccines

(Kelso et al: JACI 130:25, 2012)

(Inst Vaccine Safety - http://www.vaccinesafety.edu/components.htm)

Certain vaccines contain food proteins:
egg, gelatin, milk
But the allergy risk is very low
Passive Transfer of Food Allergy

Transfer of food allergen
Transfer of food-sIgE antibody
Transfer of the genetic trait

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Route:

- Transmammary
- Transplacental
- Blood-products infusion
- Liver transplant
- BM/SC transplant
Transplacental food allergy

Evidence for prenatal sensitization:

• Allergic reactions have occurred in young infants to the very first postnatal exposure to the food.
• Food sIgE was detected in sera from umbilical cord or of newborns.
• Detection of food allergen in cord blood.
• Relationship with maternal intake during pregnancy (Hsu et al: Ann Allergy Asthma Immunol 2013, 111:391)
Odds ratio of food sensitization in infants according to the maternal food intake during pregnancy

(Hsu et al: Ann Allergy Asthma Immunol 2013, 111:391)
Allergens cross the placenta

(Loibichler et al. Clin Exp Allergy 2002; 32:1546)

Experimental transplacental transfer of allergens:

- All 3 allergens tested were detected in the fetal outflows of all full-term & pre-term placentas.
- βLG & OVA were detectable (1.3-5.3 ng/ml) at 1 min & peaked to 88-126 ng/ml at 2-2.5 hr.
- Bet v 1 was detected at much lower concentrations than BLG & OVA; 0.1 ng/ml at 1 min & peaked to 2.4 ng/ml at 2 hr.
Sexually transmitted allergy to Brazil nuts
(Bansal et al: J Investig Allergol Clin Immunol 2007; 17: 189)

• A woman with allergy to Brazil nuts since childhood.
• Shortly after intercourse, developed local & systemic reaction. Her partner ate Brazil nuts 3 hr earlier.
• SPT with her partner’s semen without consuming nuts was negative, but was positive to semen obtained 2.5 hr after eating 4 Brazil nuts.
Transfer of peanut through contaminated platelet transfusion

- A child had anaphylaxis at 1 yr to peanut which has been avoided.
- At 6 yr, had Anx while receiving leukoreduced pooled buffy-coat with ABO-identical platelets.
- Upon contacting the blood donors, 3 recalled eating large quantities of peanuts the evening before donation.
Transfer of food-sIgE through transfusion
(Ching et al: Allergy Asthma Clin Immunol 2015)

• A non-atopic boy received platelet transfusion. subsequently had anaphylaxis following eating salmon and 1 wk later after eating peanut
• Had positive sIgE to both foods but became negative 6 mo later and he tolerated both foods.
• The platelets was suspended in plasma of a donor with severe allergy to peanut & fish.
• The donor was excluded from future blood donation!
Transfer of atopy & food Allergy by bone marrow transplant

- Yong et al; BMT 2006, 37:983
Transfer of peanut allergy by liver transplant

(Legendre et al: NEJM 1997; 337:822)

**RECIPIENTS**

<table>
<thead>
<tr>
<th></th>
<th>He</th>
<th>She</th>
</tr>
</thead>
<tbody>
<tr>
<td>PN allergy</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>PN-sIgE</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>In vitro basophil degranulation</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Peripheral chimerism</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Organ donor with severe peanut allergy

Liver and right kidney

Peanut allergy
Possible transfer of sIgE through lung transplant
(Stojanovic et al: Ann Allergy Asthma Immunol 129:517, 2022)

• A man without allergy history received lung transplant from a peanut-allergic donor.
• 16 d later, had severe anaphylaxis 5 min after eating peanut.
• 1 mo post-LTx, Peanut-sIgE & SPT were positive and became negative 4 mo later.
• Peanut challenge 18 mo post-LTX was negative

Mechanism:
Probable transfer of PN-sIgE (or B-cells or Th2 cells).
Summary & Conclusion

- FA may occur though the patient did not eat, touch, or smell the offending food.
- Allergy after eating may not be caused by the principal food.
- The reaction may be caused by an offending food hidden in another tolerated food or medication.
- Blood products may transfer a donor’s food allergen to an allergic person or of food-sIgE to a non-allergic person.
- BMT or SCT may genetically transfer FA.

A skillful history-taking is the cornerstone of suspecting FA & evaluating such cases.
If it doesn’t look like a duck, swim like a duck, or quack like a duck, it may be a duck!