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**Iranian Society of Pediatric
Gastroenterology & Hepatology**





ALLERGY PREVENTION

The Right Choice To Manage CMPA
In The First 1000 Days Of Life



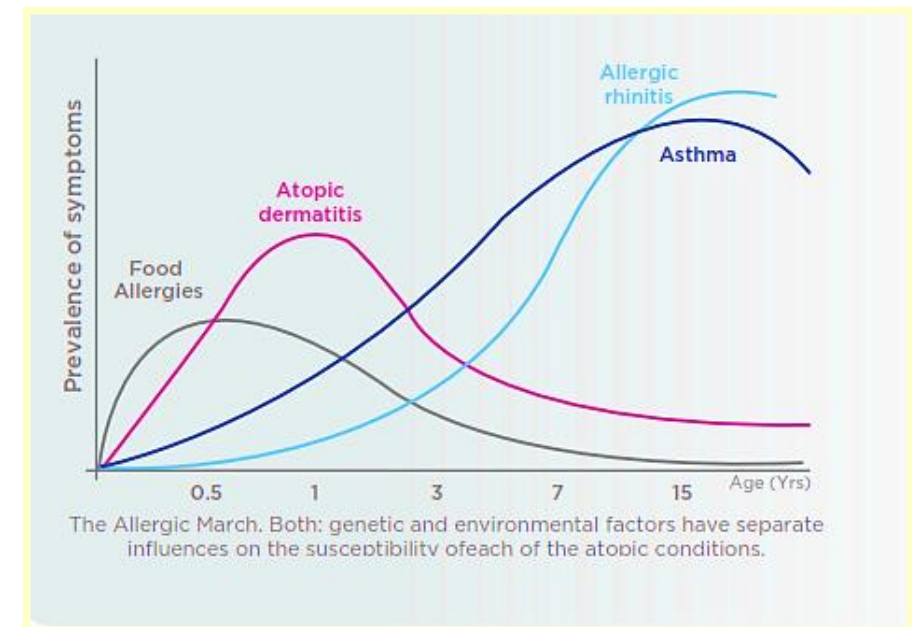
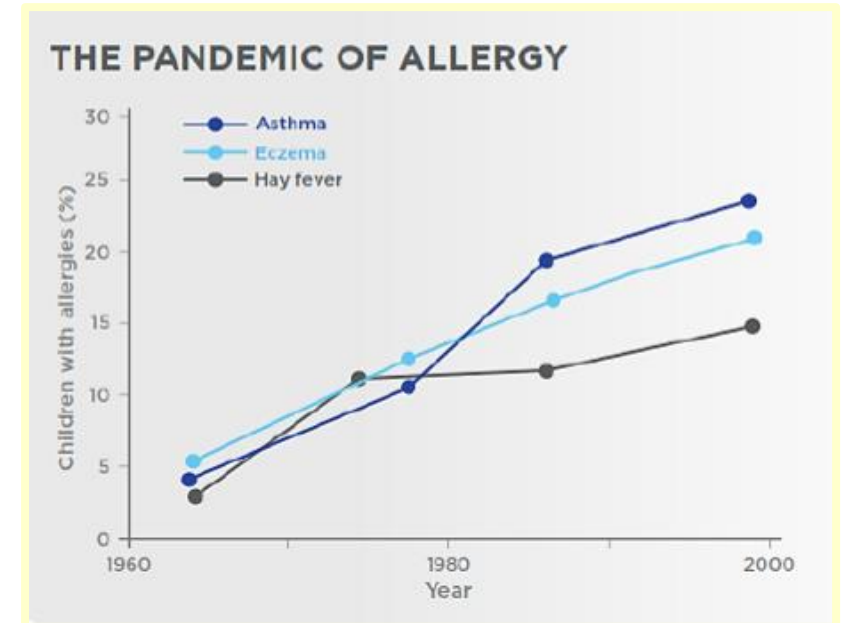
ALLERGIES ARE A GLOBAL HEALTH PROBLEM

- **The Rise In Prevalence Of Allergic Diseases Has Continued Over Decades**

Over the last decades allergies have developed to one of the biggest health problems, 1st in the industrialized, developed countries, and can now be considered as a global health problem.

- **The Allergic March - Time To Act To Change The Course**

“Allergic march”: a sequential appearance of 1st sensitization to food allergens with clinical manifestation at skin and gut, followed by additional and/or switch to sensitization to aero-allergens accompanied with manifestation at the upper and lower respiratory tract





FOOD ALLERGY: A WIDE SPECTRUM OF SYMPTOMS

- Multi organ symptoms are more common than isolated symptoms
- **CMPA** can appear at any age. In infants it happens in the second or third month of life, both in breastfed and formula-fed infants.



SKIN

Atopic eczema
Neurodermatitis
Quincke's oedema
Pruritus
Urticaria



GASTROINTESTINAL TRACT

Nausea
Vomiting
Motility disturbance
Diarrhea
Abdominal pain
Colic
Constipation
Weight loss
Dystrophy



RESPIRATORY SYSTEM

Bronchial obstruction/Asthma
Laryngeal oedema
Rhino conjunctivitis
Stridor



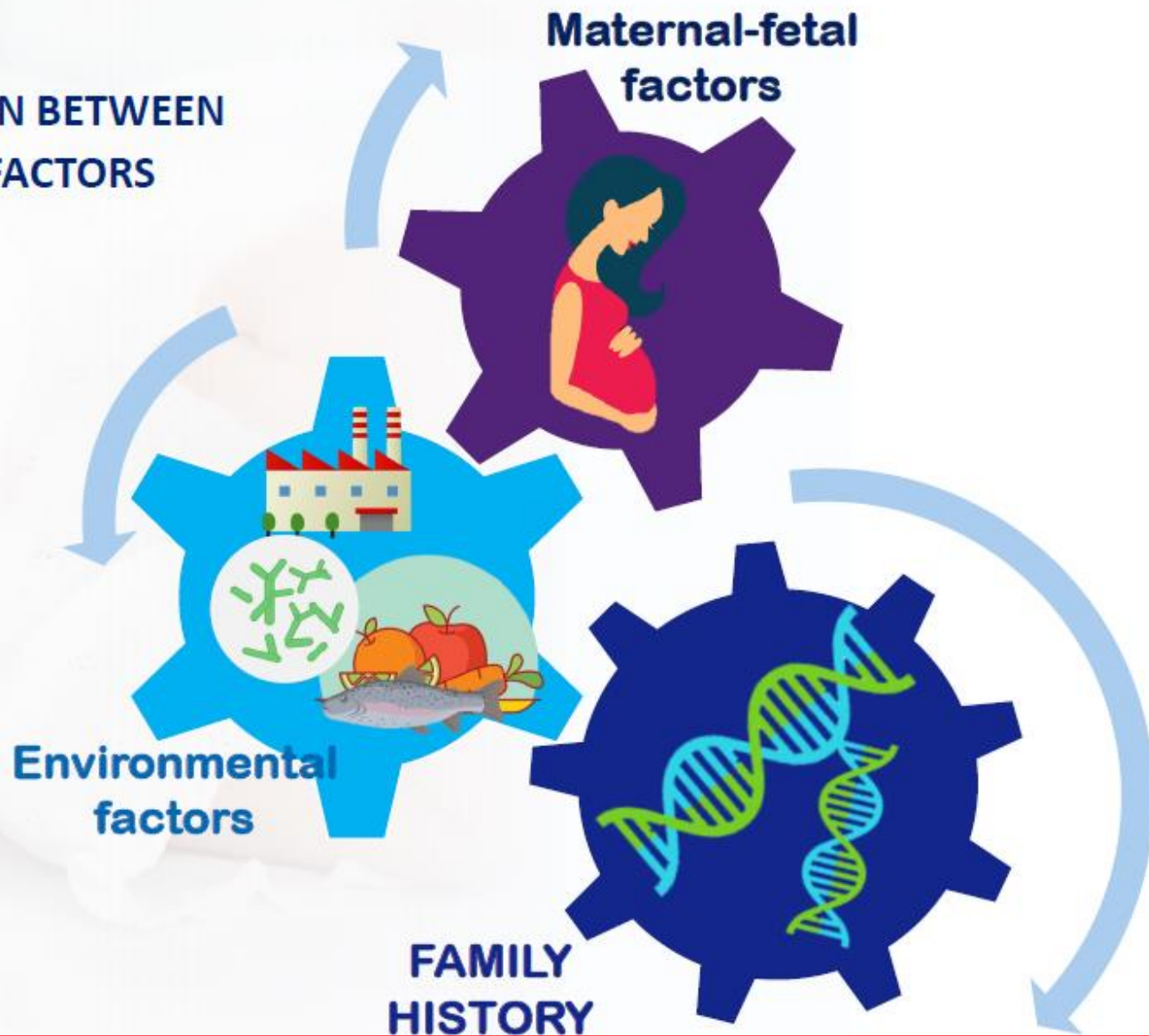
OTHERS

Inconsolable crying
Fatigue
Exhaustion
Agitation
anxiety



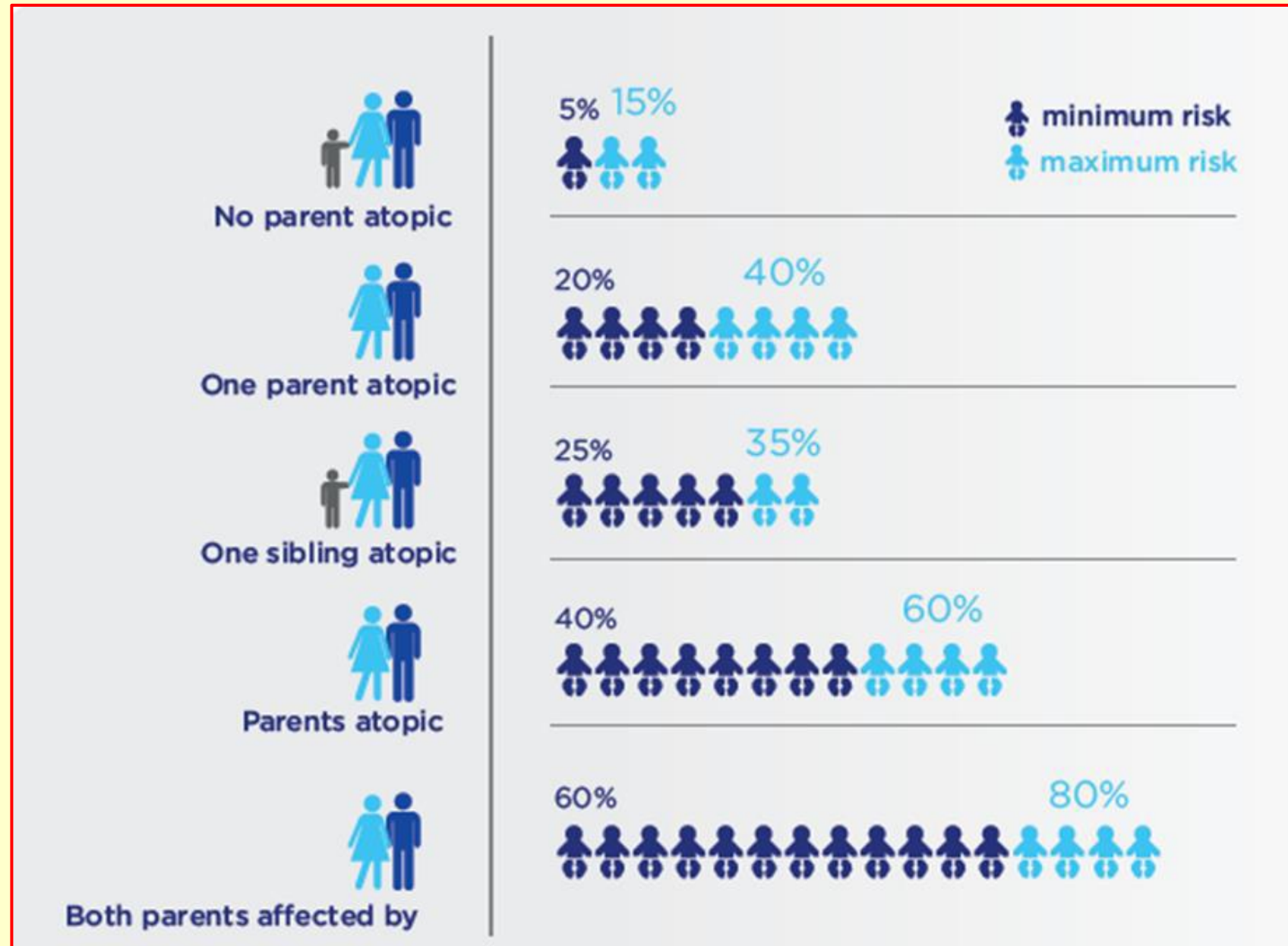
THE DEVELOPMENT OF ALLERGY

AN INTERACTION BETWEEN
DIFFERENT FACTORS



ALLERGIES RUN IN FAMILIES

The allergy risk increases with the number of immediate family members affected by an allergic disease.

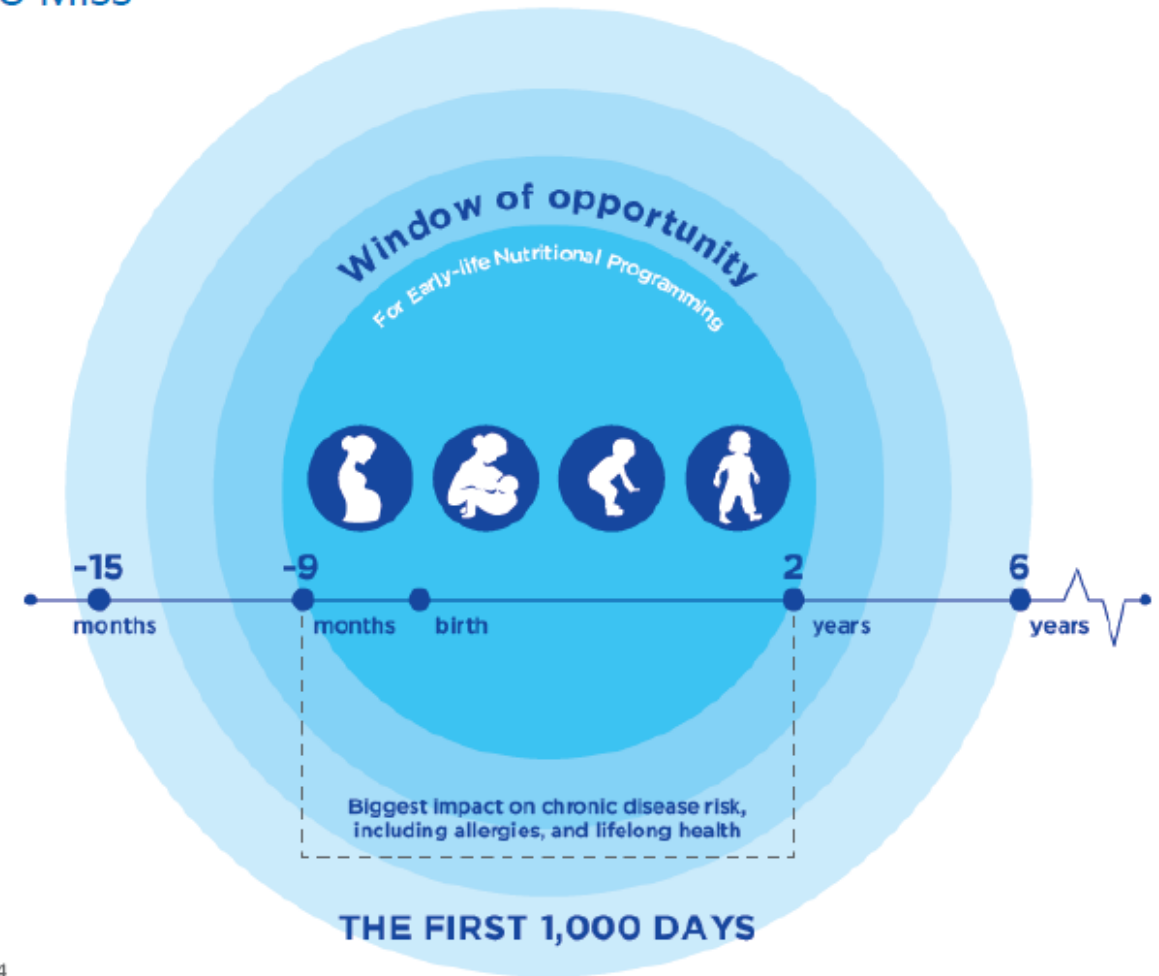




THE FIRST 1,000 DAYS

A WINDOW OF OPPORTUNITY TOO IMPORTANT TO MISS

- ✓ Genetic and environmental factors during early life, play a key role in the maturation of the immune system and disease susceptibility, including the development of allergic diseases.



1. Vanhees 2014
2. Koletzko 2005



DIETARY ALLERGEN EXPOSURE IN THE FIRST STAGES OF LIFE

NUTRITION IS SUCH A CRUCIAL ENVIRONMENTAL FACTOR



- Exposure to dietary proteins starts already during the first stages of life, starting with the diet during pregnancy, lactation and continues through the infants diet.^{1,2}
- The immune system needs to be trained to learn that these proteins are harmless (tolerance induction).



HUMAN MILK HAS PROVEN EFFICACY IN PRIMARY ALLERGY PREVENTION:

- **Allergen Exposure:** Exposure to low doses of cow's milk allergen via the maternal diet, enough to be recognized, thereby promoting oral tolerance. Avoidance to higher doses allergens, thereby limiting allergic sensitization.
- **Factors In Human Milk:** it contains immune modulatory factors that influence the environment in which the protein is presented to the immune system, thereby promoting the induction of tolerogenic immune responses (e.g. immunoglobulins, oligosaccharides, TGF-F).





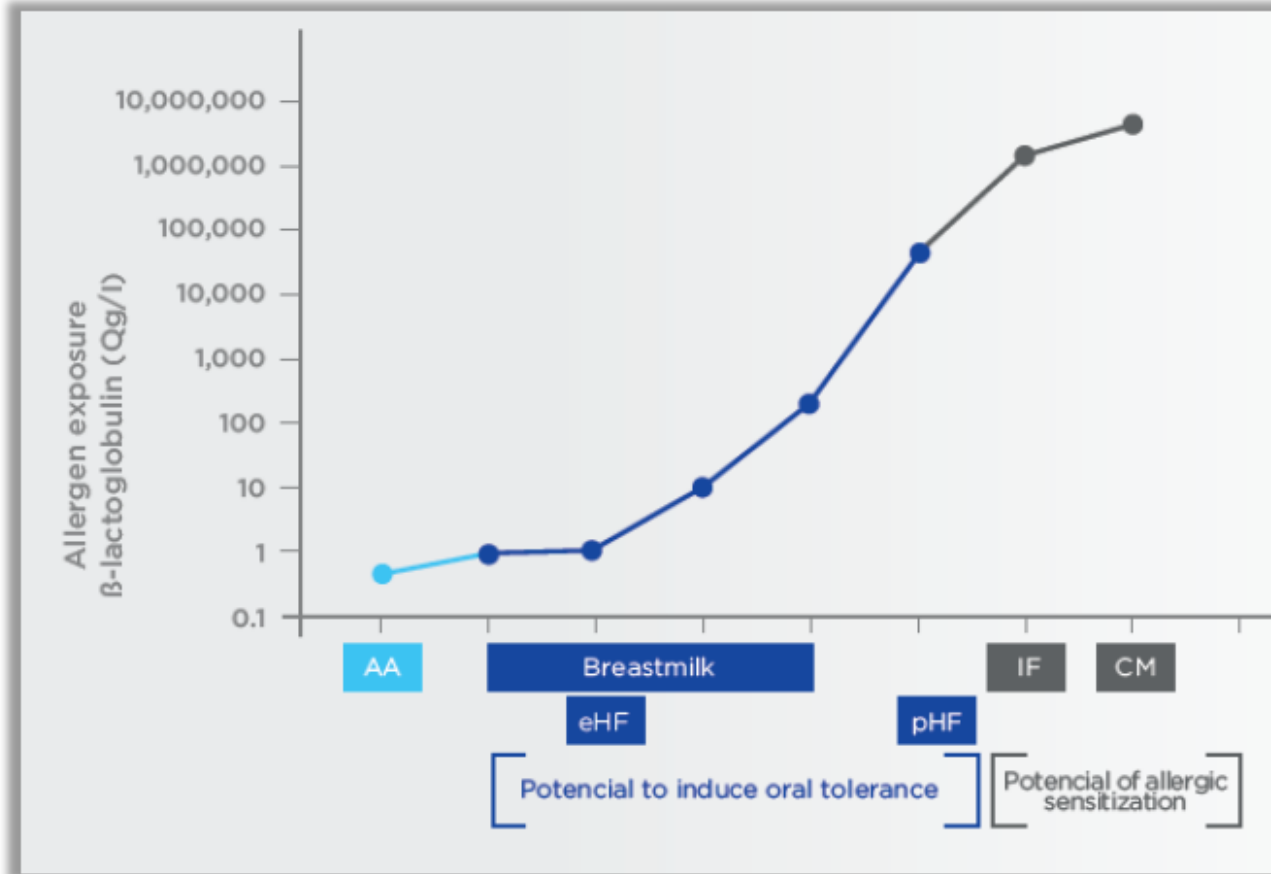
LOW DOSE EXPOSURE IS NEEDED TO INDUCE TOLERANCE

- Several studies strengthen that oral tolerance can be promoted by the exposure to low dose CM's allergens.
- There is a dose response relationship between allergen exposure and sensitization to that allergen.
- Whereas complete avoidance of allergens inhibits allergic sensitization, the immune system is not trained and tolerance is does not occur.

	COMPLETE ALLERGEN AVOIDANCE	LOW DOSE ALLERGEN EXPOSURE	HIGHER DOSES OF ALLERGEN EXPOSURE
Breastfeeding	Dietary restrictions/ complete avoidance of allergen	No dietary restrictions	Higher doses not measured in breastmilk
Infant´s diet	Amino acid based formula	Hydrolysed formulas	Intact cow´s milk protein formula
Potential for allergic sensitization	Not possible	Not very likely	More likely
Potential for oral tolerance	Not possible	More likely	Possible



TO BECOME ALLERGIC OR NOT - A QUESTION OF DOSE?



- ✓ The potential to induce oral tolerance or allergic sensitization is associated with allergen dose.
- ✓ Low dose exposure, such as breast milk and hydrolyzed formulas, are rather able to educate the immune system to develop tolerance than allergic sensitization.

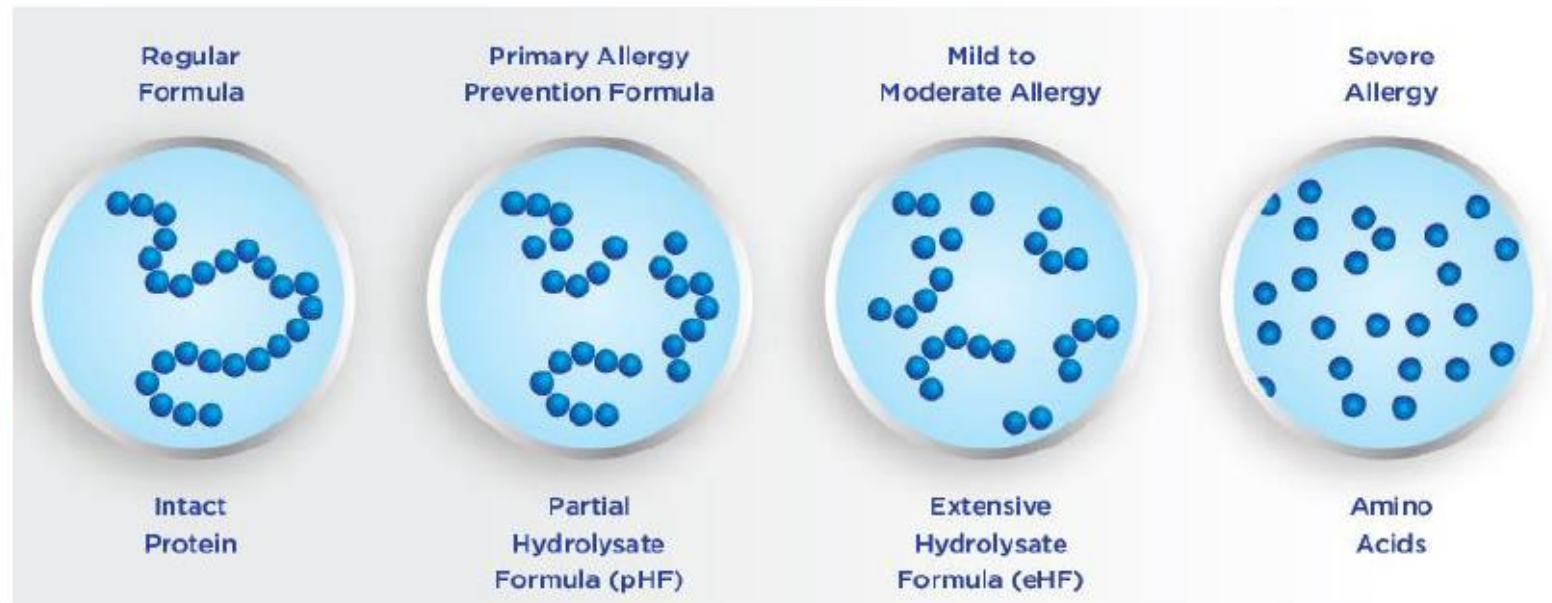


THE ROLE OF HYDROLYZED INFANT FORMULAS IN PRIMARY ALLERGY PREVENTION

Hydrolyzed CM's proteins:

- ✓ Reduce the molecular weight and the peptide size ^{1,2}
- ✓ Attenuating the allergenicity of the proteins ^{1,2}
- ✓ Efficacy approved by several studies ^{1,2}
- ✓ Processed by the gut-associated lymphoid tissue and may induce oral tolerance without allergic sensitization³

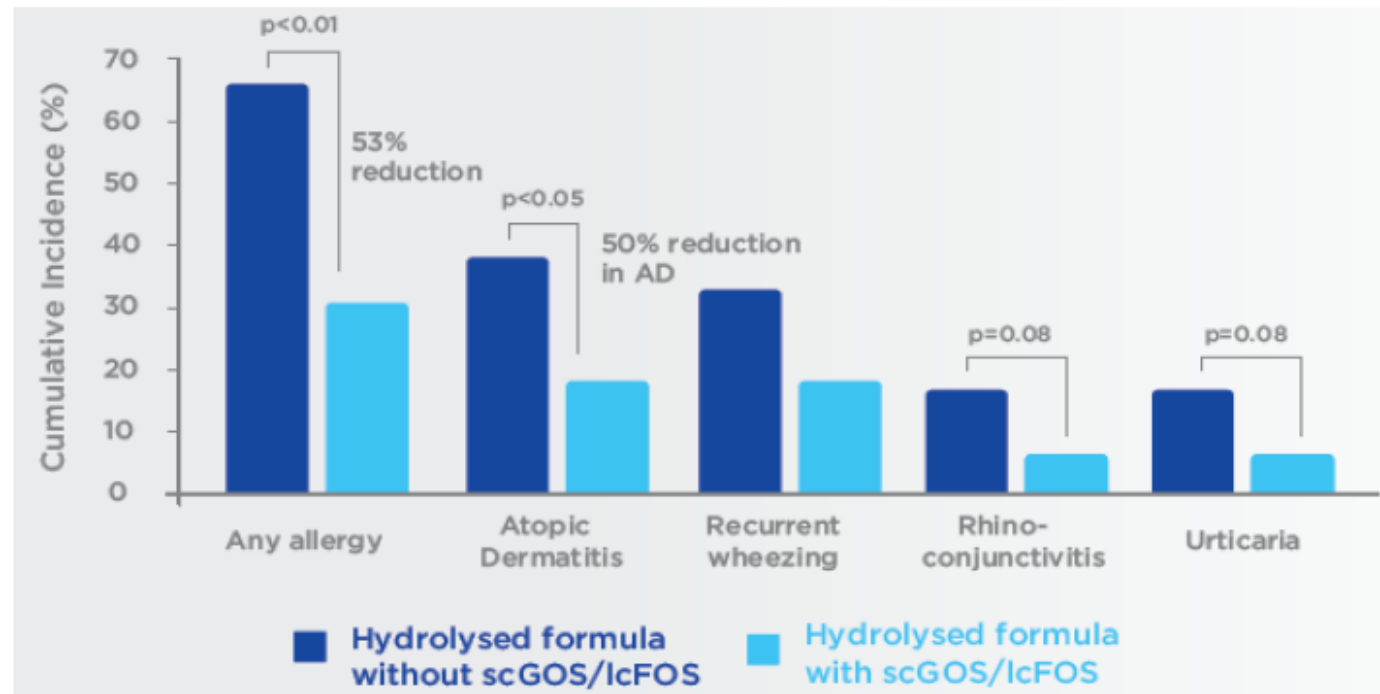
Feeding partially hydrolyzed formulas early in life is an effective approach to prevent the onset of allergies





THE ROLE OF SPECIFIC PREBIOTIC MIXTURE SCGOS/LCFOS (9:1) IN PRIMARY ALLERGY PREVENTION

- Studies on addition of a specific oligosaccharide mixture (scGOS & lcFOS 9:1) to whey hydrolysate showed a reduction in the cumulative incidence of atopic dermatitis with 50%.¹
- The follow-up study demonstrated that the allergy prevention effect remained up to at least 5 years of age.
- Indicating development of oral tolerance via immune modulation than a transient reduction of allergic sensitization.²

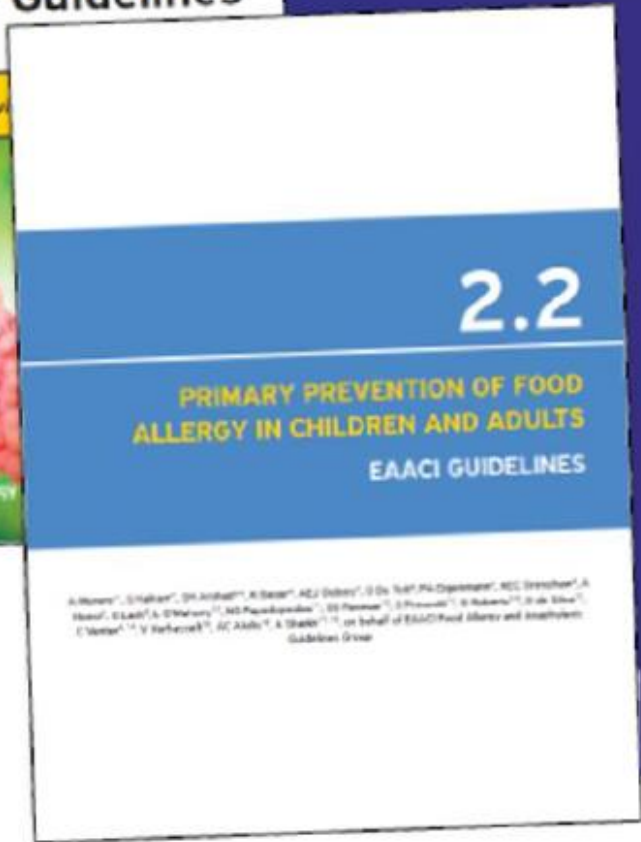
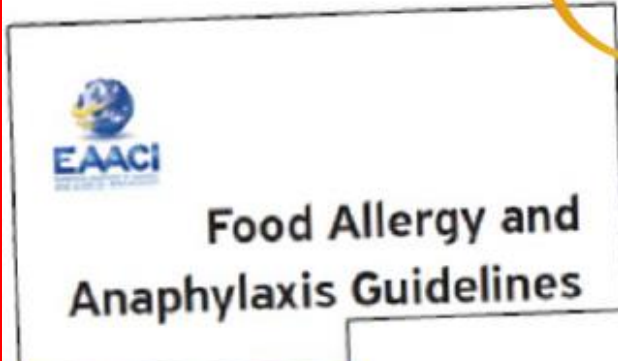




ALLERGY PREVENTION INTERNATIONAL GUIDELINES



EAACI GUIDELINE



Recommendation on formula:

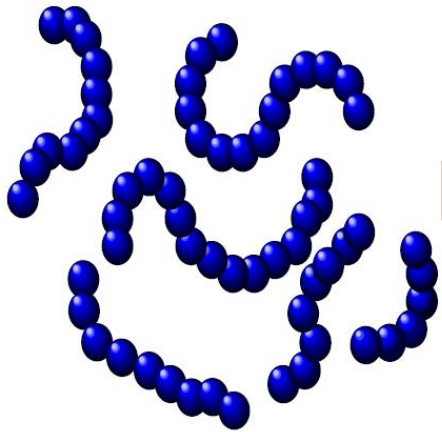
- Based on this evidence families can be provided with some practical advice about preventing food allergy, particularly amongst infants at high-risk due to parent and /or older siblings with allergic disease.
- The advice for all mothers includes the consumption of a normal healthy diet without restrictions during pregnancy and lactation. For all infants exclusive breastfeeding is recommended for the first 4-6 months of life.
- **If breastfeeding is insufficient or not possible for the first four months, infants at high risk can be recommended a hypoallergenic formula with documented preventive effect for the first 4 months of life.**
- There is no need to avoid introducing complementary foods beyond four months or for infants and children to take supplements such as prebiotics or probiotics.

Bebelac HA

DOUBLE PROTECTION

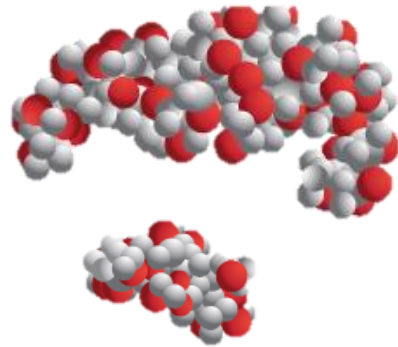
**PARTIALLY HYDROLYZED
PROTEIN**

Low consistent exposure



scGOS/lcFOS

Promotion of balanced
microbiota & prevention
of gut dysbiosis



Bebelac HA 1&2

Hypo Allergenic Formula

For prevention of cow's milk allergy in high risk infants

HA1: From birth onwards

HA2: From 6 months onwards

Contains all the nutrients for optimal growth & development

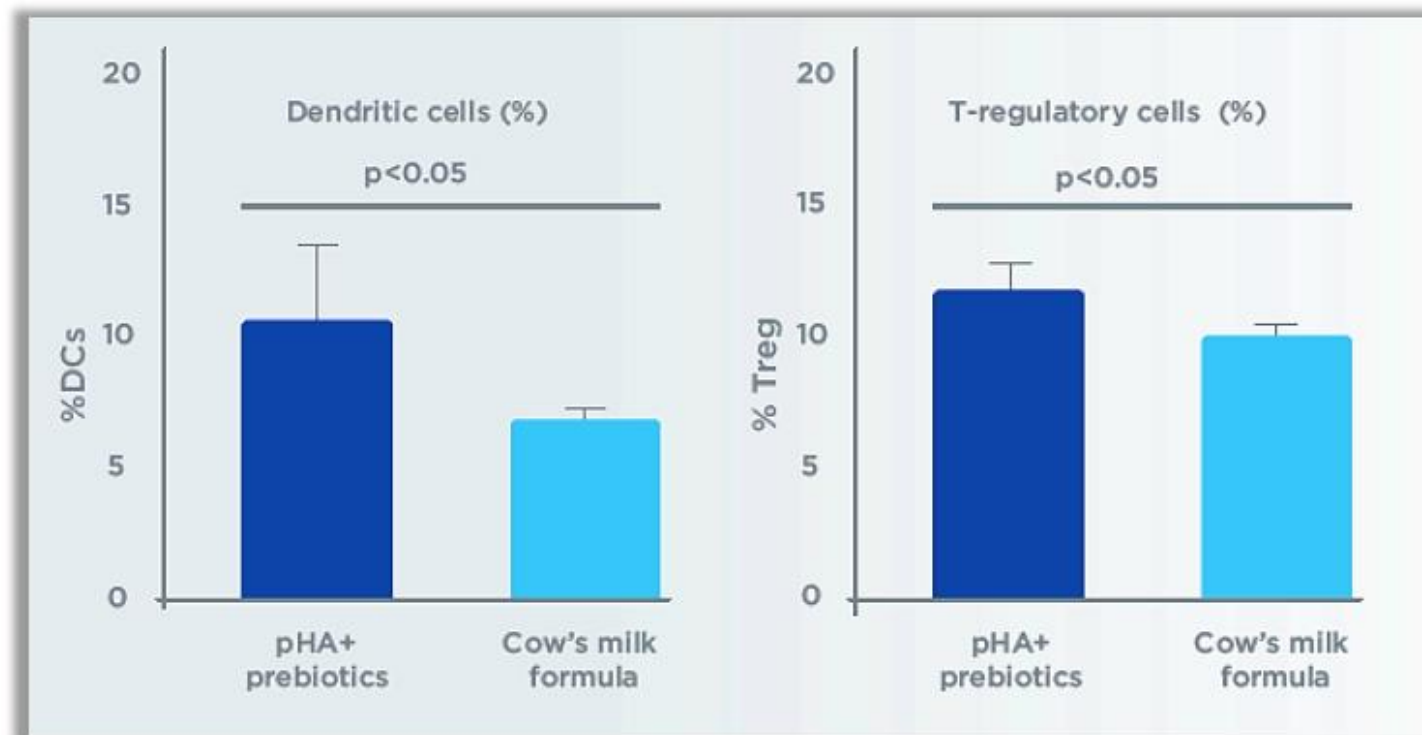


PATCH STUDY

RESULTS

- Increased numbers of specific dendritic cells and regulatory T cells in infants receiving the Danone Nutricia HA formula with specific prebiotic mixture including scGOS/lcFOS (9:1)

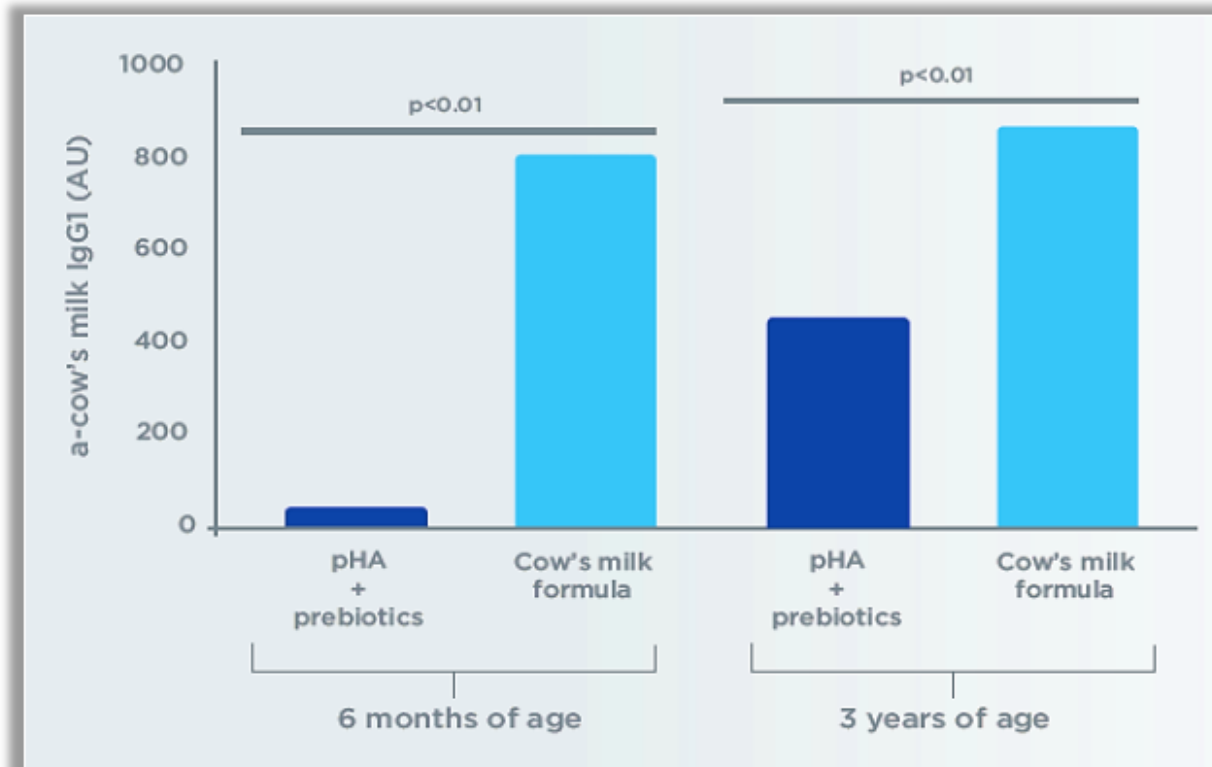
**Tolerance induction
indicated by presence of
a regulatory
immune response**



PATCH STUDY

RESULTS

- Infants with a family history of allergic diseases receiving a PHF with scGOS/lcFOS (9:1) showed a significantly reduction in CM-IgG1 compared to the control group, still present at 3 year.
- **This indicates a reduction in allergic sensitization**





SUMMARY OF CLINICAL STUDY RESULTS

NUTRICIA HA WITH SPECIFIC PREBIOTIC MIXTURE INCLUDING SCGOS/LCFOS (9:1) HAD THE CAPACITY TO MODULATE THE IMMUNE RESPONSE CONTRIBUTING TO ORAL TOLERANCE

- ✓ A dietary intervention with Nutricia HA with scGOS/lcFOS (9:1) had the capacity to modulate the immune response contributing to oral tolerance demonstrated to have the capacity to modulate the immune response

Potential for allergic sensitization Indicated by IgG1	NO	YES
Potential for tolerance induction Indicated by regulatory cells	YES	NO
	Nutricia HA with prebiotics	Intact cow's milk formula
	Allergen exposure	



SUMMARY

- ✓ To date, the family history of atopy is used to predict an individual's atopy risk.
- ✓ Dietary allergy prevention is effective and recommended for bottle-fed infants with a positive family history of atopy.
- ✓ Hydrolysis of the protein component of cows' milk based formulas (HA) significantly reduces their allergenicity.
- ✓ Danone unique prebiotic mix play an important role in allergy prevention. Apart from hydrolyzed protein (HA) infant formulas.
- ✓ Clinical trials show that Danone special prebiotic mixture reduces the incidence of allergy in formula fed babies.



Thank You

