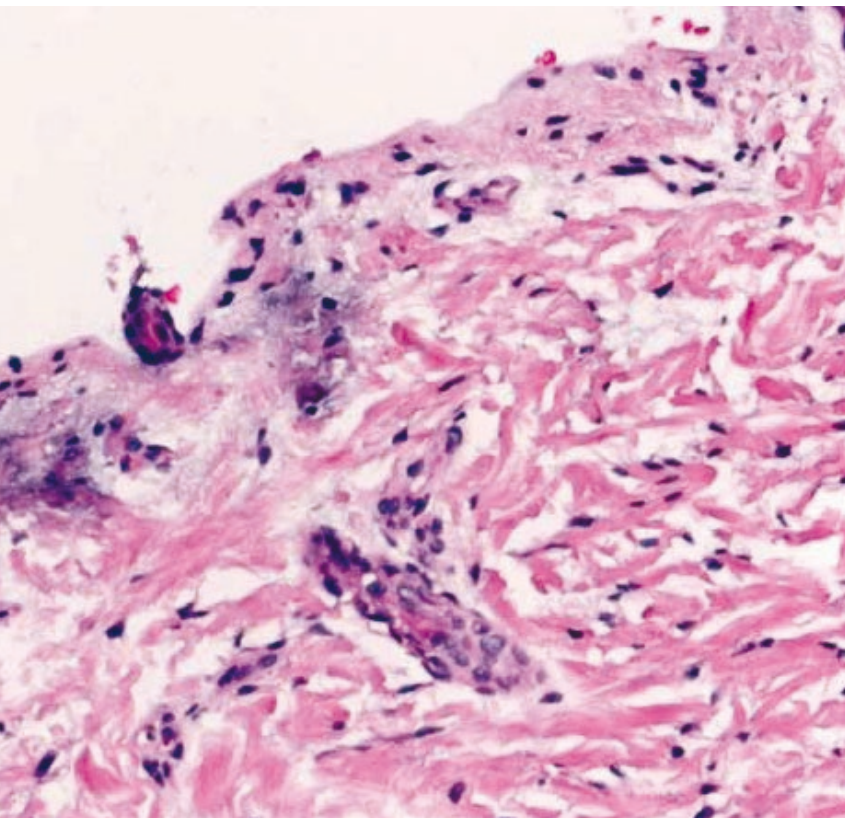


SWISS SOCIETY OF NEONATOLOGY

Epidermolysis bullosa

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This male infant was born by vacuum extraction at 39 4/7 weeks of gestation to a 35-year-old G2/P2 after an uneventful pregnancy. The mother's serologies, including HSV, were normal. No local vaginal colonisation with *B streptococci* was detected. There was no known family history of skin disorders, and his 3-year-old sister was in good health. Birth weight was 3110g (10th %ile), length 49 cm (3-10th %ile), head circumference 35cm (25-50th %ile). The newborn adapted well with Apgar scores of 7, 9 and 10 at 1,5 and 10 minutes, respectively. Immediately after birth the boy was noted to have extensive blistering of the skin on his face and both hands (Fig. 1, 2) and feet (Fig. 3, 4). Similar lesions were observed periorally and on the lips. The skin lesion on the left foot was characterized by an absence of the upper epidermal layers and two missing nails (Fig. 4), reminiscent of aplasia cutis. The infant appeared otherwise healthy and there was no evidence of an infectious process.

Histopathological examination of skin biopsies using electron microscopy demonstrated a zone of cleavage beneath the epidermal-dermal basal lamina (Fig. 5, 6). Immunofluorescence examination by antigen-mapping (Fig. 7, 8) confirmed the dermal localization (by detecting collagen IV and laminin). A thin basal lamina was attached to the epidermal surface of the blister; in contrast: no basal lamina remnant could be demonstrated on the denuded dermal surface. In addition, no anchoring fibrils (collagen VII) could

be identified, leading to the diagnosis of a dystrophic form of epidermolysis bullosa (probably EB dystrophica Hallopeau-Siemens).

Ultrastructural examination confirmed blistering at the base of the basal lamina (Fig. 9-11). The patient's further course was characterized by slow healing of the skin lesions and occasional development of new lesions. Analgesia with opioids could rapidly be weaned. At the time of discharge the boy was six weeks old, and his skin still presented older and newer lesions (Fig. 12, 13).



Fig. 1

Newly formed large blisters on the right hand.



Fig. 2

Aspect after rupture of blisters on the left hand.



Fig. 3

Extensive blistering on both feet.



Fig. 4

Skin lesion on the left foot, reminiscent of aplasia cutis.

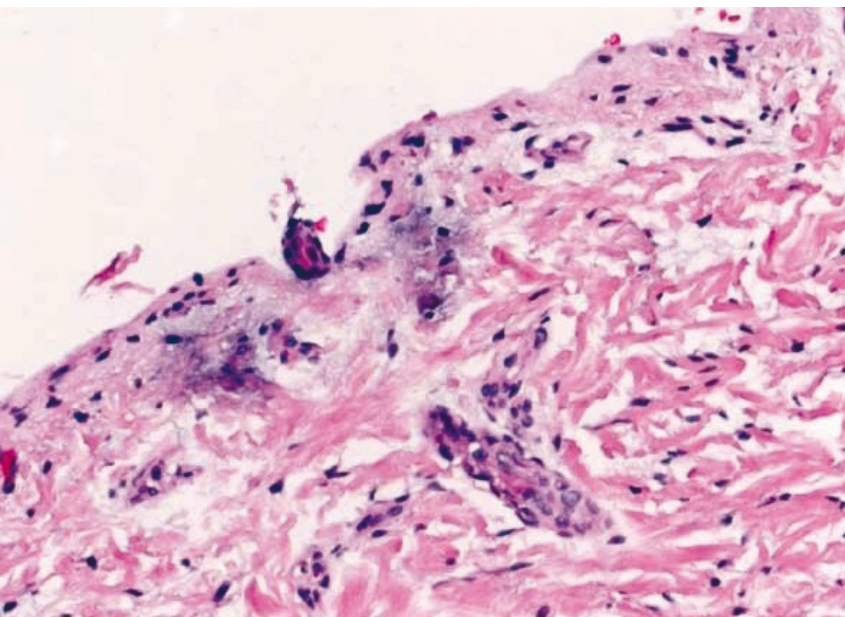


Fig. 5

Lymphocytes in aspirated pleural fluid.

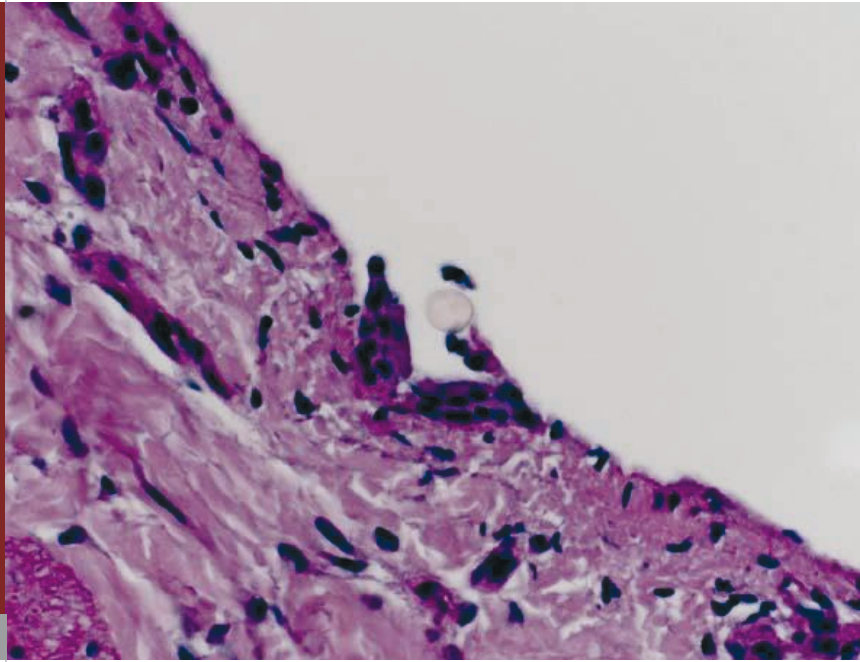
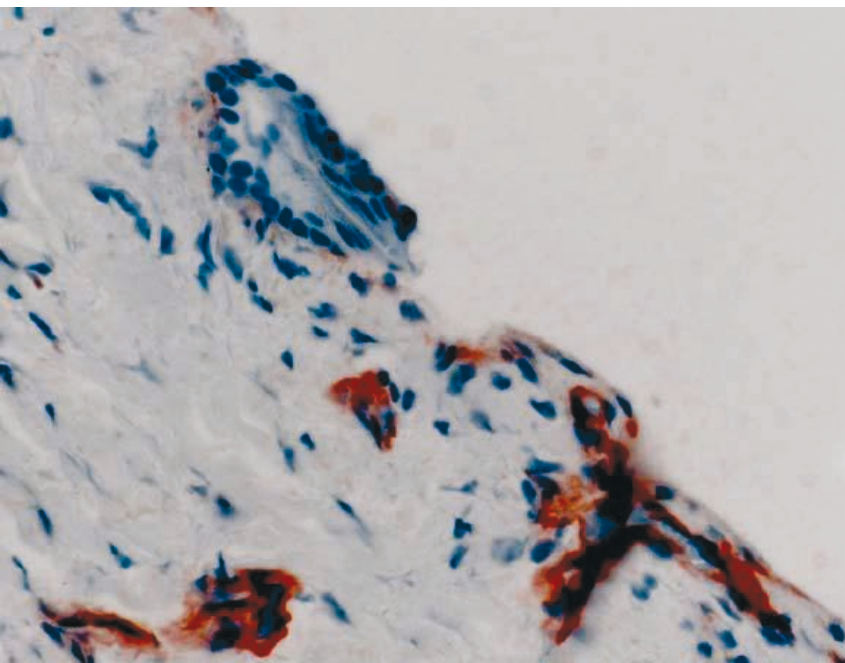


Fig. 6

Skin biopsy with completely denuded epidermis (LM: HE stain).

**Fig. 7**

*Skin biopsy with completely denuded epidermis
(LM: PAS stain).*

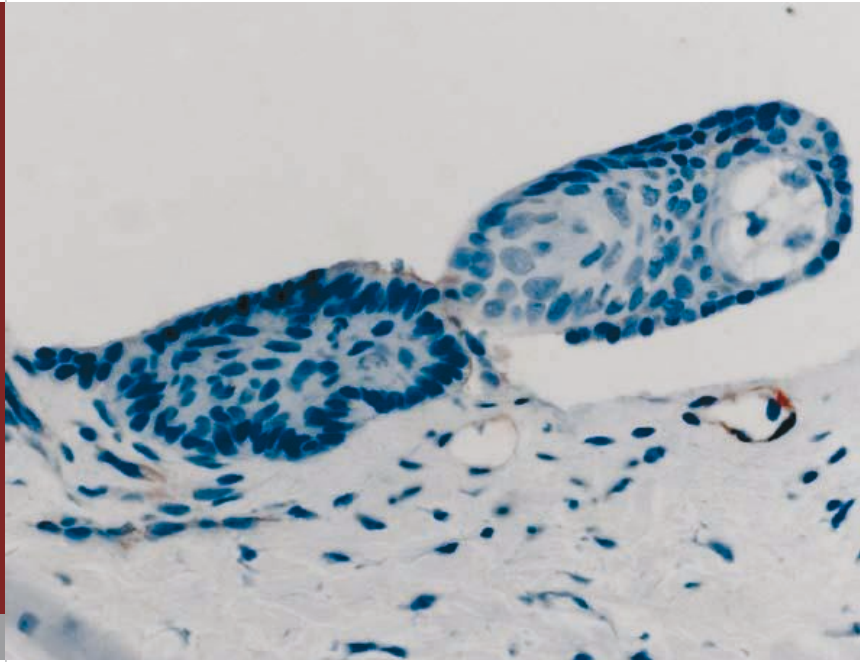


Fig. 8

Laminin immuno-histochemistry: a thin basal lamina is attached to the epidermal surface of the blister.

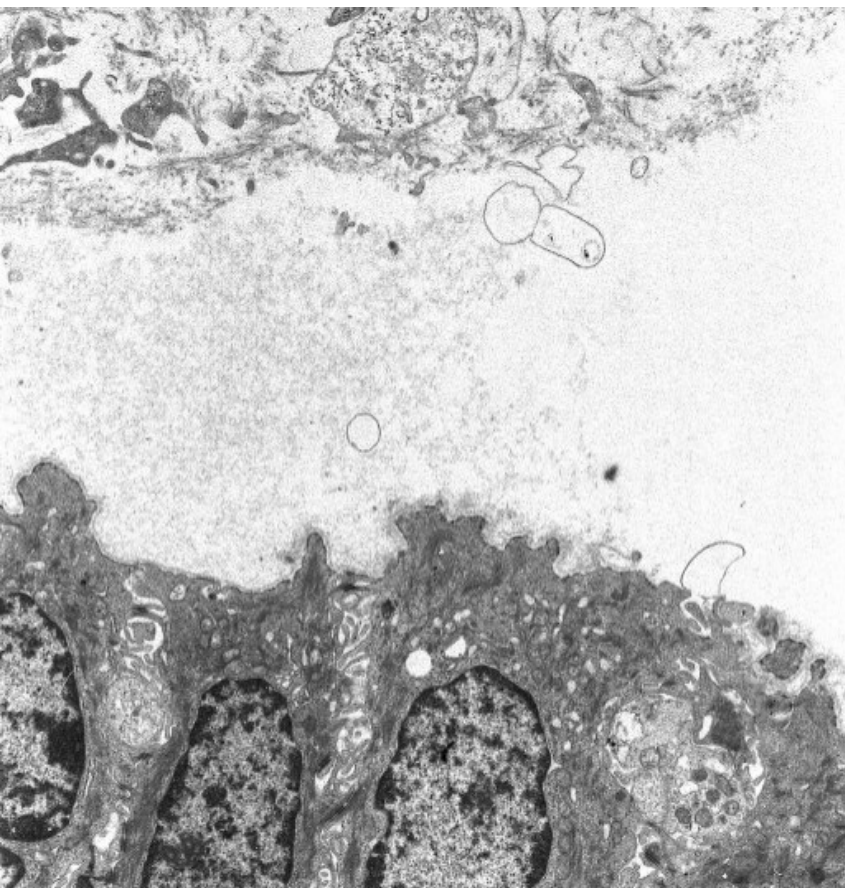


Fig. 9

TEM: Blistering at the base of the basal lamina.

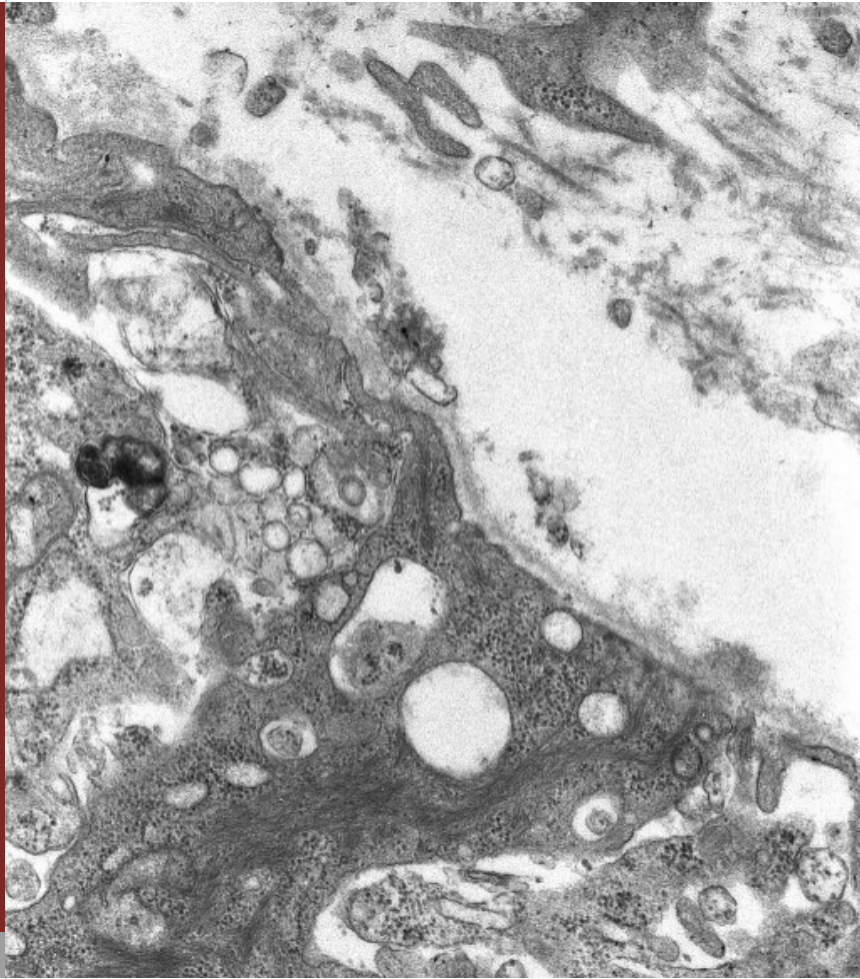


Fig. 10

TEM: Basal lamina is attached to the detached epidermis.

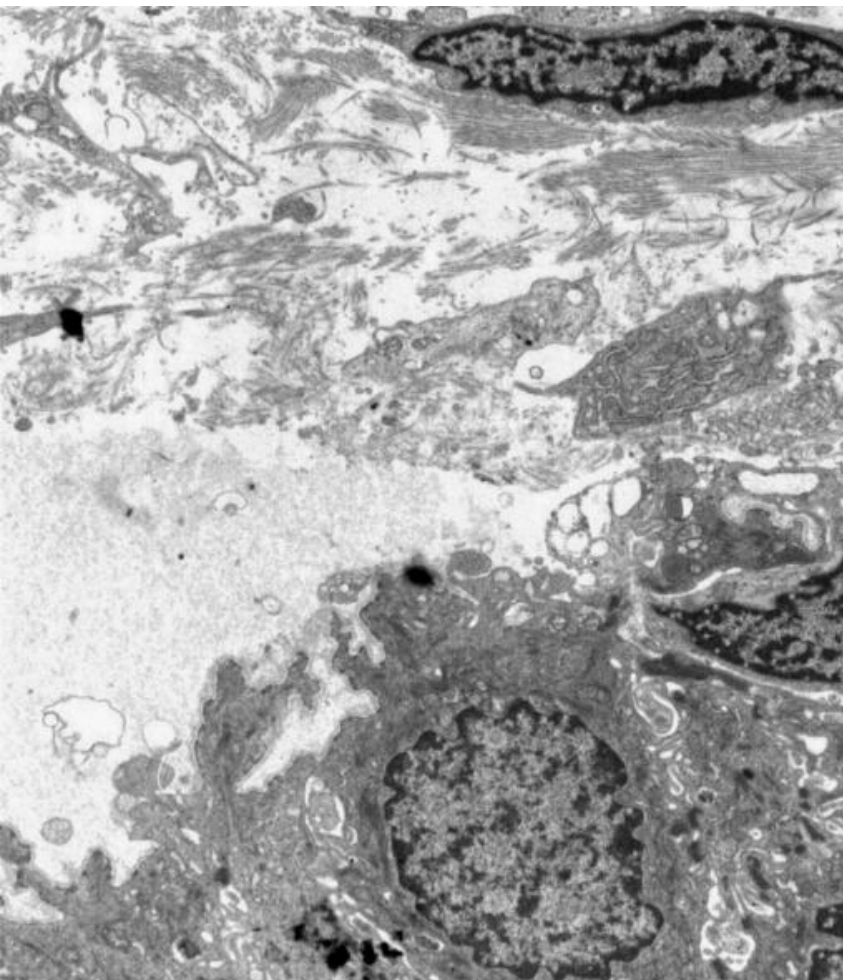


Fig. 11

TEM: No anchoring fibrils can be demon-strated.



Fig. 12

Skin condition at discharge (age 6 weeks): presence of older and newer skin lesions.

**Fig. 13**

Skin condition at discharge (age 6 weeks).

DISCUSSION

Epidermolysis bullosa (EB), a heterogeneous group of genetic skin disorders, is characterized by fragility and formation of blisters following minor trauma. The group includes up to thirty clinical-genetic entities (1) with both autosomal recessive and autosomal dominant inheritance. The clinical manifestations vary widely from a severe, mutilating condition to a relatively mild disorder, with a marked variability within each major subtype (2). The most severe forms are multior-gan disorders with a poor prognosis (3).

Based on the level of tissue separation, EB can be described as simplex or epidermolytic (in case of blistering in the epidermis), junctional (within the lamina lucida of the basement membrane zone) and dystrophic or dermolytic (if located between basal lamina and dermis) (4). Currently specific mutations in ten distinct genes expressed within the cutaneous basement membrane zone (BMZ) are known. In the simplex forms, the disorders lie in genes coding for keratins, in the junctional ones mutations are found in the laminin genes or in the genes coding for other components of the basement membrane. In the dystrophic forms, the genes affected are normally responsible for the development of the anchoring fibrils (collagen VII). Precise diagnosis is based on morphological and histological examination of the skin, as well as molecular analysis. This allows for a prenatal diagnosis in pregnancies at risk (6).

Despite improved disease characterization, specific treatment is still missing. One major goal of symptomatic treatment is to reduce blistering and to enhance wound healing. Treatment of EB is therefore based on meticulous wound care. An international support organization for families and patients, called DebRA (Dystrophic epidermolysis bullosa Research Association), has been in existence for more than 20 years (see also www.debra.org). In the severe mutilating forms of EB, frequent complications include local skin infections, amputations as well as the occurrence of squamous cell carcinomas (5). In mouse models of EB, attempts at gene therapy are in progress (7).

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