Protein and Allergy

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Objectives

• Describe manifestations of cow milk protein allergy
• Go over the relevant cow milk protein allergens
• Discuss on what hydrolyzed formula can be used to prevent allergy and why it is important to use a proven formula
• Discuss whether using a hydrolyzed formula is cost effective

Manifestations of Food Allergy to Cow Milk Proteins

IgE mediated Food Allergy

Food allergy
• Anaphylactic shock
• Hives/Urticaria
• Chest pains
• Chest tightness
• Shortness of breath
• Swelling of eyes, mouth, lips
• Wheezing

Atopic Dermatitis can be triggered by food allergy

Non IgE mediated Food Allergy

Food protein enterocolitis syndrome (FPIES)
Food protein-induced proctocolitis
How does cow milk allergy occur?

Immune Mechanisms

IgE-Mediated

- Protein digestion
- Antigen processing
- Some Ag enters blood

Non-IgE Mediated

- TNF-α
- IL-5

IgE production

Mast cell

Histamine

APC

B cell

T cell

Cow’s milk antigens

Cow’s milk antigens

β-lactoglobulin (~35%)
α-lactalbumin (~12%)
glycomacropeptide (~12%)
immunglobulins (~8%)
serum albumin (~5%)
lactoferrin (~1%)
lactoperoxidase (~0.5%)
micro proteins (~10%)

- β-lactoglobulin (in whey), casein, and bovine serum albumin are the most important antigens

Difference between Breast Milk and Cow Milk in protein

- **Cow milk**
  - Whey 20%
  - Casein 80%

- **Breast milk**
  - Whey 80%
  - Casein 20%

  total casein content varies during lactation
  (20% in early lactation, 45% in late lactation)
  - Human milk lacks αs1 and αs2 caseins and β-lactoglobulin

Are there any feeding interventions to prevent allergy in infants?

Role of breastfeeding

Breast IS BEST
Hydrolysate Formulas in Allergy Risk Reduction

- If exclusive breastfeeding is not possible in high-risk infants, a hydrolyzed formula is recommended.
- Both extensively hydrolysed and partially hydrolysed formulas have been shown to have reduce the incidence of allergy in high-risk infants compared to normal cow’s milk formula.

Smaller protein size has lower allergenicity

pHF has lower incidence of Atopic Dermatitis

The effect of hydrolyzed cow’s milk formula for allergy prevention in the first year of life: The German Infant Nutritional Intervention Study, a randomized double-blind trial

Andrea von Berg, MD, Silvia Koletzko, MD, Amin Gröbel, MD, Birgit Filipczek-Pittrich, MD, H-Enitz Wittekind, MD, PhD, Carsten Peter Bauer, MD, Dietrich Reinhart, MD, and Dietrich Brandt, MD for the German Infant Nutritional Intervention Study Group. West, Munich, and Norderney, Germany

- Independent, government-sponsored study
- Double blind randomized study
- 2,252 high-risk infants randomized at birth to:
  - Intact cow milk formula
  - Partially hydrolyzed whey formula
  - Extensively hydrolyzed casein formula
  - Extensively hydrolyzed whey formula

J Allergy Clin Immunol 2003;111:533-40

10th year result (JACI 2013)

Preventive results in allergic manifestations primarily driven by atopic dermatitis
No significance in prevention of asthma or allergic rhinitis
Risk reduction only occurred till 6 years old
No evidence ongoing preventive activity from 7 till 10 years old
GINI – 15\textsuperscript{th} year (Allergic Rhinitis)

![GINI Study](Image)

GINI Study Considerations

- One of the largest longest non industry sponsored prospective study
- Hydrolyzed formulas showed:
  - Reduction in incidence of Atopic Dermatitis
  - Reduction in Allergic Rhinitis from year 11-15
- Lack of efficacy of extensively hydrolyzed whey formula
  - Method and degree of hydrolysis matters. Why?

3D structure of whey protein

![3D structure](Image)

Cartoon depiction of epitopes

![Cartoon](Image)

Heat denaturing of Epitope

![Heat denaturing](Image)

Enzyme hydrolysis of linear epitope

![Enzyme hydrolysis](Image)
Production of HA Infant Formula: Patented Process

Analysis of hydrolyzed formula in GINI

Malaysian Allergy Prevention (MAP) Guidelines for Healthcare Professionals

Use of hypoallergenic formula in the prevention of atopic disease among Asian children

Does the studies in Western Countries translate to Asian Children?
Although there was less incidence of eczema at 30 months, it was statistically NS

Conclusions: Exclusive feeding of hypoallergenic milk formula in the first 4 months of life has a protective effect in terms of the development of atopic dermatitis in the first 2 years of life, compared to feeding with cow’s milk formula.

Is it cost effective to use proven partially hydrolyzed 100% whey formula?

Economic analyses in 5 European countries (Denmark, France, Germany, Spain and Switzerland) of the costs and cost effectiveness of a specific brand of 100% whey-based partially hydrolyzed infant formula compared to a cow’s milk standard formula and extensively hydrolyzed formulas in the prevention of atopic dermatitis in at risk children.
How about in Asia? (Less developed countries)

Table 5: Cost and ICERs for PHF-W versus SF in base-case analyses

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Negative values indicate savings.

Economic value of atopic dermatitis prevention via infant formula use in high-risk Malaysian infants

Methods: A cohort Markov model simulated the AD incidence and burden from birth to age 6 years in the target population fed with PHF-W vs. CMF. The model integrated published clinical and epidemiologic data, local cost data, and expert opinion.

Modeled outcomes included AD-risk reduction, time spent post AD diagnosis, days without AD flare, quality-adjusted life years (QALYs), and costs (direct and indirect). Outcomes were discounted at 3% per year. Costs are expressed in Malaysian Ringgit (MYR; MYR 1,000 = United States dollar [US$316.50]).

Proven milk formula for allergy

PREVENTION

- Partially hydrolyzed 100% whey
  - Taste better
  - Cheaper
- Economic savings
- Extensively hydrolyzed casein
  - Taste issue
  - More expensive
- Only formula that can be used for cow milk allergy