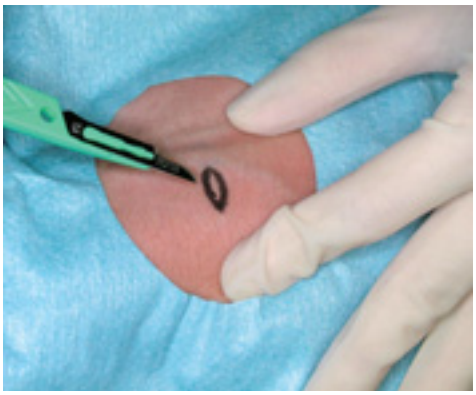


Fig. 2.1-2 Procedure of skin biopsy.
Incisional biopsy with a surgical knife.

Table 2.1 Specific stains used in dermatology.

Stain	Stained material	Stained color
Hematoxylin and eosin (HE)	Entire skin	Blue (nucleus), magenta (cytoplasm, etc.)
Elastica van Gieson	Collagen fibers	Red
	Elastic fibers	Black
Azan Mallory	Collagen fibers	Blue
Masson trichrome	Collagen fibers	Green
Periodic acid-Schiff (PAS)	Basement membrane	Red
	Glycogen	Red
	Neutral mucopolysaccharides	Red
	Fungi	Red
Toluidine blue	Mast cells	Purple (metachromasia)
	Acid mucopolysaccharides	Blue
Alcian blue	Acid mucopolysaccharides	Blue
Sudan III	Fats	Orange-red
Congo red	Amyloids	Red
Dylon	Amyloids	Orange-red
Berlin blue	Hemosiderins	Blue
Kossa	Calcium	Black
Grocott	Fungi	Black-purple
Ziehl Neelsen	Mycobacteria	Red

B. Dermatopathology

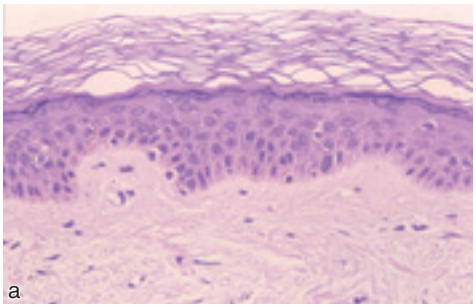


Fig. 2.2-1 Normal skin (hematoxylin and eosin staining).
a: Normal skin of the forearm. A basket-weaved horny cell layer is seen. Gaps between the stained horny cell layers are lipids that dissolved during fixation. These gaps indicate that the skin is well protected by moisturizing lipids.

When observing a pathological specimen, it is necessary to identify the abnormality in the specimen by comparison with normal findings (**Figs. 2.2-1** and **2.2-2**). This section introduces fundamental terms for skin pathological changes and diseases.

a. Epidermis

1. Acanthosis (epidermal hyperplasia) ★

Acanthosis describes thickening of the epidermis. It is classified into flat (the entire site thickens moderately; e.g., in chronic eczema), proriasiform (epidermal protrusions are extended), papillomatous (the epidermis projects upwards; e.g., with viral warts or seborrheic keratosis), and pseudocarcinomatous (pseudosquamous cell carcinomas project irregularly downward; e.g., chronic ulcer margin, deep mycoses) (**Figs. 2.3** and **2.4**).

2. Epidermal atrophy (epidermal hypoplasia) ★

Epidermal atrophy (epidermal hypoplasia) is caused by reduction of keratinocytes (**Fig. 2.5**). It leads to thinning of the epidermis. As a result, the papillary processes are diminished or lost. It

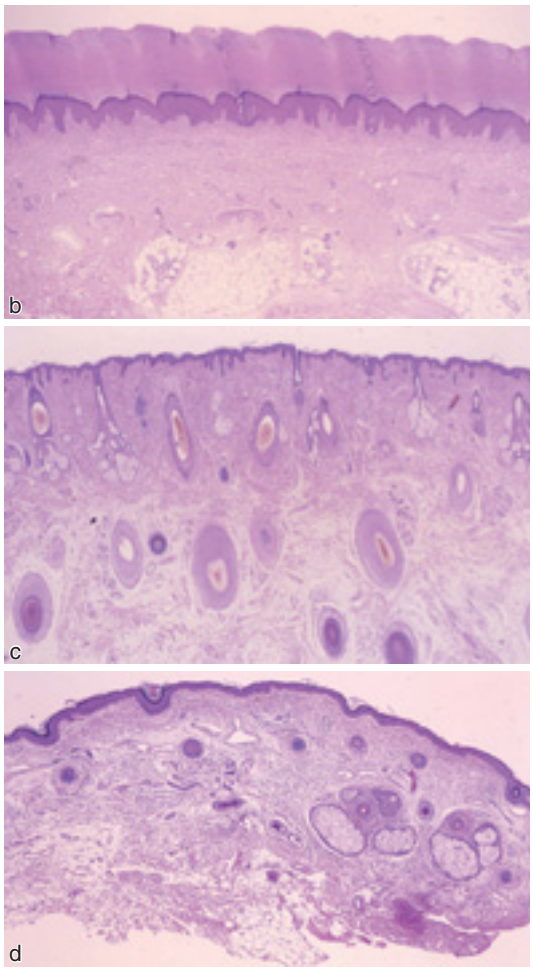


Fig. 2.2-2 Normal skin (hematoxylin and eosin staining).
b: Normal skin of the sole. A thick horny cell layer is seen. c: Scalp. Many follicles can be seen. d: Face. Sebaceous glands are abundant.

is often found in senile skin, discoid lupus erythematosus, lichen planus and actinic keratosis.

3. Hyperkeratosis ★

The horny cell layer becomes abnormally thick. This is seen in psoriasis vulgaris, ichthyosis and callus (**Fig. 2.6**). In ichthyosis, hyperkeratosis is due to detachment and exfoliation of the horny cell layer, a process called retention hyperkeratosis. Keratinization associated with hair follicles is called follicular keratosis.

4. Parakeratosis ★

Parakeratosis is caused by incomplete keratinization in which nuclei remain in the cells of the horny cell layer (**Fig. 2.7**). In normal skin, keratinocytes denucleate when they reach the horny

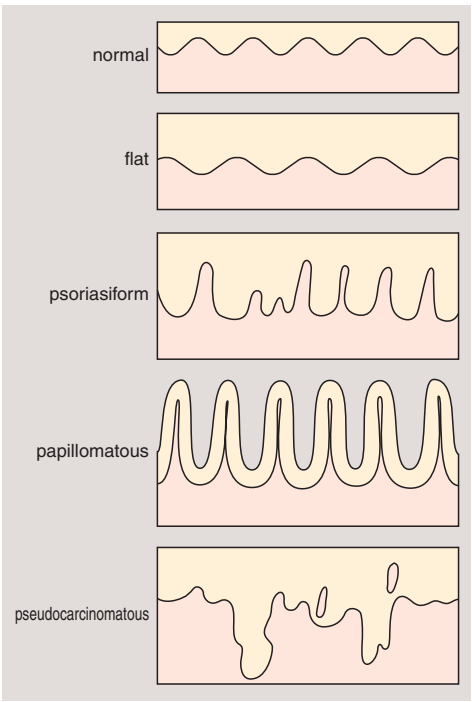


Fig. 2.3 Patterns of acanthosis.

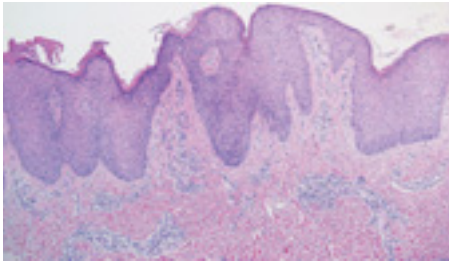


Fig. 2.4 Acanthosis.
Chronic eczema.

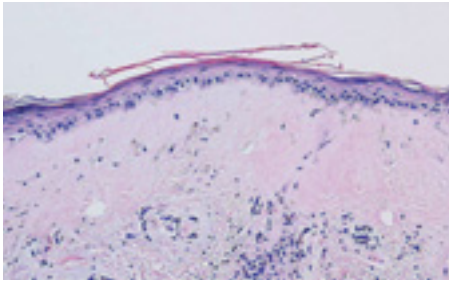


Fig. 2.5 Epidermal atrophy.
Dermatomyositis.

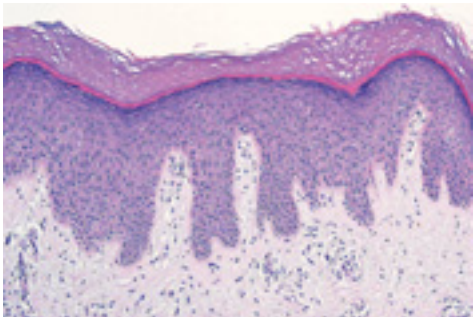


Fig 2.6 Hyperkeratosis.
Chronic eczema.

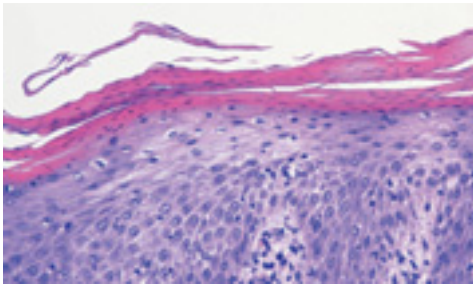


Fig. 2.7 Parakeratosis.
Psoriasis vulgaris.

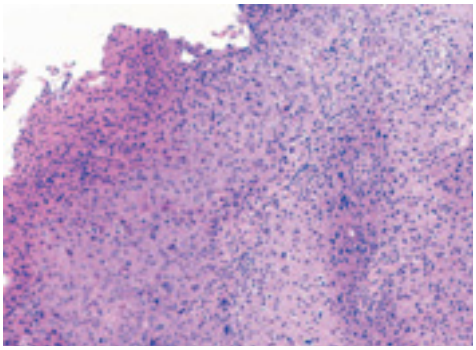


Fig. 2.8 Dyskeratosis.
Bowen's disease.

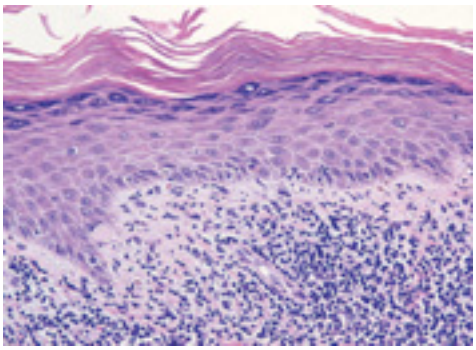


Fig. 2.9 Hypergranulosis.
Parapsoriasis.

cell layer; however, keratinocyte formation in inflammatory diseases such as psoriasis vulgaris or in tumorous diseases such as actinic keratosis and Bowen's disease takes place so quickly that most of the nuclei remain in the horny cell layer. It is frequently accompanied by hyperkeratosis and hypogranulosis. The nuclei remain physiologically in the mucous membranes.

Wedge-shaped or columnar parakeratosis, called cornoid lamellae, is observed in porokeratosis (Chapter 21).

5. Dyskeratosis ★

Dyskeratosis occurs when some keratinocytes keratinize abnormally before they reach the horny cell layer (**Fig. 2.8**). The keratinocytes become apoptotic and necrotic. The nuclei shrink and contain eosinophilic cytoplasm. Since intercellular bridges between the peripheral keratinocytes are lost, the cells become round. Dyskeratosis is often found with inflammatory diseases and malignant tumors. It is termed "grains" in Darier's disease and "individual cell keratinization" in Bowen's disease.

6. Hypergranulosis

Hypergranulosis is a thickening of the granular cell layers to four or more layers from the normal one to three layers (**Fig. 2.9**). It is often found in lichen planus, viral warts and congenital ichthyosis.

7. Granular degeneration, Epidermolytic hyperkeratosis ★

In granular degeneration, numerous vacuolated cells containing large keratohyaline granules appear in the granular cell layer and suprabasal cell layer (**Fig. 2.10**). It is characteristic of Vörner palmoplantar keratosis and bullous congenital ichthyosiform erythroderma (Chapter 15). It may also be found in epidermal nevus and even in normal skin.

8. Spongiosis, Intercellular edema ★

Spongiosis occurs when the spaces between neighboring keratinocytes are enlarged by intense edema. As a result, the intercellular space becomes extended and distinct (**Fig. 2.11**). When aggravated further, intradermal blisters (spongiotic bullae) form. It is found in eczemas and dermatitises such as contact dermatitis, atopic dermatitis and acute eczema.

9. Intracellular edema (ballooning degeneration)

Intracellular edema is the infiltration of cytoplasm into keratinocytes (**Fig. 2.12**). As the swelling develops, the cells deform

and become spherical (ballooning degeneration). If the cytoplasm swells even further, the cells break and the membranes remain in a network pattern (reticular degeneration). It is found in eruptions caused by viral infections such as that of the herpes simplex virus.

10. Acantholysis ★

Acantholysis is the dispersion of keratinocytes resulting from the dissociation of keratinocyte intercellular adhesion, particularly that of desmosomes. Intercellular spaces and blisters form, with acantholytic cells (spherical keratinocytes that have lost their intercellular adhesion) floating inside. Acantholytic cells have a tendency to become dyskeratotic (**Fig. 2.13**). The phenomenon is found in pemphigus, Hailey-Hailey disease and Darier's disease, and it may also be found in part of the lesions of actinic keratosis, keratoacanthoma, warty dyskeratoma and squamous cell carcinoma.

11. Blister, Bulla ★★

Blisters, whose contents are cytoplasm and infiltrating cells, are divided into intraepidermal and subepidermal, according to the histological findings (**Fig. 2.14**). Intraepidermal blisters are classified by formation mechanism into severe spongiosis (eczema/dermatitis group), prominent acantholysis (e.g., pemphigus vulgaris), reticular degeneration (e.g., herpes infection) and basal cell degeneration (e.g., burns, epidermolysis bullosa simplex).

Causative diseases of subepidermal blistering are autoimmune bullous diseases such as bullous pemphigoid, epidermolysis bullosa acquisita, dermatitis herpetiformis (Duhring) and epidermolysis bullosa, and burns (Chapter 4).

12. Pustule ★★

A pustule is a blister containing purulent components (mainly neutrophils). A small pustule below the horny cell layer is called Munro's micro-abscess, which characterizes psoriasis vulgaris (**Fig. 2.15**). A multilocular pustule, also called a spongiform pustule, is caused by damage to keratinocytes from neutrophilic infiltration in which intercellular junctions are retained. It resembles the network formation that is found in pustular psoriasis (Kogoj's spongiform pustule) (**Fig. 2.16**). Pautrier's microabscess is produced by infiltration of tumorous lymphocytes and is not a genuine pustule (refer to the following section).

13. Exocytosis (cell infiltration into the epidermis)

Exocytosis is the infiltration of inflammatory cells and

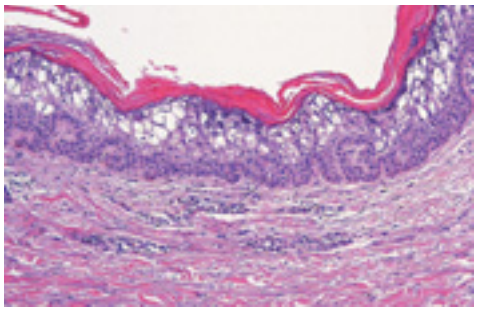


Fig. 2.10 Granular degeneration.
Bullous congenital ichthyosiform erythroderma.

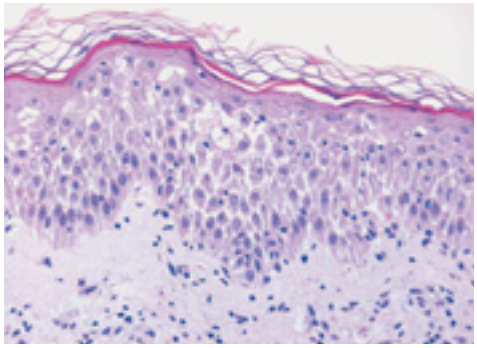


Fig. 2.11 Spongiosis.
Acute eczema.

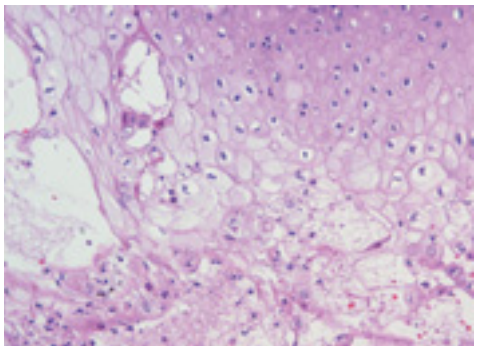


Fig. 2.12 Intracellular edema.
Herpes simplex.

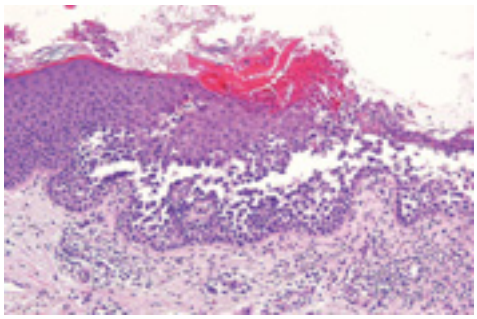


Fig. 2.13 Acantholysis.
Pemphigus vulgaris.

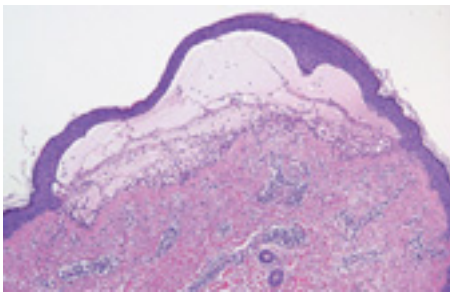


Fig. 2.14 Bulla.
Bullous pemphigoid.

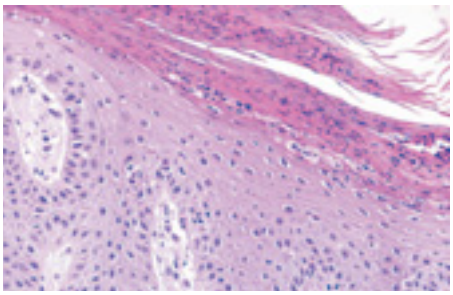


Fig. 2.15 Munro's microabscess.
Psoriasis vulgaris.

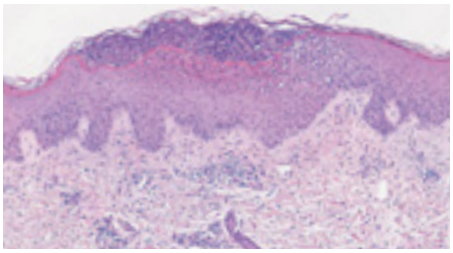
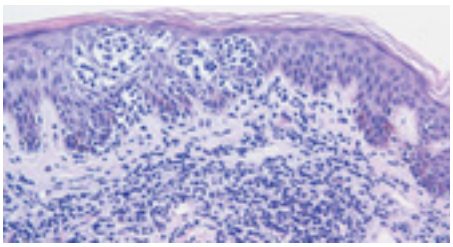


Fig. 2.16 Kogoj's spongiform pustule.
Pustular psoriasis.



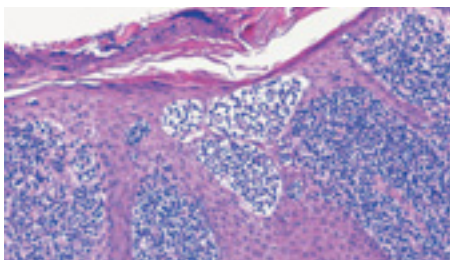


Fig. 2.17 Pautrier's microabscess.
Mycosis fungoides.

erythrocytes into the dermis. It is mostly found in spongiotic space. Infiltration of lymphocytes is seen in epidermal inflammatory diseases such as contact dermatitis and atopic dermatitis. Infiltration of multinucleated leukocytes is observed as a pustule in impetigo contagiosa, palmoplantar pustulosis and psoriasis.

In cutaneous T-cell lymphomas such as mycosis fungoides, tumorous T cell may infiltrate into the epidermis forming a mass that does not become spongiform; it is called Pautrier's microabscess for its resemblance to an abscess (**Fig. 2.17**). Langerhans cells infiltrate into the epidermis in Langerhans cell histiocytosis.

b. Dermo-epidermal junction

1. Vacuolar degeneration (hydropic degeneration) ★

Vacuolar degeneration occurs when the dermo-epidermal junctions become vacuolated and ill defined as a result of basal cell degeneration (**Fig. 2.18**). It is often accompanied by edema and lymphocyte infiltration, and the basal membranes are lost at the site. It is an inflammation that mainly occurs at the dermo-epidermal junction. When further aggravated, subepidermal blisters form. Melanin granules contained in basal cells may permeate into the dermis, a condition called incontinentia pigmenti histologica. The macrophages phagocytose melanin granules. Dyskeratosis caused by necrotic keratinocytes is seen in erythema multiforme, lichen planus, lupus erythematosus and graft-versus-host disease (GVHD). An eosinophilic Civatte body with a diameter of 10 μm may be found immediately beneath the dermis (**Fig. 2.9**).

2. Melanin synthesis abnormality

Production of melanin pigment in the basal epidermal layer is increased by exposure to ultraviolet radiation. When pigment is lost, leukoderma is observed. Generally, to diagnose melanin synthesis abnormality, a DOPA test or an immunohistological test is performed.

Albinism: A congenital abnormality of melanin synthesis. Melanin loss can be identified by Fontana Masson staining, for example.

Idiopathic guttate hypomelanosis: Melanocytes experience functional reduction by aging.

Nevus of Ota: Ectopic melanocytes are found in the dermis.

Chloasma: Melanocytes and melanin pigments increase.

Freckles: Melanocytes experience functional increase.