Cow & Breast Milk Allergy

Hussein Shamaly
24.02.2016
Foods Most Frequently Causing Allergy in Babies and Children

1. Egg
2. Cow’s milk
3. Peanut
4. Nuts
5. Shellfish
6. Fin fish
7. Wheat
8. Soy
9. Beef
10. Chicken
11. Citrus fruits
12. Tomato
Tree Nut Allergy

• Most common:
  – Walnuts – 34%
  – Cashews – 20%
  – Almonds – 15%
  – Pecans – 9%
  – Pistachio – 7%
## Major food allergens

<table>
<thead>
<tr>
<th>Food</th>
<th>Protein</th>
<th>Allergen Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow's milk</td>
<td>Casein</td>
<td>Bos d8</td>
</tr>
<tr>
<td></td>
<td>β-Lactoglobulin</td>
<td>Bos d5</td>
</tr>
<tr>
<td>Egg</td>
<td>Ovomucoid</td>
<td>Gal d1</td>
</tr>
<tr>
<td>Peanut</td>
<td>Vicilin</td>
<td>Ara h1</td>
</tr>
<tr>
<td></td>
<td>Conglutin</td>
<td>Ara h2</td>
</tr>
<tr>
<td>Fish</td>
<td>Paralbumin</td>
<td>Gad c1</td>
</tr>
</tbody>
</table>

**Table 142.1. Major Food Allergens**
Age Relationship Between Food Allergy and Atopy

{Adapted from Holgate et al 2001}
1-3 years old

- 6% Food Allergy
- 2.5% Milk Allergy
- 1.5% Egg Allergy
- 1% Peanut Allergy
Immunopathogenesis of allergy

**Epithelium**

**Sensitisation**

**APC (DC)**

- Allergen presentation DC-T cell interaction
- T cell activation
- Allergic cytokines
- B cell activation
- IgE production

**Th2**

**Cytokine production**

- IL-4, IL-5, IL-13

**B cell**

**APC = antigen presenting cell; DC = dendritic cell; IgE = immunoglobulin E; IL = interleukin.**
IgE mediated vs. non IgE mediated allergies

**IgE**
- Quick onset.
- Anaphylaxis, etc.
- Well defined mechanism.
- Easy to diagnose.
- Validated tests.

**Non-IgE**
- Delayed onset.
- Eczema, reflux, etc.
- Mechanism unclear.
- Harder to diagnose.
- No validated tests.
Symptoms Suggesting Allergy in the Infant

GIT

– Persistent colic
– Diarrhea and/or constipation
– Bloody diarrhea
– Frequent “spitting up”
– Vomiting
– Feeding problems
– Weight gain
Symptoms Suggesting Allergy in the Infant

Skin

– Urticaria
– Dry, itchy skin
– Persistent diaper rash
– Redness around anus
– Redness on cheeks
– Scratching and rubbing
– Rash
– Atopic dermatitis/Eczema
Symptoms Suggesting Allergy in the Infant

Respiratory Tract

- Rhinitis
- Persistent cough
- Nose rubbing
- Noisy breathing
- Wheezing
- Sneezing
- Itchy, runny, reddened eyes
- Atopic conjunctivitis
- Serous otitis media
Allergies are multi-system disorders

- Upper airway
- GI-tract
- Lower airway
- Skin
Current treatment options for food allergy include:

- Adequate pharmacotherapy in case of accidental exposure to the antigen.
- Strict allergen avoidance (exclusion diet).

Food allergy treatment II

Specific Oral Tolerance Induction: SOTI.
There are at least two kinds of approaches:

CONVENTIONAL
Starting with very low doses of protein, and increasing every 24 hours with less than doubling the dose administered during a period of 2-3 months.

RUSH
Also starts with a very low proteins dose, but it increases approximately every 2 hours, doubling the dose at each step in a period of 1 week.

Niggemann B. Allergy 2006
Milk Allergy

2.5% of newborn infants experience hypersensitivity reactions <1 year of age

60% are IgE-mediated; 50% then develop other food allergies

The incidence of cow's milk allergies is up to **seven** times greater in babies who are fed artificial milk formula VS human milk formula (Lawrence 1994).
Cow’s Milk Antigens

More than 25 proteins in cow’s milk can induce antibody production in humans

β-lactoglobulin (in whey), casein, and bovine

Serum albumin are the most important antigens

Casein antigens include: \( \alpha_s^1; \alpha_s^2; \beta; \kappa \)
Classification Scheme for CMA

Group 1

Immediate Reaction:
Reaction within 45 minutes after milk ingestion

Symptoms include: urticaria, angioedema, exacerbation of eczema, cough, wheeze, vomiting, anaphylaxis

Skin test positive (STP) to CMA

Elevated IgE to CMA by RAST or ELISA
Classification Scheme for CMA

Group 2: Intermediate Reaction:

- Reaction 45 minutes to 20 hours after milk ingestion
- Symptoms include vomiting, diarrhea
- Skin test negative to cow’s milk allergens
- Insignificant elevation of IgE to cow’s milk in RAST or ELISA
Group 3: Late Reactions:

- Reaction more than 20 hours after milk ingestion - weeks post ingestion
- Symptoms include diarrhea, colic, with or without wheezing, with or without exacerbation of eczema
- IgE & RAST usually normal
Atopic Dermatitis & CMPA

In some young infants there is a strong association between atopic dermatitis and CMPA.

The younger infant has more severe the atopic dermatitis,
GER and Milk Allergy

These are also symptoms of cow’s milk allergy (CMA)

Studies indicate that 40% of infants with signs of GER also have CMA

15–21% of children with suggested or proven GERD or CMPA suffer from both conditions
Diagnosis of allergy

- Clinical history of reaction
- Specific and total IgE (quantitative)
- RAST test
- Skin prick testing (SPT)
- Skin Patch Test
- Allergen challenge and/or elimination
Specific IgE

• It indicates sensitization, not necessarily allergy.

• High values are good predictors of allergy, but only for some foods (e.g. eggs, peanuts, fish) but not for others (e.g. wheat, soy).

• Does not predict severity of allergy.

• Low levels or absence do not exclude allergy.
Skin prick testing

- **Size of wheal predicts likelihood of reaction**
  
  \[ \geq 8 \text{ mm milk, egg, peanut} = 100 \% \text{ PPV} \]
  
  \[ \geq 6 \text{ mm in 0-2 years} \]

- **Size does not predict severity of reactions**

- **Negative SPT usually rules out allergy**
Patch Test

Irritated test

Positive test
Management of Milk allergy

Education of patient\ parents

- Elimination of all milk and all foods Containing cow’s milk proteins

- Breast milk of mothers following a diet devoid of cow’s milk protein is the ideal food
Extensively hydrolyzed formulas

- Extensively hydrolysed or amino - acid based formula.
  - Nutramigen, Alimentum, Pregestamil, Pepti-Junior) are usually well tolerated
  - However, some infants may have serious reactions to these formulas
  - No hydrolyzed formula should be considered completely safe for all children with IgE-mediated CMA

- In cases of allergy to these formulas, amino – acids based formulas should be used
Milk Antigens from Other Species

**Goat Milk:**
- Many goat’s milk proteins cross-react with cow’s milk proteins
- The majority of children allergic to cow’s milk are allergic to goat’s milk
- Goat’s milk is deficient in folate

**Mare’s Milk:**
- Fewer proteins are similar to cow’s milk proteins
- In research studies, most milk allergic children tolerated mare’s milk
Probiotics and their applications in human health

Application of probiotics in:
- Diarrhoea (antibiotic-associated, rotavirus-associated, *Clostridium difficile*-associated).
- Lactose intolerance.
- Vaginal infection.
- Prevention of atopic disease.
- Bowel transit.
- *Helicobacter pylori* infection.
- Irritable bowel syndrome (IBS).
- Inflammatory bowel disease (IBD).
- Necrotizing enterocolitis (NEC).
- Prevention of allergic diseases.
- Cow milk protein allergy.
- Prevention of systemic infections.
- Colon cancer.
Mechanisms of probiotic action on allergy

Milk antigens

ATC

Th0

IL-10

TGFβ

PROBIOTICS
Degrading antiagents

PROBIOTICS

Modulation Th1-Th2 response towards antigen tolerance

IFN-γ

Activated macrophages

Increase the production of secretory immunoglobulins

Antibody

Anti-inflammatory cytokines

Histamine

Mast cell/basophil degranulation

Non IgE–mediated Allergy

Oral tolerance

IgE–mediated Allergy

Prognosis

25% of infants lost all food allergy symptoms after 1 year of age

• Most infants will outgrow milk allergy by 3 years of age, but may become intolerant to other foods:
  • Peanut
  • Shillfish
  • Soy
  • Nuts
Human Milk

- Human milk is predominantly whey (80%) and Casein (20%)

- Total casein content varies during lactation: (20% in early lactation, 45% in late lactation)

- Human milk lacks $\alpha_{s1}$ and $\alpha_{s2}$ and $\beta$-lactoglobulin

- These tend to be most frequent allergens in cow’s milk
Human Milk Advantage

Decreases the incidence of:
- Diarrhea,
- Lower respiratory infection,
- Otitis media,
- Bacteremia,
- Bacterial meningitis, botulism,
- Urinary tract infection,
- Necrotizing enterocolitis.
- Sudden infant death syndrome,
- Insulin-dependent diabetes mellitus,
- Crohn's disease
- Ulcerative colitis,
- Lymphoma,
- Allergic diseases,
- Other chronic digestive diseases.
- Possible enhancement of cognitive development,
Situations in which breast feeding is not advised

• Medications:
  – Antimetabolites
  – Chemotherapy agents
  – Amphetamines
  – Ergotamine
  – Statins
  – Psychotropic agents
  – G6PD def.: mother must be alert for drugs causing hemolysis
  – Radioactive isotopes

HIV
Untreated TB
Galactosemia
PKU
Breast-feeding and Allergy

Breast-feeding is protective against allergy

– Improvement of allergic signs if:

• Baby is exclusively breast-fed

• Mother eliminates highly allergenic foods from her diet
Breast-Milk Allergy

Small amounts of cow's milk protein may appear in a mother's milk and provoke a response in her baby, even if the mother herself is not allergic to cow's milk.

Early and occasional exposure to cow's milk proteins can sensitize a baby so that even tiny amounts of cow's milk may trigger a response.
Breast-feeding and the onset of atopic dermatitis in childhood: A systematic review and meta-analysis of prospective studies

Michael Gdalevich, MD, MPH, MD, Daniel Mimouni, MD, Michael David, MD, and Marc Mimouni, MD Tel Aviv, Israel

• Conclusion:

• Exclusive breast-feeding during the first 3 months of life is associated with lower incidence rates of atopic dermatitis during childhood in children with a family history of atopy.
Conclusions: In breast-fed infants with atopy, gut barrier function is improved after cessation of breast-feeding and starting of hypoallergenic formula feeding.
Conclusions: In breast-fed infants with atopy, gut barrier function is improved after cessation of breast-feeding and starting of hypoallergenic formula feeding.
Breast-Milk Allergy

- Incidence 0.5 -1% of breast milk fed infants
- Usually at 2-6 W of age
- Some time at 1\textsuperscript{st} day of life
Pathogenesis

Cell mediated hypersensitivity

At about 6 weeks of age, Peyer's Patches begin to produce immunoglobulins or antibodies

At six months of age, a baby has a functional immature, immune system that is capable of producing secretory immunoglobulin A (sIgA), the antibody that is the first line of defense against foreign substances

Colostrum is especially rich in antibodies, including sIgA.

Mature milk continues to provide this protection and help the baby to remain healthy and allergy-free.
Immunological Factors in Human Milk that may be Associated with Allergy:

• Atopic mothers tend to have a higher level of the cytokines and chemokines associated with allergy in their breast milk

• Those identified include:
  - IL-4
  - IL-5
  - IL-8
  - IL-13

• Atopic infants do not seem to be protected from allergy by the breast milk of atopic mothers
Names

• Allergic colitis
• Allergic proctocolitis
• Benign dietary protein proctitis
• Eosinophilic proctitis
• Breastmilk – induced proctocolitis
Manifestations

- eczema
- GI symptoms: vomiting, diarrhea, restlessness
- Bloody stools
- Abdominal distention
- FTT
- “Well appearing”
Colono & Histology

• Colitis
• Bleeding
• Mucosal edema
• Focal epithelial erosion
• Eosinophilic infiltration > 20/HPF
Recommendations (1)

- **No family history of allergy:**
  - Normal nutrition practices for mother from preconception onward
  - Normal nutrition practices for early infant feeding
  - Breast-feeding is the best possible source of nutrition and protection
  - Allergen avoidance is unnecessary unless the infant demonstrates signs of allergy
Recommendations (2)

**Mother is atopic:**

- Mother eliminates all sources of her own allergens prior to and during pregnancy to reduce IgE and IgG4 in the uterine environment

- Continues to avoid her own allergens during lactation

- Exclusive breast-feeding without exposure of infant to external sources of food allergens for 6 months
Recommendations(3)

Father and or siblings atopic; mother is non-atopic:

– No recommendations for mother to restrict her diet during pregnancy

– No recommendations for mother to restrict her diet during lactation unless the baby shows signs of allergy

– Exclusive breast-feeding for 4-6 months
AAP: Breast milk and allergy

Breastfeeding infants who develop symptoms of food allergy may benefit from:

- Maternal restriction of cow's milk, egg, fish, peanuts and tree nut
- If this is unsuccessful, use of a hypoallergenic or free amino acid-based formula as an alternative to breast feeding.
נסיון אישיות

• אחמד בן חודש ימים, ללא חור הרינוון מלא, לידה
במשקל 3935 גרם, יונק בלבד

• קיבול פורמולה וvoieיה פוריה לכל הנקודות והursdayים

• כ傒יל

• הפורמולה הופכת, הדימום המשיך
בירור

• ספירה, כימיה, ת. קרייה התקין
• מיפוי לשילי MECKLE
• השלשול המשיך יחד עם הדימום
• הקולוסקופיה: 
  • רקוטום 15 ס"מ ראשונים התקין
  • בהמישר ועד לצלקות:
    • אפטות מרובות, אזוריות אל תוך דimore פעיל
    • אפטות מורבות, אזוריות אל דימו פעיל

השלשול המשיך יחד עם הדימום
Colonic mucosa with areas of marked increase of eosinophils in lamina propria, focal lymphoid aggregates.

No viral inclusion bodies.
• התנקה הפסקה
• העבר ל NEOCATE
• התלונה חלפה
• בצא נשר אנמפטומט
H.E.

• בן 24 ימים, נולד במשקל 2760 גרם, יונק בלבד 2760 גרם, יונק בלבד
• יצאות הודעות עם דם טרי, עד 10 פעמים ביום
• ללא הקאות, שלשולים ואו חום
• שקל 3850 גרם
• בדיקה במופס
• ספירה, כימיה, CRP, תרביית תאים טכני
• שחרר על אדoley
לאחר ה受理

• דימויים ממשיכים
• האימה קיבלה הדרכה להלניציה של מספר
• מאכילים
• בהמisch התלונה هلפה
H.D.

בת 5.0 חודשים
ינקה המולידה, התפתחה מיה

מגיל 4 חודשים הופיעה שיריה, דם בצואהＯystate
היא המשיכה עם דימום רקטלי פעמים כפואים ב시험 לשאות
הפסיקהモ軟り חלב, סויה ובייצים
איים הקאוז,ULSE, יפה במשקל
בדיקה: משקל 6.350 קג, בדיקה במשקל
ב=time.pause 베סר veששת – לא נראתה פיזורה
ה울ל_notes בהטריק הדנקה יאמגר תוספת חלב לתנה טומינו
ספירה, כיומת, תפקוד קריאה, צואה להוספת תקינה
ה呒ים וה"ל לא שינת את תדרות וכרויות הדימום, ולך הוזמנה לקולונוסקופיה
קולונוסקופיה

מאזור הרקטום ועד לצקומ רירית נודוליםית רבה עם התכיבות בחלקם, ללא דימום פעיל, נלקחו ביופסיות כולל ל-PCR ל-CMV ול-PCR ל-CMV בביופסיןית קולסית
Fragments of colonic mucosa one of which shows a crypt infiltrated by polymorphonuclear neutrophils, consistent with mild focal active colitis. Other colonic fragments are normal. No evidence of IBD, no parasites and no tissue eosinophilia seen. No dysplasia found. The Immunostain for CMV was negative.
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**Data and Analysis**

- **CV (Complementary) PCR**
- **Body Fluids**

**Notes**

- Data includes results of CV and PCR tests on various samples.
- Analysis of body fluids indicates positive results for CV and PCR.

**References**

- [File Path: eslabaspor/Asotolos/CommonFases/509891.html]
לאחר הקולונוסקופיה

הפסקה הנקה וכל אוכל אחר, חווה בנוקייט

הדימום המשיך בתדירות יורדת עוד שבוע ופסק

ה.dimום המשיך בתדירות ירדה עוד שבוע ופסק

6 חודשיים מאזوها והוא אסימפטומטי

• מוכנסת אוכל bíti מוגן או לולא החלב ומוצרי פרט

• לנאוקייט
Take Home Message

1. Milk allergy can be IgE mediated or non-IgE mediated.
2. Children usually develop tolerance to milk by late childhood.
3. Hypoallergenic or amino-acid based formulas are recommended in case of cow-milk allergy.
4. In breast-milk allergy, the first choice is avoidance of allergenic food from mother’s meals.
5. If no success, hypoallergenic or amino-acid based formulas are recommended with stopping breast milk.
Thank you