5) Drug challenge test

The drug suspected of causing allergy is administered to the patient to determine whether the eruptions will recur. One one-hundredth to one tenth of the usual dosage is given orally. In serious drug eruptions, there is a high risk that a drug challenge test will cause anaphylactic shock. The drug challenge test is the most reliable allergy test.

4. Skin function test

Tests for measuring various skin function, such as temperature control, secretion, and vascular regulation, are as follows.

1) Measurement of skin temperature and thermography

Thermography, which uses an infrared-camera-equipped emission pyrometer to express the distribution of skin temperature two-dimensionally, has become widely used for diagnosing diseases of the blood vessels, and nervous system disorders, inflammations, tumors, and other disorders.

2) Transepidermal water loss (TEWL)

Transepidermal water loss (TEWL) from the skin surface is measured by electric hygrometer (Fig. 5.8). This test is effective in determining the clinical condition of keratinization. The TEWL value usually is elevated in dyskeratoses, such as in ichthyosis.

3) Skin capillary resistance test

The fragility of skin capillaries can be determined by measuring ecchymosis produced in artificially pressured blood vessels. In the Rumpel-Leede test, the upper arm is pressed by a blood pressure manchette to congest the blood vessels. Two minutes after pressure between the systolic and diastolic pressures is applied to the patient’s upper arm for 5 minutes to constrict the blood vessels, hemorrhagic spots occur. When 10 hemorrhagic spots or more produced, the test is positive for dysfunction of vascular regulation. It may also be positive if there is abnormality in the capillaries or platelets, such as Henoch-Schönlein purpura or thrombopenic purpura.

5. Fungal examination

Potassium hydroxide (KOH) is used for observation and detection of fungi and mites. Scales or blister contents are swabbed (Fig. 5.9) and applied to a glass slide onto which 20% KOH solution is dripped, and a slide cover is placed on top. The slide is...
heated on a hot plate at 70°C to 80°C for 5 to 10 minutes. The components of skin such as the horny cell layers are hydrolyzed, and the fungal components become easily Fig. 25.1. By similar procedure, animals such as mites are observed. Recently, KOH solutions to which dimethylsulfoxide (DMSO) has been added have been frequently used, due to the short dissolution time and the fact that there is no need to use a hotplate.

6. **Dermoscopy (see Appendix for details)**

Dermoscopy is a test to observe the skin surface in detail under a magnifying glass with a magnification factor of ten (Fig. 5.10). Use of jelly for echography and a bright light source reduces scattering light and makes it possible to observe the lower dermal layer as well as the horny cell layer. The technique is particularly useful in distinguishing between and diagnosing pigmented lesions (e.g., malignant tumors including malignant melanomas and nevus) and subcorneal bleeding. Unlike skin biopsies, dermoscopy is not invasive; it is essential and greatly useful for dermatological examinations. Digital images of dermoscopy can also be saved.

7. **Diascopy**

In diascopy, a site with a skin lesion is pressed with transparent glass to see whether the coloration of the lesion disappears (Fig. 5.11). If so, the diagnosis is erythema. Otherwise, the diagnosis is purpura. A light brown spot is characteristically seen in a granulomatous nodule such as lupus vulgaris. The test is also effective for distinguishing between nevus anemicus and hypopigmented macule. In the case of the latter, the whitish macule remains visible under the pressure of diascopy.

8. **Needle reaction test**

When the skin of a patient with Behçet’s disease is stuck with a needle, an erythema, papule or pustule appears in 24 to 48 hours. The needle reaction test is positive for about 70% of patients with Behçet’s disease, which reflects the skin irritability of patients with this condition.

9. **Wood’s lamp test**

When skin with erythrasma, pityriasis versicolor, tinea capitis or porphyria is exposed to Wood’s lamp, a 365-nm UV light, the fluorescence has a characteristic color (Fig. 5.12, Table 5.5).

10. **Cytological diagnosis (Tzanck test)**

Cytological diagnosis (Tzanck test) is conducted by applying a slide glass to the bottom of a broken blister and staining the adhered cellular components in Giemsa (Fig. 23.8) for observation.
under a light microscope. Acantholytic cells called Tzanck cells are observed in pemphigus. In blisters of herpes simplex and herpes zoster, ballooning cells produced by viral infection are observed.

11. Dinitrochlorobenzene (DNCB) test

The strength of cellular immunity is measured by dinitrochlorobenzene (DNCB) test. First, a patch soaked in a 1% solution of DNCB acetone is adhered to the upper inner arm of the subject for sensitization. After 2 to 3 weeks, a patch soaked in 0.1 to 0.01% of the same solution is adhered to a symmetrical site on the other arm as a provocation test to observe the reaction after 48 hours. If erythema, papule or small papule is produced, the test is positive; that is, the subject is considered to have cellular immunity. Immuno-compromised patients with cancer may not always be sensitized by this test.

12. Dermographism

Some reactions of skin rubbed by something dull such as a fingernail maybe observed. If the rubbed site becomes red and elevated, it is called (red) dermographism which is a diagnostic finding of physical urticaria (Fig. 5.13). If the site becomes white, it is called white dermographism; this is usually seen in patients with atopic dermatitis (Fig. 5.14).

13. Darier’s sign

When dermography is performed on a pigmented area of a patient with mastocytosis (urticaria pigmentosa (Chapter 21)), mast cells are degranulated and the site becomes markedly elevated to form an urticarial lesion. This phenomenon is called Darier’s sign (Fig. 5.15). Urticarial lesions are usually produced shortly after rubbing. Mastocytosis can be distinguished from other pigmented lesions by Darier’s sign.

14. Sensory test

Sensory tests on touch (stroking with a brush), pain sensation (sticking with a needle), and temperature sensation (touching by tubes containing warm water or ice water) are conducted on a blindfolded patient. It is useful for the diagnosis of dissociation disability in Hansen’s disease and neurological disorders.
15. Nikolsky phenomenon

In Nikolsky phenomenon, although the skin appears normal, blistering is produced by rubbing. The result is positive in pemphigus, epidermolysis bullosa, staphylococcal scalded-skin syndrome (SSSS), and toxic epidermal necrolysis (TEN) type drug eruptions.

16. Köbner phenomenon

From stimuli such as rubbing or sunlight, a lesion is produced in normal skin; this is called the Köbner phenomenon, which is seen in psoriasis and lichen planus.

17. Auspitz phenomenon

Auspitz phenomenon is the occurrence of small droplets of blood in skin. In psoriasis, when scales exfoliate, petechia is quickly produced (Chapter 15). However, the patient may also test positive for Auspitz phenomenon in cases of eczema; it is not necessarily specific to psoriasis.

18. Enzyme-linked immunosorbent assay (ELISA)

Enzyme-linked immunosorbent assay (ELISA) is a method for measuring the amount of specific proteins, using enzymes and antibodies that are associated with fluorescent substances. For pemphigus diagnosis, it is necessary to identify whether there are autoimmune antibodies to desmoglein 1 and 3. For bullous pemphigoid diagnosis, it is necessary to identify whether there are autoantibodies to BPAG2 protein (Chapter 14).

19. Western blot

Western blot is a method to measure the amount of specific proteins using proteins that are extracted from the epidermis to be electrophoresed and reacted to the specific antibody (Fig. 5.16). It is used for detection of autoantibodies.

20. Diagnostic imaging

Diagnostic imaging using X-ray photography, CT, MRI, ultrasound, and scintigraphy is important for diagnosis of skin tumor and lymph node metastasis of a skin tumor.

21. General internal medical tests

A general blood test, bacterial culture and urinalysis are general internal medical tests.
With identification of the causative genetic mutation, accurate diagnosis and classification of diseases are possible for hereditary skin diseases caused by single-gene mutation (Fig. 5.17, Chapter 29). The characteristic configuration of DNA in tuberculosis and atypical mycobacterial diseases is detectable by magnifying the DNA extracted from the lesion or reproducing it by PCR.

Fig. 5.16 Western blotting.
Serum of bullous pemphigoid patient reacts against skin antigens (molecular weight of 180 kD and 230 kD).

Fig. 5.17 DNA analysis of type VII collagen in a patient with epidermolysis bullosa.
Point mutation (C6761G, exon 86) causes nonsense mutation; stop codon (TGA) occurs at 2261 amino acid instead of arginine (CGA).

Photodynamic diagnosis (PDD), Photodynamic therapy (PDT)
When δ-aminolevulinic acid is applied as topical occlusive dressing therapy or when it is locally injected or orally administered for lesions such as those that occur in extramammary Paget’s disease, basal cell carcinoma, and actinic keratosis, there is accumulation of protoporphyrin IX that contains red fluorescence. Taking advantage of this, non-invasive diagnosis (photodynamic diagnosis; PDD) and treatment (photodynamic therapy; PDT) is possible. In PDD, by irradiation of Wood’s lamp 4 to 6 hours after topical application of δ-aminolevulinic acid, red fluorescence is observed (Fig. 5.12). In PDT, irradiation is by 100 J/cm² 630-nm excimer dye laser instead of by Wood’s lamp.