trauma are observed, and instead we should ask the question 'Do you have any pain related to your AD or are your skin lesions painful?' If the answer is 'yes', then we should address the frequency and intensity of pain as this can impact treatment decisions moving forward.

We should also consider whether rapid treatment initiation results in improvements in pain and thus QoL. Thyssen *et al.*[5] also explored the use of analgesic medication and found no increased use of analgesics in patients with AD compared with controls. The authors extrapolate these findings to suggest that treatment of AD reduces skin pain. However, care should be taken when interpreting these results as the study does not address the reasons why analgesics were being prescribed. Future longitudinal studies are needed to examine this issue further, as an increased understanding of the full burden of AD, including assessment of pain, is necessary if we are to develop better and more efficient treatment strategies for our patients.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

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Growth profile and anaemia in children with epidermolysis bullosa

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Linked Article: Reimer *et al.* Br J Dermatol 2020; **182**:1437–1448.

In the severe variants of epidermolysis bullosa (EB), extensive skin fragility with generalized trauma-induced blistering and wounding of skin and mucosal sites as well as extracutaneous multiorgan involvement cause significant morbidity and mortality.[1]

Malnutrition and feeding difficulties are prototypic for these EB phenotypes and commonly result from the disruption of epithelial linings within the oropharyngeal and gastrointestinal tract that limit nutritional intake and/or nutrient absorption.[2] Painful blistering, scarring and strictures may cause dysphagia, gastroesophageal reflux, constipation and secondary anorexia. Nutritional impairment is further enhanced by transcutaneous/transmucosal loss of nutrients and hypermetabolism associated with accelerated skin turnover, permanent wound healing, natural growth as well as chronic inflammation and infection following skin barrier disruption.[3] Malnutrition also results in complications including failure to thrive, osteopenia/osteoporosis, secondary hypogonadism with delayed puberty as well as anaemia.[3,4]

Facing this significant burden, a timely diagnosis of macro- and micro-nutrient deficiencies and accurate supplementation are considered essential to improve growth, pubertal development, bowel function, immune status and wound healing in EB.[2,5,6] With the aim of determining the course of growth and anaemia in children with EB and the impact of nutritional compromise, inflammation and genetic factors Reimer *et al.* publish, in this issue of the BJD, a retrospective monocentric study of 200 young patients aged 0–25 years with recessive dystrophic EB (RDEB) and junctional EB (JEB) generalized intermediate.[7] Their growth charts were correlated with contextually relevant milestone clinical events (such as oesophageal stenosis, dilatation, gastrostomy and death), laboratory parameters (for anaemia, nutrition and inflammation as an indicator of wound burden) as well as molecular aberrations.

In the RDEB cohort, the authors found weight impairment to start early at 12–18 months and to be common with > 80% of young adults being underweight. Half of the patients showed stunting (impairment of height gain) after 10 years of age. Low levels of haemoglobin (detected in 91% of patients with RDEB and 75% of those with JEB from the second year of life onwards), iron, vitamin D, zinc and albumin, high levels of C-reactive protein and the absence of collagen VII in immunofluorescence staining correlated significantly with low weight only in RDEB, with no correlation observed in JEB.

In the context mentioned above, the investigations of Reimer *et al.* have implications of great clinical relevance, that include (i) clues regarding impact and the time frames for

weight measurement and sampling of distinct blood profiles to allow accurate prognostication and therapy planning in children; (ii) provision of EB-specific growth charts as more feasible assessment tools in daily practice that consider EB peculiarities; and (iii) data on scheduling gastrostomy and nutritional interventions to counteract profound nutritional deficits that in this cohort were shown to start before the age of 2 years.

The retrospective nature of the single-centre study harbours some limitations as mentioned by the authors: laboratory analyses were rarely performed within the first year of life; concomitant nutritional intakes, wound extent and compliance were not systematically recorded; the socioeconomic impact of resource-limited settings was not further delineated; and there was no further stratifying analyses of EB subtypes.

Notably, translating weight and height measurements (the latter may be challenging in affected individuals because of immobility or joint contractures) or distinct laboratory values into supplementary dosing regimens, accurate time points to start enteral nutrition and, more importantly, sustainable clinical benefit in patients with EB is as much critical as complex, and requires a highly individual approach. The latter depends on a broad spectrum of key variables being considered, including disease severity and extent of organ involvement, the presence of infection and an inflammatory state as well as the clinical milestones that alter an individual's nutritional requirements and daily feeding modalities such as weaning, teething, childhood diseases or start of school.[2]

Prospective studies are highly warranted, in particular to assess modalities and effects of nutritional interventions and supplementation in affected individuals – a challenging task in clinical research on rare diseases. Against this background, the paper by Reimer *et al.* provides relevant information and further evidence for the EB community that is valuable and that can be incorporated into clinical practice guidelines to target better wound healing, inflammatory pathways and anaemia as pathogenic traits in EB.

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The changing transcriptome in human skin following *in vivo* exposure to erythemal solar-simulated ultraviolet radiation

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The detailed and rigorous study by Bustamante *et al.* gives further insights into how sun-sensitive skin responds acutely to erythemal sunlight.[1] When buttock skin biopsies were taken 6 h after the exposure of seven sun-sensitive individuals to approximately double an erythemal dose (six standard erythema doses) of fluorescent solar-simulated radiation (FSSR), transcriptional changes in 4071 genes, i.e. approximately 20% of the human genome, were recorded. After 24 h, only 30% of those genes were expressed at levels different to those measured in unexposed skin. A sequential transcriptional response by human skin to erythemal ultraviolet (UV) radiation (UVR) emerged, as changes to mRNA levels for genes coding for apoptosis and keratinization were prominent after 6 h while, after 24 h, inflammatory and immunoregulatory genes were differentially expressed, as well as those for hyaluronan biosynthesis. Small changes in microRNA expression 6 and 24 h after exposure to FSSR were detected, suggesting minor regulatory effects. To help interpret outcomes, transcriptional changes were reported in skin from another cohort of volunteers 6 h and 24 h after exposure to a single erythemal dose