

Differentiating milk allergy (IgE and non-IgE mediated) from lactose intolerance:

understanding the underlying mechanisms and presentations

INTRODUCTION

Children with food allergy and, in particular, infants with suspected adverse reactions to cow's milk, commonly present to primary care. It is thought that 6–8% of children aged <3 years have a food allergy¹ and up to 4.9% have a cow's milk allergy.²

Inconsistencies in the management of food allergy prompted the commissioning of projects such as the National Institute for Health and Care Excellence (NICE) clinical guideline on the diagnosis and assessment of food allergy in the community¹ and in 2014 the NICE Clinical Knowledge Summary looking specifically at the management of milk allergy.³

It has been shown that GPs' knowledge of these guidelines is poor. Inconsistencies remain in the management of milk allergy, with a particularly lengthy time period and multiple consultations before diagnosis.⁴

There is anecdotal evidence of confusion between lactose intolerance and milk allergy among both patients and physicians, which could result in unnecessary dietary restriction or avoidable reactions. Terminology such as suspected 'milk allergy', 'milk intolerance', and also 'lactose intolerance' are often used without a clear sense of the different meanings, understanding of the different mechanisms that underlie them, or the dietary implications of the diagnosis. The management of these conditions is distinctly different, and inappropriate recognition or management may have significant implications for the patient. In the last 15 years, there have been many discussions on the nomenclature of reactions to foods, including milk. The currently accepted nomenclature is determined by the mechanism likely to be producing the symptoms, with cow's milk allergy being immune mediated and lactose intolerance not immune mediated.^{1,2}

MECHANISM AND SYMPTOMS

Lactose intolerance

Lactose intolerance results from a reduced

capacity to digest lactose, a sugar. It causes symptoms only in the bowel, for example, abdominal pain, bloating, flatus, and diarrhoea. Importantly, it is not a cause of rectal bleeding.⁵ Congenital lactose intolerance is very rare and presents only in isolated populations, for example, some Finns and Russians.⁶ Primary lactose intolerance develops when levels of the enzyme lactase naturally reduce, which usually occurs after 3 years of age in some populations (for example, Africans and Asians). Secondary lactose intolerance presents as a result of mucosal damage, usually following severe gastroenteritis but also when the epithelium is damaged such as in coeliac disease and cow's milk allergy. It is usually reversible once the epithelial lining has repaired. Except after a gastrointestinal infection, infants with gastrointestinal symptoms on exposure to cow's milk are more likely to have cow's milk allergy than lactose intolerance.⁷

Cow's milk allergy

Milk allergy can be either immunoglobulin E (IgE) or non-IgE mediated. IgE-mediated reactions typically occur immediately after ingestion whereas non-IgE mediated are delayed and take up to 48 hours to develop, but still involve the immune system. It is the symptoms of non-IgE mediated disease, which are commonly wrongly labelled as symptoms of intolerance, using either the terms 'lactose intolerance' or 'milk intolerance'. See Box 1 for symptoms of food allergy.

MANAGEMENT

Lactose intolerance

Children with suspected lactose intolerance do not usually require any testing and should improve within 48 hours on a low lactose diet. (It is the sugar, lactose, which needs to be reduced in the diet.) In secondary lactose intolerance, for example after severe gastroenteritis, lactose can usually be tolerated again by 6 weeks. The World

Joanne Walsh, MSc, MBChB, GP, Castle Partnership, Norwich. **Rosan Meyer**, PhD Paediatric, Dietician, Imperial College, London. **Neil Shah**, MD, MRCP, Consultant Paediatric Gastroenterologist, Department of Gastroenterology, Great Ormond Street Hospital for Children NHS Foundation Trust, University College London, London.

James Quekett, FRCGP, DRCOG, Director for Primary Care Doctors.net.uk, Abingdon.

Adam T Fox, Consultant Paediatric Allergist, MA (Hons), MD, MSc, DCH, FRCPCH, FHEA, Dip. Allergy, MRC & Asthma UK Centre in Allergic Mechanisms of Asthma, King's College London, London. Guy's and St Thomas' Hospitals NHS Foundation Trust, London.

Address for correspondence

Joanne Walsh, Castle Partnership, 101–103 Magdalen Street, Norwich, Norfolk NR3 1LN, UK.

E-mail: joanne.walsh@nhs.net

Submitted: 21 March 2016; Editor's response: 6 April 2016; final acceptance: 28 April 2016.

©British Journal of General Practice 2016

This is the full-length article (published online 29 Jul 2016) of an abridged version published in print. Cite this article as: **Br J Gen Pract** 2016; DOI: 10.3399/bjgp16X686521

Box 1. Signs and symptoms of possible food allergy as set out by NICE in Clinical Guideline 116¹

IgE mediated	Non-IgE mediated
Skin	
<ul style="list-style-type: none"> • Pruritus • Erythema • Acute urticaria (localised or generalised) • Acute angioedema (most commonly in the lips and face, and around the eyes) 	<ul style="list-style-type: none"> • Pruritus • Erythema • Atopic eczema
Gastrointestinal system	
<ul style="list-style-type: none"> • Angioedema of the lips, tongue, and palate • Oral pruritus • Nausea • Colicky abdominal pain • Vomiting • Diarrhoea 	<ul style="list-style-type: none"> • Gastro-oesophageal reflux disease • Loose or frequent stools • Blood and/or mucus in the stools • Abdominal pain • Infantile colic • Food refusal or aversion • Constipation • Perianal redness • Pallor and tiredness • Faltering growth plus one or more gastrointestinal symptoms above (with or without significant atopic eczema)
Respiratory system (usually in combination with one or more of the above symptoms and signs)	
<ul style="list-style-type: none"> • Upper respiratory tract symptoms (nasal itching, sneezing, rhinorrhoea, or congestion, with or without conjunctivitis) • Lower respiratory tract symptoms (cough, chest tightness, wheezing, or shortness of breath) 	
Other	
<ul style="list-style-type: none"> • Signs or symptoms of anaphylaxis or other systemic allergic reactions 	

Health Organization suggests an infection should have lasted for 2 weeks before consideration of lactose intolerance. Breast feeding should continue, despite the high lactose content of breast milk, and maternal dietary restrictions will not reduce this.

Unless there is an enteropathy, with

Box 2. Comparison of non-IgE mediated cow's milk allergy and lactose intolerance

	Non-IgE-mediated milk allergy	Lactose intolerance
Symptoms	Gastrointestinal, skin, or respiratory	Bowel only, for example, pain, flatulence, diarrhoea
Mechanism	Immune reaction to milk protein	Non-immune. Reduced ability to digest lactose
Tests	Exclusion diet (NO MILK PROTEIN) (symptom improvement) and then reintroduction (symptom recurrence). May take 4–6 weeks for symptoms to improve	Exclusion diet (LOW LACTOSE) (symptom improvement) and then reintroduction (symptom recurrence). Usually improve within 48 hours of exclusion
Dietary advice (including formulas)	A diet free from cow's milk protein. Exclude all cow's milk and products. Consider tolerance acquisition and introduction of, for example, extensively baked products after 6 months	Low lactose diet — exclude cow's milk and foods containing cow's milk, although some with low lactose may be tolerated by some individuals If secondary, should resolve by 6 weeks

small bowel damage causing secondary lactose intolerance, most infants with cow's milk allergy can tolerate lactose.²

Cow's milk allergy

An infant with suspected IgE-mediated milk allergy will require testing for specific IgE to milk (skin prick test or blood tests). Infants with suspected non-IgE-mediated disease do not need these tests.^{1,3,8} Dietary management involves removing the allergenic protein from the diet. All dairy products must be removed from the diet of a breastfeeding mother if milk allergy is suspected in the infant and calcium supplements given.^{3,8} In a formula-fed infant, choice of formula is determined by the severity of the symptoms.^{3,8} Most infants respond to extensively hydrolysed formulas, where the milk protein is broken down. Amino acid formulas should be reserved for severe symptoms and those not responding to an extensively hydrolysed formula.^{3,8}

An amino acid formula should also be used first line if top-up feeds are required in an infant who is exclusively breast fed and shows symptoms suggestive of cow's milk allergy.⁸

Acquisition of tolerance in cow's milk allergy should be considered after at least 6 months on a diet free from milk protein. It is likely that tolerance to extensively baked milk products will occur before that to less well cooked milk.⁸

Box 2 summarises the differences between non-IgE-mediated cow's milk allergy and lactose intolerance. Some other important facts on diet in milk allergy:

- soya is not recommended before 6 months of age due to it containing isoflavones, which may exert a weak oestrogenic effect. There is also a risk of cross-reactivity: up to 14% of those with IgE-mediated cow's milk allergy also react to soya and up to 60% of those with non-IgE-mediated cow's milk allergy;⁴
- rice milk is not recommended in those aged <4.5 years due to the arsenic content; and⁹
- there is cross-reaction between mammalian milks. Goat's milk and products are not suitable for infants with cow's milk allergy.⁴

CONCLUSION

There are important differences between lactose intolerance and milk allergy. Knowing these differences should result in increased recognition of milk allergy

and reduce the incorrect 'labelling' of children as having 'lactose intolerance' or 'milk intolerance'. The appropriate tests can then be requested and appropriate diets commenced. As a result, symptoms should resolve more quickly, reducing the economic burden and giving children and their families an improved quality of life.

Further details on the appropriate management of milk allergy in primary care, along with an algorithm for assessment and diagnosis, are available in the form of the Milk Allergy in Primary Care (MAP) guideline.⁸

Provenance

Freely submitted; externally peer reviewed.

Competing interests

James Quekett is employed by Doctors.net.uk, who have received educational grants from companies producing infant formulas for the management of milk allergy and lactose intolerance. The other authors have acted as consultants, given educational lectures, or received educational grants for travel and meeting attendance from companies producing infant formula feeds for medical purposes.

Discuss this article

Contribute and read comments about this article: bjgp.org/letters

REFERENCES

1. National Institute for Health and Care Excellence. *Food allergy in children and young people: diagnosis and assessment of food allergy in children and young people in primary care and community settings*. CG 116. 2011. <https://www.nice.org.uk/guidance/cg116/evidence/full-guideline-136470061> [accessed 27 Jun 2016].
2. Fiocchi A, Brozek J, Schünemann H, *et al*. World Allergy Organization (WAO) diagnosis and rationale for action against cow's milk allergy (DRACMA) guidelines. *World Allergy Organ J* 2010; **3(4)**: 57–161.
3. National Institute for Health and Care Excellence. *Cows' milk protein allergy in children*. 2015. <http://cks.nice.org.uk/cows-milk-protein-allergy-in-children> [accessed 27 Jun 2016].
4. Lozinsky AC, Meyer R, Anagnostou K, *et al*. Cow's milk protein allergy from diagnosis to management: a very different journey for general practitioners and parents. *Children* 2015; **2(3)**: 317–329.
5. du Toit G, Meyer R, Shah N, *et al*. Identifying and managing cow's milk protein allergy. *Arch Dis Child Educ Pract Ed* 2010; **95(5)**: 134–144.
6. Büller HA, Rings EH, Montgomery RK, *et al*. Clinical aspects of lactose intolerance in children and adults. *Scand J Gastroenterol Suppl* 1991; **188**: 73–80.
7. Ludman S, Shah N, Fox AT. Managing cow's milk allergy in children. *BMJ* 2013; **347**: f5424.
8. Venter C, Brown T, Shah N, *et al*. Diagnosis and management of non-IgE-mediated cow's milk allergy in infancy — a UK primary care practical guide. *Clin Transl Allergy* 2013; **3(1)**: 23. DOI:10.1186/2045-7022-3-23.
9. Food Standards Agency. *Survey of total and inorganic arsenic in rice drinks*. 21 May 2009. <http://webarchive.nationalarchives.gov.uk/20120206100416/http://food.gov.uk/news/newsarchive/2009/may/arsenicinriceresearch> [accessed 4 Jul 2016].