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# Which formula for a cow's-milk-protein-intolerant infant?

Katero formulo predpisati dojenčku, ki ne prenaša beljakovin kravjega mleka?

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## Abstract

Breast milk is the best for infant nutrition, but sometimes it is necessary to use an adapted milk formula. All infant formulas must support the normal growth and development of infants.

Cow's milk allergy is used to describe reactions involving the immune system, while other reactions are normally called cow's milk intolerance. Management includes diet modification for nursing mothers and special formulas for formula-fed infants.

## Izveček

Materino mleko je najboljša za prehrano dojenčkov, čeprav je včasih treba uporabiti prilagojeno mlečno formulo. Vse formule za dojenčke morajo zagotoviti normalno rast in normalni razvoj otrok.

Alergija na kravje mleko je reakcija imunskega sistema, medtem ko druge reakcije navadno imenujemo neprenašanje kravjega mleka ali netoleranca. Zdravljenje vključuje spremembo prehrane za doječe matere in posebne formule adaptiranega mleka za dojenčke.

## Introduction

Breastfeeding is the best nutrition for most infants and should be promoted, supported and protected at all times. Besides that, it is good for the mother and infant's health, development, immune system, acute infections protection and other.

There are several adverse food reactions, mainly due to immaturity of the local and systemic immune system, often in association with increased gut permeability to large molecules. Food allergy represents the failure to achieve or maintain immune tolerance to one or several food proteins. Clinical symptoms are different and may involve skin, respiratory and digestive tract.<sup>1</sup>

Food allergy may be classified as antibody mediated (e.g. IgE mediated – asthma, laryngeal oedema, atopic dermatitis, urticaria, immediate gastrointestinal hypersensitivity and oral allergy syndrome, nausea and vomiting, colic, diarrhoea), or cell mediated (e.g. T-cell mediated – contact rash, atopic dermatitis, gastroesophageal reflux, dietary

protein enteropathy, protein induced enterocolitis and proctocolitis).<sup>2</sup>

Food intolerance is characterized by an adverse reaction to non-protein food ingredient without interacting with the immune system. Sometimes it may indicate the presence of underlying digestive tract or metabolic disease.<sup>2</sup>

The treatment of food allergies is based on the elimination of specific food proteins until tolerance has developed. It is important to select a suitable infant formula based on the infant's individual needs and medical condition.

Any food ingested could induce allergic reaction, but most common are cow's milk, egg, wheat and soya. The exclusion diet is generally based on an underlying family history of atopy (hay fever / allergic rhinitis, asthma, eczema), allergies and organ-specific autoimmunity combined with the age at presentation of symptoms with food intake at that time.<sup>3</sup>

Cow's milk is the most common food to cause a reaction in infants. About 2–3 % of infants in developed countries have cow's milk protein intolerance or allergy. But also 0.5 % of breast fed infants are reported to be food-allergic or intolerant, reacting to exogenous food proteins secreted into the mother's milk.<sup>3</sup>

In breast-fed infants, the mother's diet needs to be modified by the removal of cow's milk and any other foods allergenic to the infant, ensuring that the maternal diet continues to include adequate amounts of calcium, fluid, energy and protein. In formula-fed infants it is important to give a proper milk formula instead of a formula based on cow's milk protein.<sup>4</sup>

## Clinical manifestation

In IgE mediated food allergy, symptoms generally appear within minutes after ingestion of a very small amount of food. They include vomiting, abdominal pain, urticaria, angioedema, erythema, pruritus, wheeze and cough. The most severe are symptoms of upper and lower airway obstruction, hypotension, cardiac arrhythmias and even heart failure – anaphylactic shock.<sup>5</sup>

Non-IgE mediated food allergy symptoms are the classic delayed hypersensitivity reactions. The mechanism involves sensitised T-cells reacting with the antigen to produce cytokines and cause inflammation, tissue damage and the formation of epitheloid and giant cells. Gastrointestinal and nutritional manifestations include gastroesophageal reflux, esophagitis, gastritis and failure to thrive, sometimes only crying inconsolably and feeding refusal. These symptoms are particularly challenging owing to their non-specificity and a wide differential diagnosis.<sup>6</sup>

Non-allergic food hypersensitivity is not caused by an immune reaction and is often a result of enzyme deficiencies. They are characteristic for older population rather than infants.<sup>2</sup>

Sometimes it is very difficult to differentiate allergic reaction from gastroesophageal reflux, colics or other nutritional problems, so the main symptom should be managed as start.

## Diagnosis

Double-blind, placebo-controlled food challenge has long been regarded as the criterion standard for confirming the diagnosis of cow's protein allergy. Children tend to grow out of some food allergies and so food reintroductions will need to be considered from time to time.<sup>7</sup>

Other investigational options include skin-prick testing, serum measurement of IgE antibodies to the specific allergen and patch testing. Other laboratory investigations are not diagnostic but can support a diagnosis made on clinical grounds (decreased albumin, increased platelets and C-reactive protein, fecal leukocytes).<sup>7,8</sup>

## Therapy

The main principle is to avoid allergens while maintaining a balanced, nutritious diet for infant and mother. An elimination diet may also be used in the diagnosis of food allergy. Breastfeeding can be continued if allergens are avoided. In the case of cow's milk allergy, it is important that breastfeeding mother sequentially eliminate all cow's milk protein, than all bovine protein (milk and meat), and occasionally, if symptoms continue, other protein sources such as soy.<sup>9</sup>

When clinical history and diagnostic tests strongly indicate which food causes the symptoms, exclusion of the food is very easy.

In some cases it may not be clear which foods are causing the problems. An empirical diet is used where food hypersensitivity is suspected and causative agents are not known.<sup>9,10</sup>

## Protein hydrolysate formulas

Protein hydrolysate (semielemental) infant formula is often a choice for an infant with immediate or delayed adverse reactions to cow's milk. There is some variation in the degree of hydrolysis, sugar content and sources of fats. Sometimes these products have bad palatability, but infants will take them quite readily.<sup>11</sup>

The partially hydrolysed whey based formulas are much more palatable than exten-

sively, and are also much cheaper. They are intended for prophylactic use and are not suitable for the treatment of cow's milk allergy because of the relatively high level of large peptides present, which may cause an adverse reaction.<sup>2</sup>

In cow's milk sensitive enteropathy, both casein and extensively hydrolysed whey formulas have been shown to be satisfactory. The best enteropathy milk formulas also contain medium chain triglycerides.<sup>2,6,11</sup>

Besides anaphylactic reactions, late onset adverse reactions have also been described with both casein and whey hydrolysates. The majority of cow's milk allergic infants will tolerate any of these formulas. A highly allergic infant may tolerate one and not the other. It is possible that in such case, casein hydrolysate will be most successful.<sup>11,12</sup>

## Amino acid formulas

Amino acid formulas are suitable for infants who cannot tolerate an extensively hydrolysed formula. Such infants usually have multiple allergic reactions. Protein source are synthetic amino acids and sugar source is glucose. However, amino acid formulas usually contain soy lecithin, also potentially allergenic material, so they must be used with caution. In infants with allergic colitis, they are not recommended owing to high osmolality. Additionally, cross-sensitization of milk proteins correlates with increased intestinal permeability.<sup>6,12,13</sup>

## Human milk

It is known that allergens from the mother's diet can appear in breast milk. Breast fed infants with multiple allergies

have also been described. The breastfeeding mother should avoid milk and eggs as well as any other food that causes allergic reaction. If symptoms cannot be controlled by maternal allergen avoidance, breast feeding may be stopped for a while. Breast feeding mothers on exclusion diets should be receiving a calcium supplement.<sup>14,15</sup>

## Other

Soy formula can be given for the treatment of cow's milk allergy after the age of 1 year and can be given between 6 and 12 months of age if amino acid of extensively hydrolysed formulas is not tolerated because of palatability.<sup>2,6</sup>

Sheep and goat milk are not suitable for infants with cow's milk allergy as their nutritional composition is unsuitable for infant feeding, there is sometimes concern about microbial content and their proteins can be sensitising as cow's milk protein.

Introduction of solid food can occur at the usual age barring complications such as feeding aversion.

## Conclusion

Milk protein allergy can occur in both formula-fed and breastfed infants, usually in the first year of life. It can entail cutaneous as well as respiratory, gastrointestinal and other manifestations. When milk protein allergy is suspected, investigational procedures include food challenge, skin-prick testing, serum IgE antibodies and patch test. The main principle in management is to avoid allergens in infant's and/or mother's diet.

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