Atopic Dermatitis and Skin Barrier Function in Infancy and Early Childhood

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Teresa Løvold Berents, a dermatologist at Oslo University Hospital, on September 7, 2017 defended her doctoral thesis titled "Atopic dermatitis and skin barrier function in infancy and early childhood" with Petter Gjersvik as main supervisor. Opponents were Åke Svensson, Malmö, Sweden, and Marit Saunes, Trondheim, Norway.

Atopic dermatitis is a common, chronic and relapsing eczematous disease, typically manifesting in early life. The pathogenesis of atopic dermatitis is complex, with interactions of multiple genetic, biological and environmental factors leading to skin barrier dysfunction, altered immunological response and increased susceptibility to *Staphylococcus aureus* (*S. aureus*) colonization.

The overall aim of the studies was to investigate some established and potential risk factors for the development of atopic dermatitis in early life, especially the role of skin barrier dysfunction, *filaggrin* mutation status, upper airway colonization of *S. aureus*, excessive weight-for-length and vitamin D levels. Infants living in south-east Norway and participating in a clinical trial on acute bronchiolitis treatment, either as patients ($n=404$) or as controls recruited from the general population ($n=240$), were assessed in infancy (mean age 5.1 months) and at a follow-up visit 18 months later (mean age 24.6 months), all within the period 2010–2014. Atopic dermatitis was diagnosed using the Hanifin & Rajka criteria and/or based on caretakers' history of physician-diagnosed atopic dermatitis. Disease severity was assessed using the SCORing Atopic Dermatitis (SCORAD) index. Data on weight and length at birth were obtained. Weight and length in infancy and at two years of age were measured at the clinical investigations. Transepidermal water loss (TEWL) was measured using an open chamber device on volar forearm and lateral upper arm to assess skin barrier function, with high levels indicating reduced barrier function. Samples for bacterial cultures were taken from the vestibulum nasi and fauces. Blood samples were analysed for vitamin D levels and for *filaggrin* mutations common in the European population.

Measurements of TEWL on the lateral upper arm and volar forearm appeared equally appropriate to assess skin barrier function in infants (1). *S. aureus* colonization in vestibulum nasi and/or fauces was not associated with high TEWL (1). In children without atopic dermatitis in infancy, high TEWL in infancy was significantly associated with atopic dermatitis at follow-up 18 months later, indicating that skin barrier dysfunction may precede the development of atopic dermatitis, although the sensitivity, specificity and positive predictive values were low (2). Atopic dermatitis at both time visits was associated with excessive weight-for-length in infancy, but not with excessive weight-for-length at birth or with early weight gain velocity (3). Vitamin D levels were not associated with

From left to right: Siri Rostoft (acting dean), Marit Saunes (2nd opponent), Åke Svensson (1st opponent), Teresa Løvold Berents, Petter Gjersvik (main supervisor), Karin Lødrup Carlsen (co-supervisor), and Tom Stiris (evaluation committee chair).

atopic dermatitis, and in children without atopic dermatitis in infancy, vitamin D levels did not predict atopic dermatitis 18 months later (4). Having a *filaggrin* mutation was significantly associated with high TEWL and atopic dermatitis (1, 2), but not with weight-for-length (3) or with vitamin D levels (4).

The results confirm the role of skin barrier dysfunction and *filaggrin* mutations in the development of atopic dermatitis in early life. Also, the results suggest that upper airway colonization of *S. aureus* is related to atopic dermatitis by factors other than skin barrier dysfunction, and that excessive weight-for-length in some way appears related to the development of the disease. The results do not support a hypothesis that vitamin D levels are associated with atopic dermatitis in early life, questioning the use of vitamin D supplements to prevent or treat atopic dermatitis.

List of original publications

1. Berents TL, Carlsen KC, Mowinckel P, Skjerven HO, Kvenshagen B, Rolfsjord LB, et al. Skin barrier function and Staphylococcus aureus colonization in vestibulum nasi and fauces in healthy infants and infants with eczema: a population-based cohort study. PloS One 2015; 10: e0130145.
2. Berents TL, Lødrup Carlsen KC, Mowinckel P, Skjerven HO, Rolfsjord LB, Bradley M, et al. Transepidermal water loss in infancy associated with atopic eczema at 2 years: a population-based cohort study. Br J Dermatol 2016 Nov 3. [Epub ahead of print]
3. Berents TL, Carlsen KCL, Mowinckel P, Skjerven HO, Rolfsjord LB, Nordhagen LS, et al. Weight-for-length, weight gain velocity and atopic dermatitis in children during infancy and at two years of age. BMC Pediatr 2017; 17: 141.
4. Berents TL, Lødrup Carlsen KC, Mowinckel P, Sandvik L, Skjerven HO, Rolfsjord LB, et al. Vitamin D levels and atopic eczema in infancy and early childhood in Norway: a cohort study. Br J Dermatol 2016; 175: 95–101.