



Cow's Milk Protein Allergy

"From Gastroenterology Perspective"

Prof. Dr. Aydan Kansu

**Ankara University, School of Medicine,
Department of Pediatric Gastroenterology, Hepatology and Nutrition**

- **Definition**
- **Epidemiology**
- **Risk factors**
- **Pathogenesis**
- **Clinical presentation**
- **Evaluation**
- **Management**
- **Prognosis**

Food allergy

Adverse immune mediated reaction

Proteins in the food

Symptoms and findings

**The prevalence of allergic diseases
in the world is increasing**

**Asthma / Rhinitis / Anaphylaxis / Eczema / Urticaria /
Angioedema / Food allergy**

(prevalence ~10%)

Environmental factors?

Food Allergy

- Cow's milk
- Egg white
- Peanut, tree nut
- Soy
- Sea food
- Wheat

CMA = CMPA (Cow's Milk Protein Allergy)

**Immune reaction to proteins in cow's milk
(casein, whey)**



F (cow's milk-based F)

Breastmilk (passed through BM)

Cow's Milk Protein Allergy (CMPA) – Prevalence?

- Geographical differences
 - Methodological differences
 - Qualified, challenge-based screening (epidemiological studies)
-

- Children 2-7.5%

- 3 y ↓

- Prevalence at 1st year: 2-7.5%

age 6 ↑: <1%

- Exclusively breastfed → 0.5%
-

Growth!

Different from other food allergies

Sensitizing proteins in cow's milk

Whey

Casein

α lactalbumin

α lactoglobulin

Bovin Ig

Casein allergens

➡ Industrial processings

➡ Pastorisation

➡ Ultra high temperature

*Baked products

No effect on the antigenic properties of cow's milk protein

Physiological Barriers

- Breakdown of antigens: enzymes / lysozyme / peristaltism
- Intestinal epithelial barrier
- Blocking of antigen entrance: mucus / membrane / tight junction / peristaltism

Immunological Barriers

- Blocking of antigen entrance: sp IgA
- Clearance of antigen: serum IgA, IgG, macrophages, RES,....)

Immune-mediated reaction



IgE-mediated
Non IgE-mediated
Mixed

Non-immune-mediated reaction



Lactase deficiency

Lactose intolerance

CMPPA

- Nonspecific GIS symptoms and signs
- Pathognomonic symptom or sign Ø
- Common functional GIS conditions
- Diagnostic laboratory findings Ø

Underdiagnosis

Overdiagnosis

Underdiagnosis

Pediatricians



**Unnecessary,
ineffective treatment**

Overdiagnosis

Parents

Pediatricians



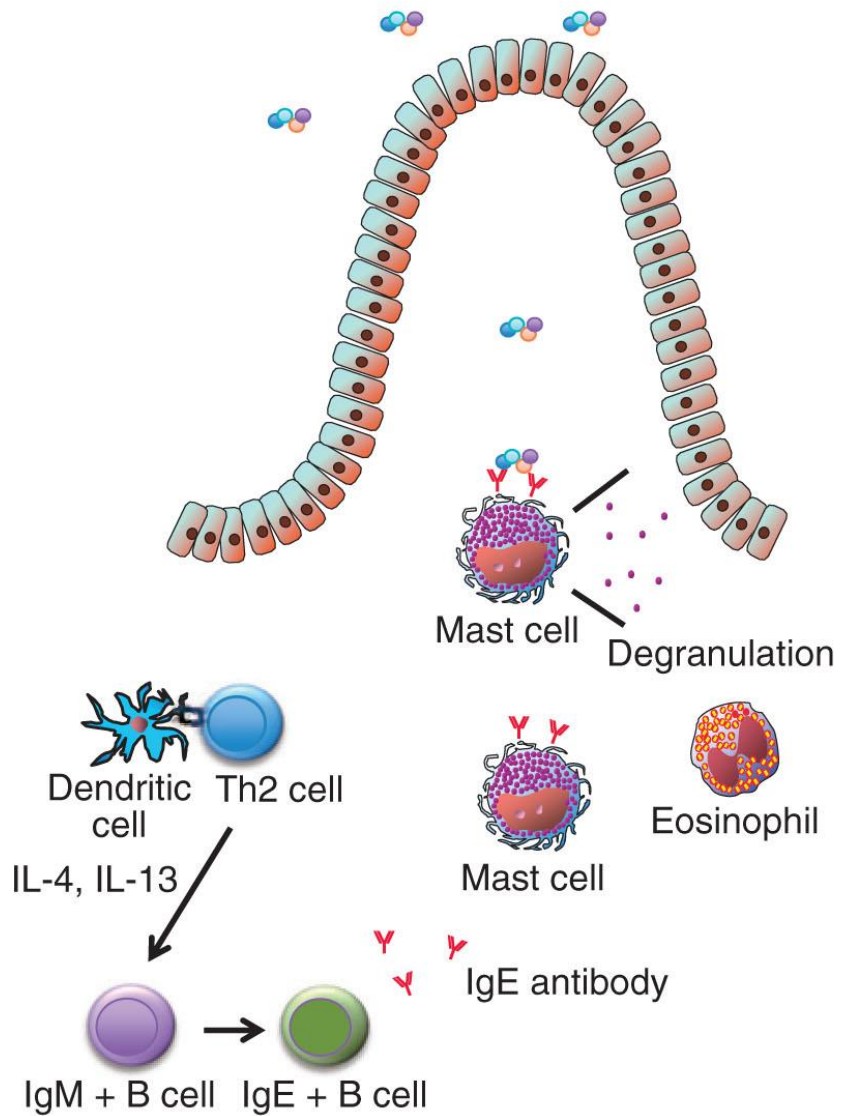
**Unnecessary
dietary
restrictions**

Clinical Presentation

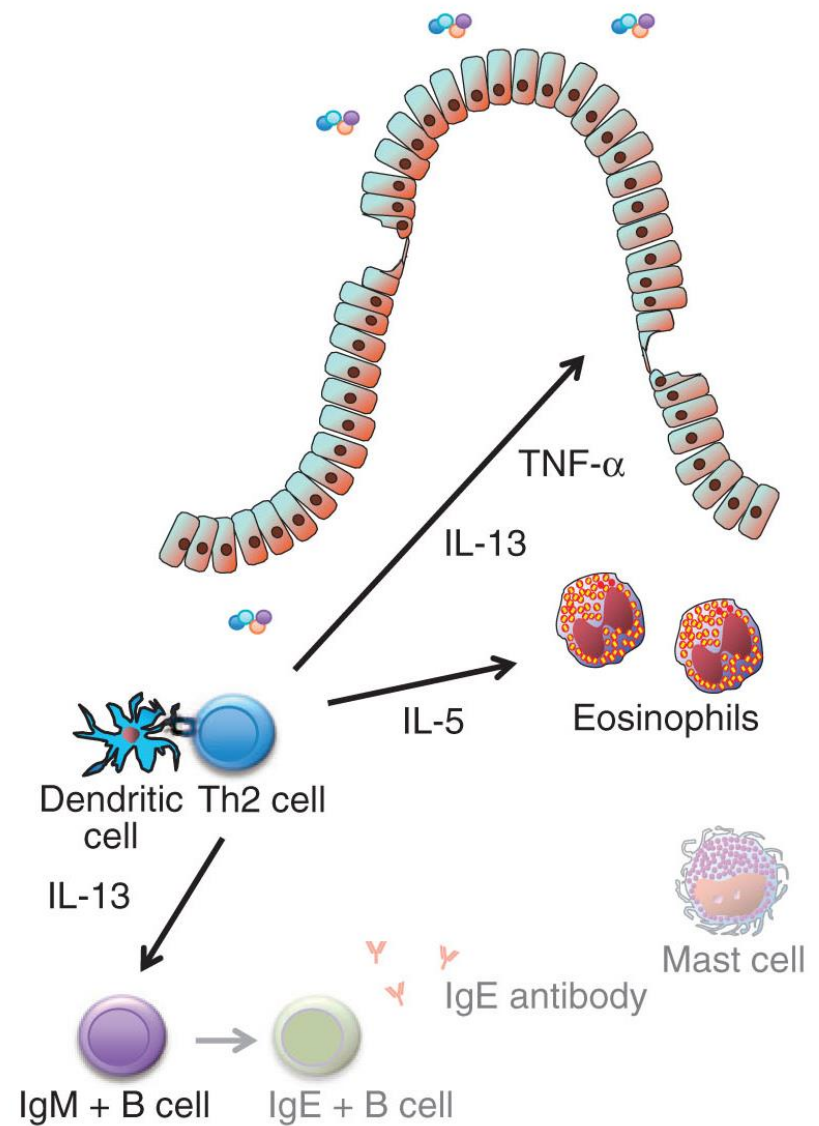


a

Food proteins

**b**

Food proteins



Clinical Presentation

- **First months of life / rarely after 12 months**
- **Usually 2⁺ symptoms, 2⁺ systems**
 - **Gastrointestinal symptoms (50-60%)**
 - **Skin symptoms (50-60%)**
 - **Respiratory symptoms (20-30%)**

IgE-mediated CMPA

15% : stridor, wheezing

9% : anaphylaxis

85% : mild

- Oral pruritis
- Urticaria
- Rhinorrhea
- Rhinoconjunctivitis
- Angioedema
- Eczema
- Vomiting
- Diarrhea

Non IgE-mediated CMPA

Gastrointestinal Symptoms

inflammation
dysmotility



GERD
Vomiting
Diarrhea
Malabsorbtion
Constipation
Bloody stool

Colic, irritability
refusal to feed

FTT
IDA

Skin

Atopic dermatitis

Respiratory

Wheezing
Cough

Non IgE-mediated CMPA

Diagnosis is difficult

- Time of symptoms
- GIS and skin symptoms (very common symptoms)
- No laboratory for diagnosis or exclusion

Non IgE-mediated CMPA

Typical gastrointestinal manifestations

- Allergic proctocolitis
- Enteropathy
- Eosinophilic esophagitis / enterocolitis
- Enterocolitis

Diagnosis

Challenge

Elimination

Laboratory

Physical Examination

Family History

Medical History

Diagnosis

History

- Symptoms?
- Severity?
- Timing?
- Treatments? Efficacy?
- Dietary Exclusion? Results?

- Breastmilk? F?

- Atopic dermatitis
 - Allergic rhinitis
 - Asthma
- in the family?

Non-response
to conventional
therapy?

Diagnosis

Laboratory

Skin prick test

Specific blood IgE level



**IgE-
mediated
CMPA**

- **Non IgE-mediated CMPA**
- **GIS involvement**

**Laboratory tests have no value for
diagnosis**

TYPICAL GASTROINTESTINAL PRESENTATIONS

CMPPA - PROCTOCOLITIS

- Rectal bleeding in an infant
- First months of life
- Adequate weight and height
- No other complaints
- Stool normal other than fresh blood
 foamy frequency N
 mucoid volume N

CMPA - Proctocolitis

Thinning of the mucosa

Mucosal ulcerations

Friability



Rectal bleeding

CMPA – Proctocolitis

Elimination of CMP ➡ Resolution of Symptoms

Other causes are ruled out

- **anal fissure**
- **diaper dermatitis**
- **A. gastroenteritis**

CMPA - ENTEROCOLITIS

months – 2 years
Non IgE-mediated

Repetitive vomiting
Lethargy
Pallor / cyanosis
Shock
Metabolic acidosis
Diarrhea
Dehydration

Failure to thrive
Protein losing enteropathy
Anemia

Dermatitis / Urticaria Ø
Respiratory symptoms Ø

A. Gastroenteritis?
Sepsis?
Metabolic disease?
Acute abdomen?
Intestinal obstruction?
Anatomic anomaly?

CMPA – ENTEROPATHY

Chronic diarrhea

inadequate weight gain / loss of weight

hypoalbuminemia - edema

Celiac disease?

Gold Standard – Diagnosis – Non IgE-mediated CMPA

**Elimination diet
(Cow's milk and products)**



Resolution of symptoms



Oral challenge



**Recurrence of symptoms
(other causes are ruled out)**

Elimination Diet for Diagnosis

- **Breast fed babies**

- Elimination of CM in mother's diet

- **F fed babies**

- Elimination of CM in baby

- ➡ – Switching to special F

2-8 weeks

Elimination Diet for Diagnosis

Breastfed babies

Elimination of CM in mother's diet
(2-8 weeks)



no improvement in symptoms



Multiple food allergy?

CMPA Ø?



restriction of other allergenic food in mother's diet



no improvement



therapeutic F



no improvement in symptoms



CMPA Ø
other causes?



Improvement in Symptoms

Improvement in Symptoms



Challenge (gradually)



Symptoms recur



CMPA



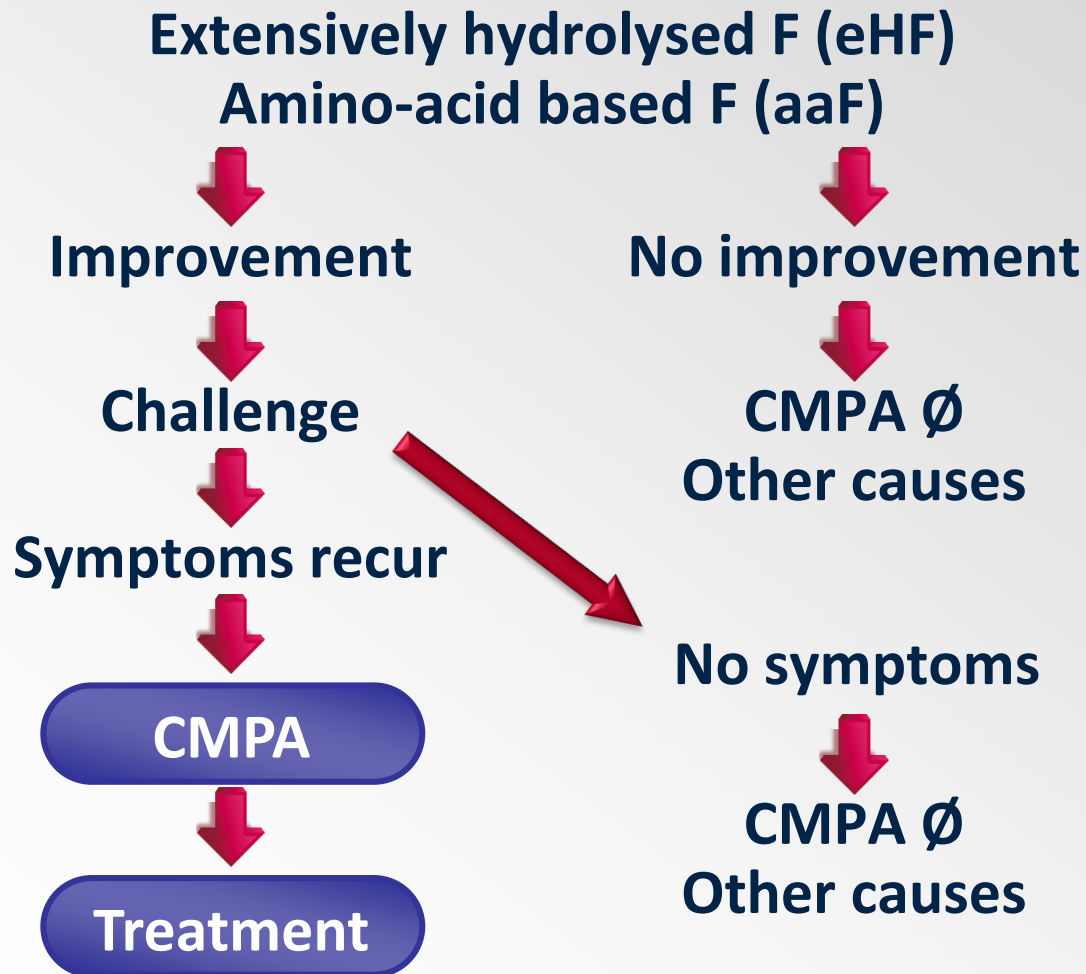
No symptoms



**CMPA Ø
Other causes?**

Elimination Diet for Diagnosis

Formula-fed babies



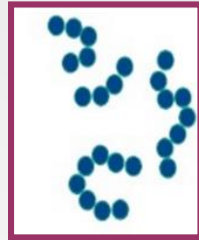
Mol. Wt. (kD) Allergenicity Taste Cost

- Standard F (CMP-based)



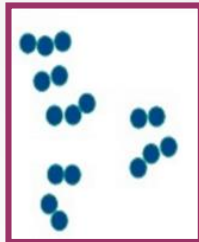
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- Partially hydrolysed F (pHF)



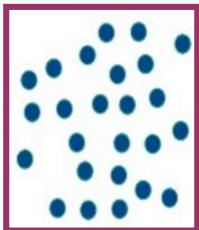
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- Extensively hydrolysed F (eHF)

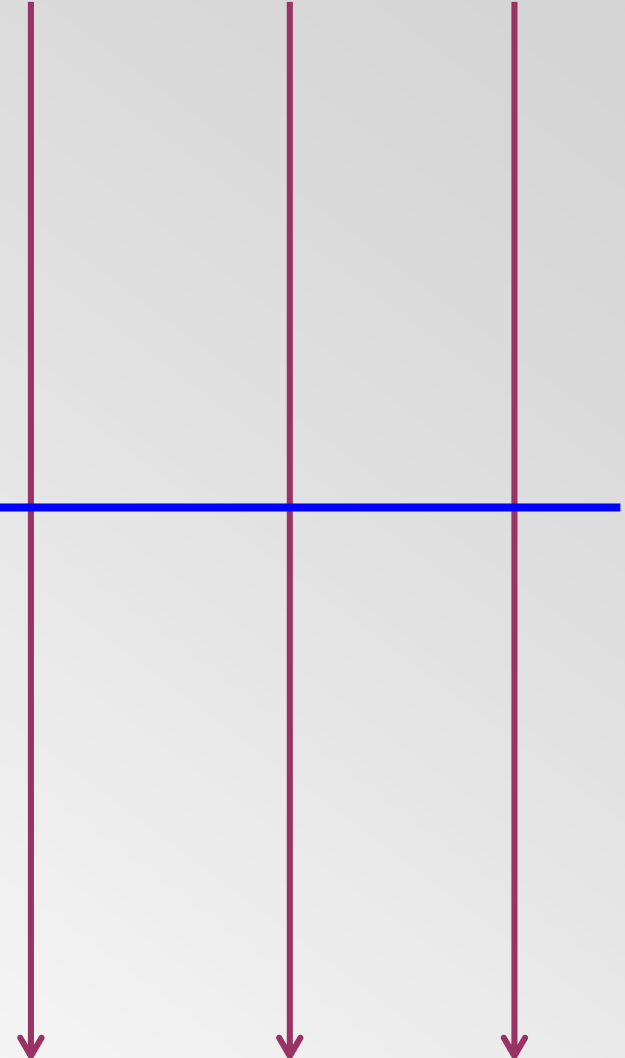


<3

- aa-based F



aa



Extensively hydrolysed F



aa-based F



Indications for aaF in CMPA

- Anaphylaxis / severe reactions
- Growth failure / hypoproteinemia / severe anemia (enteropathy)
- Persistence of symptoms with eHF
- (Multiple food allergies?)

Treatment

Breastfed babies

- Continue BF
 - CMP elimination in mother's diet
 - Processed food!
 - Hidden sources!
 - Ca 1000 mg/day
 - Vitamin D 400 IU/day
- for the mother

Treatment

Formula-fed babies

- Extensively hydrolyzed F
- Amino-acid based F

more affordable
well tolerated
90% success

Complementary Feeding

The goals of therapy in CMPA

1. Preventing allergic reaction
2. Promoting optimal nutrition and growth
 - ➡ • Exclusion of CMP and products
 - ➡ • Usual introduction of other food
Do not delay!
 - ➡ • Reading labels!
(casein, whey, lactalbumin...)

- ✖ ● **Soy-based Formula**
 - Cross-reactivity (60%)**
 - Isoflavins (estrogen effect)**
 - Phytate (absorbtion of minerals and trace elements ↓)**
- ✖ ● **(Rice Formula)**
- ✖ ● **Goat, sheep, donkey, horse, camel.... milk**
 - Cross-reactivity (80%)**
 - Not nutritionally appropriate**
- ✖ ● **Almond, coconut, chest nut juices**
 - Not nutritionally appropriate**

CMPA



**bovine serum albumin
beef and veal meat allergy
13% - 20%**



**excluding beef and veal
is not recommended**

Beef allergy



**CMPA
92%**

Duration of Treatment

Tolerance

When?
How?

Non IgE-mediated

- After at least 6 months of elimination diet
- Until the baby is 9-12 months-old

Challenge

at home
gradually

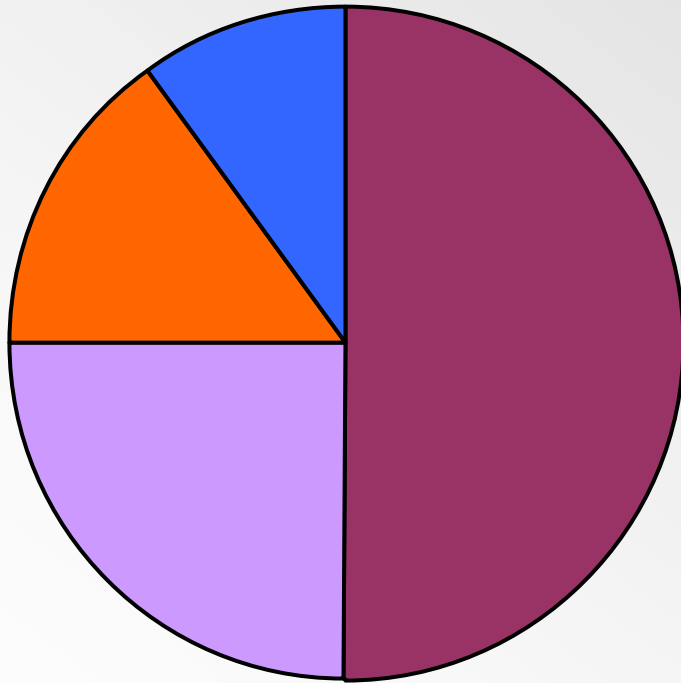
IgE-mediated

After 12-18 months of elimination diet

Challenge

at hospital
after checking IgE levels / skin prick test
very carefully-closely observed!

Prognosis



1 y : 30-50%

2 y : 60-75%

3 y : 85-90%

IgE-mediated CMPA

tolerance ↓

5 years: 50% - 60%

baked milk products

(cake, pastries,...)

**helps to development of
tolerance**

Factors Related to Tolerance and Persistence of CMPA

Favor tolerance

Non IgE-mediated
>1 mo at presentation
GIS Symptoms
Tolerance to baked products
Family history \emptyset
IgE levels \downarrow at D_x and follow-up

Favor Persistence

IgE-mediated
<1 mo at presentation
Respiratory Symptoms
Intolerance to baked products
Family history (+)
IgE levels \uparrow at D_x and follow-up
Multiple food allergy

Clinical Suspicion

Differential diagnosis

CMPA?



Elimination diet



Challenge



Diagnosis

Breast-fed infants can have CMPA

Diagnosis must be definite

Elimination diet must be strict

Prognosis is good

Avoid unnecessarily long elimination diet



Growth failure

Quality of life ↓

Health expenses ↑