dominant or recessive. For Hallopeau-Siemens recessive DEB with severe clinical symptoms, prenatal diagnosis is made by fetal skin biopsy, amniocentesis and chorionic villis biopsy.

**Treatment**

Synthetic type VII collagen therapy has been attempted on DEB patients in recent years. Friction is avoided and topical therapies are applied. Fluid therapies, nutritional management and genetic counseling are conducted for recessive DEB.

**b. Other genetic blistering diseases**

**1. Skin fragility syndrome**

Skin fragility syndrome, an autosomal recessive inherited disease, is caused by abnormality in the gene that codes for plakophilin 1, a desmosomal structural protein. Epidermal fragility, painful hyperkeratosis in the hands and soles, and abnormalities of hair, nails and perspiration are found.

**2. Hailey-Hailey disease**

*Synonym: Familial benign chronic pemphigus*

**Outline**

- Vesicles aggregate on an erythematous base in areas exposed to friction. The appearance resembles that of impetigo.
- It is autosomal dominantly inherited and occurs in adults in their 30s.
- It is caused by a mutation in the ATP2C1 gene that codes for a calcium pump in the Golgi apparatus within keratinocytes.
- The pathology is acantholysis and villi formation. It is somewhat similar to Darier’s disease.
- Topical steroid application is the main treatment.

**Clinical features**

Hailey-Hailey disease is inherited. It tends to manifest in adults in their 30s, appearing as aggregated erythema and blistering in areas that are exposed to friction, such as the cervical regions, axillary fossa, inguinal regions and anus. On an erythematous blistering base there are crusts, pustule formation and pigmentation, and secondary infection produces impetigo-like lesions (Fig. 14.17). Itching is usually present. Although it heals without scarring, it leaves abnormal pigmentation and is recurrent. The disease worsens in summer, and subsides in winter. It is worsened by external friction, perspiration, infection and UV radiation.

**Pathology**

Acantholysis of the epidermis leads to intradermal lacunae
formation immediately above the basal layer. The dermal papillae, which are covered by basal cells in the single layer that is left in the lacunae, protrude and resemble villi. Dyskeratotic cells are occasionally found. Acantholytic cells in the lacunae are connected loosely to each other by a few desmosomes (Fig. 14.18). Autoantibodies to the epidermis are not detected by immunofluorescence.

**Diagnosis**

Hailey-Hailey disease is diagnosed by the clinical symptoms and pathological diagnosis. As it is autosomal dominantly inherited and frequently occurs within a family, it is important to take a thorough family history. Genetic diagnosis can identify the mutation in the ATP2C1 gene.

**Treatment**

Topical application of steroids and antibiotics ointments is useful. Oral etretinate (a vitamin A derivative) and surgical ablation may be performed in intractable cases.

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### B. Autoimmune blistering diseases

#### a. Diseases with intra-epidermal blistering (pemphigus group)

**Outline**
- Middle-aged and elderly people are the most commonly affected. Intra-epidermal blistering with flaccid blisters occurs.
- The two main pemphigus groups are the pemphigus vulgaris group and the pemphigus foliaceus group.
- They are an autoimmune diseases. Acantholytic intra-epidermal blistering is produced by autoantibodies against desmoglein (intercellular substances; MEMO).
- Anti-desmoglein antibodies are detected by ELISA. In vivo IgG deposition and IgG antibodies are observed by immunofluorescence (IF). Nikolsky’s sign and Tzanck test are positive (i.e., for acantholytic cells).
- Oral steroids and immunosuppressants are mainly administered.

**Classification**

Diseases with intra-epidermal blistering (pemphigus group) are divided into two groups according to pathogenesis: pemphigus vulgaris and pemphigus foliaceus. Pemphigus vegetans is a type of pemphigus vulgaris; pemphigus erythematous is a type of pemphigus foliaceus. The characteristics of each type are summarized in Table 14.2. Pemphigus vulgaris accounts for 60% of...