

## Department of Dermatology

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Akihiko Asahina, *Professor*  
Yoshinori Umezawa, *Professor*  
Yoshimasa Nobeyama, *Associate Professor*  
Koichi Yanaba, *Associate Professor*  
Yozo Ishiujii, *Assistant Professor*  
Tomohiko Onoe, *Assistant Professor*

Takaoki Ishiji, *Professor*  
Arihito Ota, *Associate Professor*  
Toshihiro Ito, *Associate Professor*  
Munenari Ito, *Assistant Professor*  
Michie Katsuta, *Assistant Professor*

### General Summary

We have organized special clinics for selected skin diseases, including viral diseases, neurofibromatosis type 1, atopic dermatitis, psoriasis, contact dermatitis, and skin cancers. Integrating concentrated clinical efforts and related basic research should provide a significant contribution to excellent clinical practice.

### Research Activities

#### *Psoriasis*

Various systemic therapies, including oral cyclosporin microemulsion preconcentrate, methotrexate, etretinate, biologics, and topical therapies, such as vitamin D3, and corticosteroids, have been used, depending on disease severity and the degree to which quality of life (QOL) is impaired in individual patients. Also, phototherapy is effective and has been performed in our skin-care clinic. We have evaluated patients' QOL and have developed Japanese versions of the Psoriasis Disability Index and the Work Productivity and Activity Impairment questionnaire for psoriasis. In a special psoriasis clinic, we select patient-based treatments to satisfy patients' demands. Biologic agents, including infliximab, adalimumab, ustekinumab, secukinumab, brodalumab, ixekizumab, and guselkumab, are available and have been used to treat severe, intractable psoriasis. Clinical trials have been performed with new biologic agents and new topical agents.

#### *Atopic dermatitis*

Recently, psychosocial factors have been suggested to affect the exacerbation of atopic dermatitis. Therefore, we are treating patients on the basis of both evidence-based medicine and QOL issues. We obtain a precise medical history from each patient and evaluate the degree of QOL impairment. We are also doing some basic experiments with a mouse model of atopic dermatitis to reveal the mechanism of pruritus in this disease. An antibody agent (dupilumab) against the interleukin (IL)-4/IL-13 receptor is available and has been used to treat moderate-to-severe atopic dermatitis. Clinical trials have also been performed of a topical phosphodiesterase 4 inhibitor and an antibody agent against the IL-31 receptor.

#### *Malignant skin tumors*

We have been studying clinical courses, postoperative outcomes, and genomic and

expression changes in patients with malignant melanoma, extramammary Paget's disease, squamous cell carcinoma, basal cell carcinoma, cutaneous T-cell lymphomas, and a wide variety of soft-tissue sarcomas, including malignant peripheral nerve sheath tumors. For the accurate diagnosis of pigmented tumors, we always perform dermoscopic examinations and sentinel lymph-node biopsies. For patients with advanced disease, we have performed multidisciplinary treatment, including immune check point inhibitors, molecular targeted agents, chemotherapy, and radiation therapy.

### *Neurofibromatosis*

Because the number of registered patients in our clinic is the largest in Japan, we concentrate on long-term follow-up and the improvement of impaired QOL by means of accurate diagnosis and the resection of neurofibromas. The estimated lifetime risk of malignant peripheral nerve sheath tumor (MPNST) in patients with neurofibromatosis 1 is approximately 10%. We have used the methylation-specific polymerase chain reaction (PCR) and real-time reverse transcriptase PCR to analyze the methylation status of tumor suppressor genes and cancer-testis genes in established MPNST cell lines.

### *Herpes virus infection*

#### 1. Herpes simplex virus

Rapid diagnostic procedures by means of immunohistochemical staining with monoclonal antibodies against herpes simplex virus 1 and 2 and varicella-zoster virus are performed in this clinic. After the diagnosis is confirmed, suppressive therapies with valaciclovir are started to improve QOL.

#### 2. Herpes zoster and postherpetic neuralgia

Initial treatments are performed in this clinic for herpes zoster and postherpetic neuralgia (PHN). To prevent PHN, we prescribe tricyclic antidepressants. Posthoc analyses of a subgroup of patients have shown that amitriptyline in combination with acyclovir reduce the incidence of PHN. We prescribe pregabalin, tricyclic antidepressants, selective serotonin reuptake inhibitors, and opioid analgesics, such as Tramacet® (Grünethal Ltd., Stockenchurch, UK), which contains tramadol hydrochloride and acetaminophen.

### *Human papillomavirus infection*

In addition to ordinary cryotherapy, agents that have been used to treat viral warts include topical vitamin D3, salicylic acid, glutaraldehyde, and monochloroacetic acid. Contact immunotherapy with squaric acid dibutylester, CO<sub>2</sub> lasers, and pulsed dye lasers has also been used to treat severe intractable viral warts. Human papillomavirus infection typing with the PCR has regularly been performed.

### *Contact dermatitis/drug eruption*

We have regularly performed patch testing to identify causes of contact dermatitis and drug eruption.

### *Laser*

The Q-switched 694-nm ruby laser is useful for treating nevus of Ota, acquired dermal

melanocytosis, and ectopic Mongolian spots. On the other hand, nevus spilus/café-au-lait spots are difficult to treat with this laser because they often recur after 1 to 2 months. The recently introduced 595-nm V-beam laser (long pulsed dye laser) is effective for treating intractable vascular lesions. The ultrapulse CO<sub>2</sub> laser can be used to quickly remove lesions of actinic keratosis, seborrheic keratosis, syringoma, and epidermal nevus.

### *Skin Care Clinic*

Narrow-band ultraviolet B irradiation is performed for patients with psoriasis, alopecia, atopic dermatitis, prurigo nodularis, vitiligo, or cutaneous T-cell lymphomas. Other special clinics, including those for skin care lessons, therapeutic make-up, acne care, mental care, and *kampo* medicine, are available for patients on demand.

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