

### **Practical Tips for Paediatricians**

# Practical tips for the use of the Canadian milk ladder for paediatricians

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#### BACKGROUND

Cow's milk allergy is a common cause of anaphylaxis in children although most milk-allergic children can ingest extensively baked milk (BM) without an allergic reaction (1,2). BM ingestion in these children can accelerate milk tolerance (1,2). Milk ladders are home-based tools to support parents with introducing milk products into a milk-allergic child's diet (3). This approach carries a risk of allergic reactions and needs informed consent. In parallel to the milk ladder, public health efforts should be made to prevent milk allergies through education about the importance of early and sustained exposure to cow's milk formula (4-6).

#### MILK ALLERGENICITY AND TOLERANCE

Heating milk causes conformational changes in milk protein altering its ability to induce allergic reactions (1). Approximately 75% of children who are allergic to liquid, pasteurized milk are non-reactive to milk which has been baked into wheat-based muffin (1).

## MEDICALLY-SUPERVISED ORAL FOOD CHALLENGE TO BAKED MILK

To discover if a child can tolerate BM, allergists can offer a medically-supervised BM oral food challenge (OFC). The child would eat a BM muffin over a few hours. The OFC reveals the child to be allergic or not allergic that very day. Children who tolerate BM muffins will likely outgrow their milk allergy and are encouraged to routinely eat BM (1). Children who are BM reactive may have a severe allergic reaction (1,5).

#### THE HOME-BASED MILK LADDER

An alternative approach to introducing BM is the milk ladder. Milk ladders outline a home-based graded introduction of milk products (3). The ladder can be more accessible than waiting for referral and scheduling an OFC. One version of the ladder has four steps containing increasingly less cooked milk ingredients (3). If there is no existing knowledge of a child's tolerance/reactivity to BM, selected children are advised to start on step 1: extensively BM (e.g., muffin or cookie) with daily, grain-sized amounts that increase in quantity over days/weeks until they reach a serving size. After 1 to 3 months at a full serving, the child may advance to step 2: a grain-sized amount of waffles or pancakes. The third step is baked cheese and boiled milk, and the final stage begins with unbaked milk products such as cheese and pasteurized milk. If the child develops any allergic symptoms, they go back to the previous tolerated step for a month before re-attempting the higher step again.

#### PATIENT SELECTION

If the milk ladder is initiated with no knowledge of a child's BM tolerance, some will be BM allergic and therefore have a risk of severe reactions (1,5,7). This risk can be reduced by choosing low-risk children.

Age is a dominant consideration. BM ingestion can be considered a form of oral immunotherapy (OIT) (7). Milk ladder safety studies have been mainly done in the infants and preschoolers (3,8,9), but can be inferred from OIT studies demonstrating safety in preschoolers compared to older children (3,9).

Baked milk reactivity can rapidly resolve in young milkallergic children, especially in children under 2 years old (10,11). In milk-allergic children who are BM-tolerant, the first steps of the ladder identify and support their BM tolerance and prevent total avoidance of milk products. For these children, cautious progression to steps 3 and 4 is low risk of a severe reaction because they will likely outgrow their allergy (1).

Overall, the home introduction of BM by a ladder has the most evidence for preschool-aged children (<6 years old), with well-controlled/no asthma, no history of anaphylaxis to milk, whose families will follow the instructions (9). A Food Ladder Safety Checklist has been proposed with the mnemonic 'the 4 A's', looking at age, asthma control, anaphylaxis history and adherence (9).

#### PARENT PREPARATION

Food ladders should be administered with informed consent and a shared decision-making model by clinicians with food allergy expertise (9). Counselling is required so parents understand each stage and how to treat IgE-mediated reactions including how to administer an epinephrine autoinjector (9). Parents should also be aware that if there are any co-factors that decrease the allergic threshold, such as excessive exercise, febrile illness, hot baths, an empty stomach, increased allergenic exposure (i.e., pollen season), milk products should be offered with close monitoring (12). Follow-up every 6 months to evaluate safety and progress has been suggested (3,9). During follow-ups, a general paediatrician can optimize asthma management to ensure excellent asthma control (9).

#### **CONCLUSIONS**

Cow's milk ladders are a home-based opportunity for dietary expansion and to reveal and support development of milk tolerance in children with low-risk milk allergies, while reducing the need for in-office OFCs. With more families using milk ladders, paediatricians play a central role in supporting these patients.

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#### POTENTIAL CONFLICT OF INTEREST

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#### REFERENCES

- Upton J, Nowak-Wegrzyn A. The impact of baked egg and baked milk diets on IgE- and non-IgE-mediated allergy. Clin Rev Allergy Immunol 2018;55:118–38.
- Kim JS, Nowak-Wgrzyn A, Sicherer SH, Noone S, Moshier EL, Sampson HA. Dietary baked milk accelerates the resolution of cow's milk allergy in children. J Allergy Clin Immunol 2011;128:125–131.e2.
- Chomyn A, Chan ES, Yeung J, et al. Canadian food ladders for dietary advancement in children with IgE-mediated allergy to milk and/or egg. Allergy Asthma Clin Immunol 2021;17:83.
- 4. Anagnostou A, Upton J, Nowak-Wegrzyn A. Cow's milk formula each day may keep milk allergy away. Ann Allergy Asthma Immunol 2023;130:151–2.
- Yonkof JR, Mikhail IJ, Prince BT, Stukus D. Delayed and severe reactions to baked egg and baked milk challenges. J Allergy Clin Immunol Pract 2021;9:283–289.e2.
- Lachover-Roth I, Cohen-Engler A, Furman Y, et al. Early, continuing exposure to cow's milk formula and cow's milk allergy: The COMEET study, a single center, prospective interventional study. Ann Allergy Asthma Immunol 2023;130:233–239.e4.
- Mack DP, Greenhawt M, Anagnostou A. Are there hidden dangers associated with milk and egg dietary advancement therapy? J Allergy Clin Immunol Pract 2023;11:1056–62.
- Ball HB, Luyt D. Home-based cow's milk reintroduction using a milk ladder in children less than 3 years old with IgE-mediated cow's milk allergy. Clin Exp Allergy 2019;49:911–20.
- Chua GT, Chan ES, Yeung J, et al. Patient selection for milk and egg ladders using a food ladder safety checklist. Allergy Asthma Clin Immunol 2022;18:51.
- 10. Cogurlu MT, Simsek IE, Aydogan M, Uncuoglu A, Acar HC. Prospective evaluation of tolerance to unheated milk-boiled egg after baked milk-egg tolerance under 2 years. Ann Allergy Asthma Immunol 2022;129:742–50.
- 11. Wong D, Eiwegger T, Upton J. Avoiding avoidance in milk and egg allergy. Ann Allergy Asthma Immunol 2022;1129:657–658.
- Wasserman RL, Factor J, Windom HH, et al. An approach to the office-based practice of food oral immunotherapy. J Allergy Clin Immunol Pract 2021;9:1826–1838.e8.