Exploring immunological mechanisms in cow’s milk allergy
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DIAGNOSIS AND MANAGEMENT OF COW’S MILK PROTEIN ALLERGY

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LETTER TO THE EDITOR

To the editor,

With interest we have read the review by VandenPlas and coworkers(1) in which guidelines for the diagnosis and management of cow's milk protein allergy (CMPA) in infants are discussed and general recommendations with respect to these issues are given. The authors present two diagnostic algorithms, on which we would like to comment.

The authors developed separate diagnostic algorithms for exclusively breast-fed and formula-fed infants with a suspicion of CMPA. In both algorithms a clinical assessment divides the flow chart into two branches: suspicion of mild to moderate CMPA or suspicion of severe CMPA. Symptoms that put the child at an immediate life-threatening risk or may interfere with the child's normal development, differentiate severe from mild to moderate CMPA. Children with a suspicion of severe CMPA are referred to a paediatric specialist and a food challenge will be performed in a hospital setting.

Our first comment on the presented diagnostic algorithms concerns the manner at which the diagnosis CMPA is confirmed. Nowadays the food challenge, preferable a double blind placebo controlled challenge (DBPCFC), is the gold standard for the diagnosis of food allergy. The food challenge is part of a diagnostic procedure that includes three phases: elimination of the suspected food, challenge with the suspected food, and re-elimination. For simplicity and socio-economic reasons an open food challenge instead of a DBPCFC is recommended by the authors. It is well known that the diagnosis of food allergy based on an open food challenge will result in large numbers of false positive diagnoses. To limit this number of false positive diagnoses, the diagnostic procedure should include the three phases mentioned above. Unfortunately, in both diagnostic algorithms the re-elimination phase is not mentioned.

Second, in the algorithm for formula-fed infants angio-edema and urticaria are described as mild to moderate symptoms. This implies that children with these symptoms are not referred to a paediatric specialist and a food challenge will be performed in a non-hospital setting, with which we strongly disagree. Urticaria and angio-edema are both manifestations of a systemic reaction and are the most common manifestations of anaphylaxis.(2,3) No clear data are available that describe the risk of a severe life threatening allergic reaction in children suspected of CMPA with initial symptoms such as urticaria and angio-edema. For other food allergies such as nut allergy, it is known that severity of subsequent reactions can not be predicted by history alone.(4) Furthermore, in children with initial mild symptoms such as atopic eczema dermatitis syndrome, acute allergic reactions to cow's milk after a prolonged cow's milk protein diet are described.(5) In our opinion children with initial symptoms of angio-edema and generalized urticaria are at risk of a similar or even severe allergic reactions when they are challenged with the suspected food. Therefore, a challenge test should be performed in a hospital.
setting supervised by a medical staff experienced in recognizing and managing severe allergic reactions.

Third, the instructions how to perform a food challenge in formula-fed infants are incomplete. The authors propose a challenge protocol with a stepwise increased dose scheme expressed in milliliters formula. No instructions are given about the amount of cow’s milk protein needed in each dose step. The amount of cow’s milk protein is different in each infant formula. Therefore the guideline should provide information about the amount of cow’s milk protein in milligrams needed in each challenge step.

Furthermore, no instructions are given by the authors how to perform a food challenge in breast-fed infants. According to the national guideline of the baby health clinics in the Netherlands,\(^6\) we propose that a food challenge in breast-fed infants is performed by instructing the mother to drink a stepwise increasing amount of milk on three consecutive days (up to 500ml daily). If symptoms of CMPA re-appear, the challenge is followed up by a re-elimination phase of one week. If no reaction occurs, the mother is instructed to drink 500ml milk each day for the next two weeks and the parents are told to observe the child for late reactions.

In summary, children suspected of CMPA need to complete a diagnostic procedure including a re-elimination phase to confirm the diagnosis CMPA. Furthermore, children suspected of CMPA with initial symptoms such as urticaria and angio-edema should be referred to a paediatric specialist and a food challenge needs to be performed in a hospital setting. Finally, instructions on how to perform a food challenge should include the amount of cow's milk protein needed in each challenge step.
REFERENCES