

News Summary

Advancing on Allergy: Experts gaining ground in managing cow's milk protein allergy in infants

- ***Cow's milk protein is one of the leading causes of food allergy in infants and young children below three years of age***
- ***Success factors emerging: closing gap between Guidelines and practice remains a continuing priority***

Vevey, Switzerland, August 2014 – Speaking at two Nestlé Nutrition Institute (NNI) Satellite Symposia organised during EACCIⁱ and ESPGHANⁱⁱ 2014, leading experts in the field of allergy and paediatric health indicated that they are gaining ground in the science and practice of how to best manage cow's milk protein allergy (CMPA), which is a major type of food allergy in children below three years of age.ⁱⁱⁱ If not suitably managed, CMPA not only has short-term clinical implications (such as eczema and gastrointestinal symptoms) but can have long-term implications on healthy growth and development, not to mention the considerable emotional and physical challenges it poses for the child and their parents. A more structured and informed approach to CMPA management is emerging – helping to close the gap between guidelines and practice – vitally important for a condition prevalent in upwards of 2-3% of infants.^{iv}

Start point: Early and effective diagnosis

Speaking at the ESPGHAN NNI event, **Dr. Ralf Heine** (Department of Gastroenterology & Clinical Nutrition, Royal Children's Hospital, Murdoch Children's Research Institute, University of Melbourne, Australia), crystallised the importance of an early and pro-active approach to diagnosis and intervention in infants with gastrointestinal (non-IgE-mediated) CMPA. He explained the main goal of intervening early is to prevent the gastrointestinal complications of growth failure, micronutrient deficiencies, aversive feeding behaviours and sleep pattern disturbance and also, of course, family stress. *"We need to recognise the allergy and intervene early to prevent growth and health complications. If children are not improving with our interventions, we must reconsider our diagnosis."* According to Dr. Heine, this translates into healthcare professionals ruling out other relevant gut pathology, confirming the diagnosis by elimination followed by re-challenge, and then re-assessing the child's progress, including key growth parameters.

Dr. Heine explained that in everyday clinical practice, early intervention can be a real challenge and be delayed due to diagnostic confusion. This is because symptoms for gastrointestinal CPMA can be fairly non-specific and overlap with several common childhood conditions. These include coeliac disease, gastro-oesophageal reflux disease and lactose malabsorption. Primary lactose intolerance is rare in infancy, whereas secondary (transient) lactose intolerance is relatively common after viral gastroenteritis. There are also different types of food allergy for healthcare professionals to consider. For example, there is confusion between IgE-mediated and non-IgE-mediated food allergy, and also multiple food protein intolerance: *"Multiple food protein intolerance of infancy is a complex, multi-factorial disease in which infants do not appear to tolerate any food, even breast milk or simple weaning solids. Clinically, they only respond to amino acid-based formula,"* advises Dr Heine.

At EACCI NNI event, further insights into the complexity of the condition and the value of starting the diagnosis process early were shared by **Professor Arne Høst** (Department of Paediatrics, Hans Christian Andersen's Children's Hospital, Odense University Hospital, Denmark). He explained that most infants with CMPA develop symptoms before one month of age, or within one week of the introduction of CMP-based formula, adding, *"There are more than 25 different cow's milk proteins and a child may react against one or more of them."*

Multidimensional management central to expert guidelines

To assist healthcare professionals in managing CMPA, the GI committee of ESPGHAN recently published a practical algorithm for the diagnostic work-up for children with suspected CMPA, management and follow-up of children with proven CMPA.^v The algorithm includes a strict diagnostic elimination of cow's milk protein from the child's diet, with documentation of signs and symptoms followed

in most cases by a timely challenge procedure: “If stringent diagnostic criteria are not applied, including food challenge procedures, the risk of over- and under-diagnosis – and thus over- and under-treatment – is high,” explained **Professor Sibylle Koletzko** (Dr. von Hauner Children’s Hospital, Ludwig Maximilians University Munich, Germany) when presenting and discussing how to apply the ESPGHAN guidelines in clinical practice.

In addition, the EACCI Food Allergy and Anaphylaxis guidelines^{vi} also provide evidence-based advice to help healthcare professionals manage CMPA, translate evidence into best practice, as well as reduce current variation in practice. The EACCI guidelines, presented by **Professor Antonella Muraro** (Veneto Region Referral Centre for Food Allergy Diagnosis and Treatment, Padua General University Hospital, Italy) advise on when to use extensively hydrolysed cow’s milk formula, amino acid formula, soy formula and probiotic supplements:^{vi}

- Use extensively hydrolysed cow’s milk formula as first choice for the treatment of cow’s milk allergy, especially in infants and young children
- Amino acid formula can also be recommended, especially for patients with more severe symptoms
- Soy formula should not be recommended before six months of age, nor at any age in the presence of GI symptoms, but can be considered on a case-by-case basis from 6-12 months of age
- Probiotic supplements cannot be recommended for the management of food allergy.

Professor Muraro summarises: “The conclusions for cow’s milk substitute is that this should be adequate for growth, development and full nutrition and that the selection of a proper formula should be balanced against age, type of food allergy, severity of food allergy, the extent of gastrointestinal symptoms, history of life-threatening reactions and nutritional requirements. Studies show the usefulness of extensive hydrolysed formula, and amino acid formula as a long-term treatment. Soy formula can be considered as a nutritional option in children who refused extensive hydrolysates and who don’t present GI symptoms. She also called for more research on rice hydrolysed formulas. As additional guidance, **Professor Muraro** noted, “Hypoallergenic formulas, both for therapy and prevention, show remarkable differences according to the commercial brand. Therefore tolerance or reaction to one hypoallergenic formula cannot be extrapolated to another.”

Closing the gap between guidelines and clinical practice

Whilst the simplicity of available guidance, such as the ESPGHAN algorithms, is adding to their uptake and implementation, still too often guidelines are not being followed, according to Professor Koletzko. In line with **Dr. Heine’s** observations, she explained that there are many reasons for this, including confusion between the signs and symptoms of CMPA and lactose intolerance, and low awareness/recognition of CMPA. Whatever the reasons - which may differ in each country and in each individual case - they must be identified and addressed since, if the diagnosis of CMPA is missed, consequences include failure to thrive and needless suffering; alternatively, if management is introduced but is inappropriate, children might be kept on a cow’s milk protein-free diet unnecessarily.

Professor Koletzko expressed the view that the healthcare profession needs to take responsibility to ‘educate’ and shift practice further: “The task required of healthcare professionals is to spread the word as there is a high risk of over- and under-diagnosis and over- and under-treatment in CMPA. This results in a risk of poor nutrition for the child, potential child under-development, burden for the family, reduced quality of life and increased costs for society.”

A public health imperative

Considering that the incidence of cow’s milk protein allergy (CMPA) in early childhood is approximately 2-3% and even higher in some developed countries, as shown by **Professor Høst**, it is apparent that this is now an important public health challenge needing to be addressed at the local, national and international level.

Some countries, such as Finland, have chosen to address CMPA and other allergies head on in public health programmes, as explained at the NNI EACCI event by **Erkka Valovirta** (Department of Pulmonary Diseases and Clinical Allergology, University of Turku, and Terveystalo Allergy Clinic, Finland). He gave insights into the comprehensive nature of his home country’s plan to reduce the allergy burden in society and change attitudes to allergy. The Finnish Allergy Programme (2008-2018)^{vii} is positioned as an integral part of healthy lifestyle for all children, whether allergic or not. It also emphasises the need to focus on severe allergies and reduce allergic attacks. Despite only having been introduced five years ago – a relatively short timescale for a public health initiative - this programme has already shown impressive

population benefits in raising awareness of allergies and significantly reducing their incidence in children. In the near future, 'Case Finland' will be published providing a model for other countries to build upon and adapt to their local needs. It will describe the Finnish Allergy programme and how it has been embedded throughout the healthcare system and public mindset.

A positive future

Expert-driven guidelines for managing CMPA from both EACCI and ESPGHAN now clarify the recommended approach to CMPA and with on-going education effort - as outlined by **Professor Koletzko** - this should help avoid inconsistencies in approach to this problem and reduce variation in clinical practice.

Looking to the future, **Dr Heine** highlighted that the diagnosis of non-IgE-mediated food allergy "*is still fraught with difficulties and that we urgently need (research to establish) better in vitro markers*". **Professor Muraro** envisions an increasingly holistic approach will be beneficial, "*The management of CPMA as well as food allergy in general should be multi-disciplinary and multi-faceted, with dietary avoidance, education, pro-active treatment and networking between centres of excellence and primary care are the main pillars.*"

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Notes to editors:

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Link to the Symposium [Abstract](#):

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Key references for further reading:

- ⁱ European Academy of Allergy and Clinical Immunology (EAACI) 2014, 7-11 June, Copenhagen, Denmark: NNI Satellite Symposium 'Success Factors for Preventing Food Allergies, Diagnosing and Managing Cow's Milk Protein Allergy in Line with Recommendations'.
- ⁱⁱ 47th Annual Meeting of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), 9 -12 June, Jerusalem, Israel: NNI Satellite Symposium 'Success Factors for Preventing Food Allergies, Diagnosing and Managing Cow's Milk Protein Allergy in Line with Recommendations'.
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- ^v Koletzko S., Niggemann B, Arato A, Dias JA, Heuschkel R, Husby S, Mearin ML, Papadopoulou A, Ruemmele FM, Staiano A, Schäppi MG, Vandenplas Y. Diagnostic approach and management of cow's-milk protein allergy in infants and children: ESPGHAN GI Committee practical guidelines. JPediatr Gastroenterol Nutr 2012; 55: 221-29.
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- ^{vii} Haahtela T, von Hertzen L, Mäkelä M, Hannuksela M; Allergy Programme Working Group. Finnish Allergy Programme 2008-2018-time to act and change the course. Allergy. 2008 Jun;63(6):634-45.