# Department of Dermatology

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## 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, and 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) has been impaired in individual patients. Phototherapy is also 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, brodalmab, 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*
Psychosocial factors have recently 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 to evaluate the degree of QOL impairment. We are also doing 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 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 (MPNSTs). To accurately diagnose 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 patients registered in our clinic is the largest in Japan, we concentrate on long-term follow-up and improving impaired QOL by means of accurately diagnosing and then resecting neurofibromas. The estimated lifetime risk of MPNSTs in patients with neurofibromatosis 1 is approximately 10%. We have used the methylation-specific and real-time 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 viruses 1 and 2 and varicella-zoster virus are performed in this clinic. After the diagnosis is confirmed, suppressive therapies with varaciclovir are started to improve the impaired 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 reduces the incidence of PHN. We prescribe pregabalin, tricyclic antidepressants, selective serotonin reuptake inhibitors, and opioid analgesics, such as Tramcet® (Grunethal Ltd., Stokenchurch, UK), which contains tramadol hydrochloride and acetominophen.

*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, $CO_2$ 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 $CO_2$ 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.

## Publications

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