Department of Dermatology Activity Report 2011–2012

WINSELSPITAL

UNIVERSITÄTSSPITAL BERN HOPITAL UNIVERSITAIRE DE BERNE BERN UNIVERSITY HOSPITAL



Foreword

Introduction

The Department of Dermatology of the University Hospital of Bern is pleased to provide its second activity report under the chairmanship of Professor Luca Borradori. In the past 5 years the Department has undergone substantial changes in spirit, in the medical staff as well as in overall organisation. Requisite changes positioned the Department to correctly face the new challenges imposed by the new developments in the Swiss health care system, the current economic landscape as well as the new strategic medical and financial objectives set by the direction of the University Hospital .

The overall goals are to provide high level medical care and services in close collaboration with both other Hospital Departments and external specialists to carry out translational clinical and basic research, and, finally, to ensure the best possible preand post-graduate teaching. Nevertheless, efficient management and optimal engagement of the various resources with improvement of the processes have emerged as crucial factors in increasing budgetary constraint as well as in both given and enforced yearly objectives.

Professor Luca Borradori Director and Chairman



Therese Zürcher Chief nurse



Staff and collaborators	(as at 31. 12. 2012)
Director and Chairman	Professor L. Borradori
Vice-Chairman	Professor Th. Hunziker (up to 2011)
	Professor N. Yawalkar (from 2012)
Chief Nurse	Th. Zürcher
Faculty and Chiefs	Professor R. Hunger
	Professor D. Simon
Research & development	Dr B. Favre
Chief physician clinical ward	Dr N. Pelivani
Dermatopathology sector	Dr H. Beltraminelli
	PD Dr I. Hegyi (up to 2011)/Dr R. Blum

Attending physicians

Dr R. della Torre (from 2012), Dr N. Dietrich (from 2012), Dr N. Irla (from 2012), Dr K. Kernland, Dr P. Oberholzer (from 2012), Dr L. Parmentier (until 2012), Dr Th. Schneiter (until 2011)

Consultants and lectors

Dr M. Adatto (Laser), Dr U. Büttiker (Phlebology), Dr P. de Viragh (Trichology), Dr K. Fritz (Laser), Professor E. Haneke (Nail diseases, Surgery, Histopathology), Dr H. Nievergelt (Histopathology), Dr Dr A.A. Ramelet (Phlebology), Dr A. Skaria (Mohs Surgery)

Residents

C. Blazek, Dr M. Corti, Dr S. Häfliger, Dr K. Heidemeyer, Dr C. Houriet, Dr B. Jamnicki (2011), Dr D. Perruchoud, Dr T. Renker, Dr Ch. Schlapbach, Dr Z. Spanou, M. Stieger, Dr A. Surovy (2011)

Background

- The Department of Dermatology is part of the Inselspital, University Hospital of Bern. The Inselspital belongs to a private foundation, the *Inselstiftung*. The latter has an agreement with the Canton of Bern to serve as a tertiary health care centre for the population of the Canton of Bern and as a University teaching hospital.
- The Department of Dermatology within the Inselspital is a tertiary referral centre for skin and sexually-transmitted diseases. Patients are referred from all over Switzerland. More than 20% of the treated patients come from outside the Canton of Bern.

Structural organization, medical staff and nurse team

- Our Department comprises an in-patient section with 14 beds, an out-patient section with several specialized clinics, a day hospital for management of complex cases with emphasis on chronic wounds, a phototherapy unit, a surgical unit, a laser platform, as well as a dermatopathology unit.
- The medical staff consists of 11 senior physicians and 9 junior physicians.
 There are one full Professor, four associate Professors and one senior lecturer.
 Furthermore, there are 8 part-time board-certified consultants and lecturers.
 The Department regularly hosts a number of guest physicians in training as well as board-certified dermatologists from European and non-European countries for elective periods.
- The medical staff works in tight collaboration with the specialized out-patient and in-patient nursing teams. The latter take particular care in ensuring the best education and practice quality in nursing. These high quality levels and standards have been accredited for activities both in the in-patients ward and as well as for distinct out-patient activities.

Specialized nursing team

- The nursing team is headed by Mrs T. Zürcher, member of the department's directorate. The nursing team constitutes the largest group among medical personnel working in the Department of Dermatology and represents the critical backbone requisite to providing the specialized high level medical care of patients. Mrs Zürcher and her closest collborators (Mrs T. Gross, Mrs B. Nydegger, Mrs S. Hale) have been faced with a number of significant organizational changes and new goals over recent years.
- The most significant challenges have been to deal with a new management pathway of in-patients with a significant reduction in the length of the hospital stay and a rapid turnover of patients in the clinical ward, an increased number of out-patient surgical cases related amongst others, to the introduction of the micrographic Mohs surgery, as well as the implementation of new therapeutic approaches with related training, including UVA1 phototherapy and lasers. Furthermore, in the light of increasing budgetary restriction, the personnel pool has to be constantly adapted to needs with always the ultimate goal of increased efficiency. Finally, the nursing team is keen to maintain a high standard of care. These efforts are reflected by the regular internal and external controls meeting the quality management standards required to maintain certification.

Patients and technical statistics

The number of dermatological in-patients is approximately 550 per year. There are up to 33,000 out-patient consultations per year, 3,600 patients are cared for at the wound care clinic, up to 5,500 phototherapy treatments and 2,300 surgical procedures are routinely performed. The dermatohistopathology sector processes and analyses 13,000 skin biopsy specimens per year and is one of the largest dermatopathology units still fully integrated within a University Hospital in Switzerland.

Objectives

The main goals of the Department of Dermatology are

- 1. to provide *high quality medical care and service* by offering a spectrum of specialised outpatient consultations as well as appropriate evaluation and management of patients requiring hospitalisation. Respect of patients' dignity and overall ethical issues are of constant concern for patient treatment,
- 2. to carry out *clinical, translational and basic research*. The ultimate objective is to ensure best patient care, state of the art therapy and to have a better understanding of disease mechanisms,
- 3. to provide intensive teaching for *pre-graduate and post-graduate* students in medicine and biomedical sciences, residents, physicians and specialists of dermatology and venereology, as well as other specialisations.

Overall, the Department is very enthusiastic and highly motivated to share experiences in clinical evaluation, management and treatment of dermatological patients through interface with other partners within the Canton of Berne and in the rest of Switzerland. Joint ventures with focus on consultative activities for dermatological patients have been established with neighbouring Cantons (Fribourg, Solothurn). Finally, the Department is keen on developing and carrying out clinically oriented and basic investigative research projects in collaboration with either other researchers or with pharmaceutical companies.

Current challenges

The structure of the Swiss health system is undergoing a substantial reorganisation. The Swiss health system is one of the most expensive in the world. Measures are being taken in an effort to reduce expenditure for both in-patient and out-patient services. This situation has put hospitals under pressure with budget cuts and rigorous budgetary control, making the implementation of cost-containment measures and the reassessment of the running of the Department including patient management and medical services essential. Since 2012 the hospital directorate has set a number of objectives each year for each Department in the hospital to meet. The goals invariably encompass a defined budget, a given number of hospital admissions, outpatient cases, medical treatments, as well as management improvement processes and a campaign of quality projects.

Activity and areas of expertise

Our interest is currently focused on the evaluation and management of:

- 1. Skin cancers including clinical evaluation, management and systematic followup of melanoma and non-melanoma skin cancer patients using video-microscopy and digital imaging devices
- 2. Dermatosurgery, including Mohs micrographic surgery
- 3. Inflammatory skin diseases, such as psoriasis and atopic dermatitis
- 4. Autoimmune blistering disorders of the skin and mucous membranes
- 5. Paediatric dermatology, congenital vascular malformation, inherited blistering and fragility syndromes of the skin
- 6. Acne and hidradenitis suppurativa
- 7. Medical lasers
- 8. Hair and nail diseases with specific conservative and surgical treatment
- 9. Skin ageing and pigmentation disorders with development of autologous cell-based therapeutic approaches
- 10. Phlebology as well as chronic wound care with use of tissue-enginered skin equivalents and novel wound dressing techniques
- 11. Skin ageing and pigmentation disorders with development of cell-based therapeutic approaches and lasers
- 12. Dermatopathology

Detailed clinical services

In the following section the specialised out-patient clinics available in our Department and specific areas of clinical and research interests are both presented.

Melanoma and pigmented lesion clinic

(responsible: Professor R. Hunger)

The incidence of malignant melanoma is rapidly growing. The current incidence rate in Switzerland is 22 new cases per 100,000 inhabitants followed by over 200 melanoma related deaths each year. While early stages can be cured by surgical excision, late stages have a poor prognosis. To best follow up patients with malignant melanoma and to recognise these tumours at an early stage two specialised consultations are available:

Malignant melanoma and pigmented lesions

- 1. We provide regular clinical follow-ups for our patients with atypical moles and malignant melanoma. The regular examinations are important to exclude disease progression as early as possible. Since patients with melanoma have an increased risk to develop a second melanoma, regular full skin examination is essential.
- 2. Dermoscopy/videomicroscopy. Patients with multiple dysplastic naevi and other patients at high risk for melanoma are regularly evaluated using a digital dermoscopic system (Fotofinder). This technique allows the detection of even the slightest changes in the pigment pattern of the lesions, increasing the sensitivity and specificity of diagnosis.

Non-melanoma skin cancer consultation

(responsible: Dr P. Oberholzer)

Non-melanoma skin cancers (NMSC) such as basal cell carcinoma and squamous cell carcinoma represent a medical and epidemiological challenge in Western countries. This is related first to the significant increase of skin cancers (4-8 % in Europe per year) as a consequence of the current life style (sun exposure) as well as the ageing of the population. In this context, there is a growing demand for treating these patients, and e.g. for skin surgical approaches ensuring good aesthetic results. Since the Inselspital is one of the Swiss referral centres for organ transplantation, we are also frequently involved in the evaluation and management of skin tumours in this high-risk organ recipient population. Our clinic has thus a strong commitment to management of skin tumours of peculiar complexity. A close collaboration with the Department of Plastic and Reconstructive Surgery (Chair: Professor M. Constantinescu) and with the Department of Radiation Oncology (Chair: Professor D. Aebersold) exists.

To address these issues, specific platforms and therapies are developed and performed, respectively

- 1. Tumour board: Interdisciplinary evaluation of patients with complex cutaneous cancers together with the Department of Plastic and Reconstructive Surgery and Department of Radiation Oncology
- 2. Dermatologic surgery, with particular focus on Mohs micrographic surgery

- 3. Non-invasive therapeutic approaches, such as radiation therapy, photodynamic therapy (PDT), cryosurgery, and non-invasive topical immunomodulatory therapies
- 4. Collaboration with the Department of Nephrology for the dermatological followup of renal transplant patients.

Dermatosurgery clinic: Micrographic surgery

(responsible: Dr A.M. Skaria, Dr R. della Torre, Dr M. Stieger)

In 2008 Mohs micrographic surgery was introduced in Bern by Dr A.M. Skaria. About 100 patients/year benefit from this special technique. Mohs micrographic surgery combines the surgical procedure with an immediate intraoperative three-dimensional histopathological assessment of the excised tumour. Since the operator evaluates the histological slides himself, the orientation for subsequent resection is optimal. Mohs surgery decreases the recurrence rate of epidermal tumours down to 1-4%, compared to classical surgery. The latter shows recurrence rates of up to 20%. Furthermore this technique leads to an improvement of the cosmetic result due to smaller defects. Indications for Mohs surgery are mostly non-melanoma skin cancers, especially those located on the face. In addition to the traditional dermatosurgery and the micrographic surgery, we offer another specific surgical technique called slow-Mohs surgery, which allows the treatment of certain special forms of tumour, such as sarcomas. In cases of complicated and excessive tumours, this two-stage surgical approach is realised in close cooperation with Professor M. Constantinescu and his team from the Department of the Plastic and Reconstructive Surgery.

Psoriasis clinic

(responsible: Professor N. Yawalkar)

Psoriasis is a common inflammatory skin disease of variable severity with significant morbidity and impact on quality of life. Evidence exists indicating that psoriasis may be associated with serious comorbidities such as cardiovascular and metabolic diseases. The underlying pathomechanisms are not yet fully understood. Recent advances in our understanding of the pathomechanisms of psoriasis have opened the way for new therapeutic strategies in psoriasis, such as the use of targeted therapies with biologic treatments.

In our specialised psoriasis clinic the following services are provided:

- topical and systemic treatments including phototherapy, traditional immunosuppressive agents (methotrexate, retinoids, and ciclosporin) and biologics such as tumour necrosis factor inhibitors (etanercept, infliximab, adalimumab) and anti-IL-12/23p40 monoclonal antibodies (ustekinumab) are routinely used
- interdisciplinary medical education courses provided by dermatologists, psychologists and nutritionists are offered to affected patients and their families, an opportunity exclusive to Switzerland
- clinical research studies aimed at testing novel biologic treatments are carried out.
 The clinic participates in phase 2 and phase 3 trials.

The clinic is also directly involved in basic investigative studies focused in the characterisation of the immune and inflammatory response in psoriasis (see research part).

Eczema and atopic dermatitis clinic

(responsible: Professor D. Simon)

Eczematous skin diseases are very common and concern over 20% of dermatologic patients. For instance, atopic dermatitis affects more than 10% of children between the ages of 6 to 7 years. Irritant and allergic contact dermatitis as well as occupational eczema is common in adults. These groups of cutaneous diseases are characterised by an acute and/or chronic inflammation of the skin and intense itch. Therefore, they have an enormous impact on the quality of life and are of medical as well as socioeconomic importance.

This specialised clinic provides all diagnostic and therapy facilities for patients with eczematous skin diseases. Diagnostic tests comprise blood and skin tests (patch test, skin prick test, atopy patch test, and provocation tests) to identify exogenous and endogenous pathogenic factors. Comprehensive management of affected patients encompasses installation of adequate anti-inflammatory topical and systemic therapies, skin care and skin protection teaching courses and practical instructions, psychological advice and support, as well as avoidance of triggers in daily life and occupational activities. Finally, we offer specific medical education courses for atopic dermatitis patients provided by dermatologists, allergists, psychologists, nutritionists, which are unique in Switzerland.

Our on-going research projects include clinical studies focusing on pathogenic mechanisms of allergic skin diseases such as atopic dermatitis and contact dermatitis, as well as eosinophilic skin diseases. Furthermore, we are involved in epidemio-logic studies on hand eczema as well as contact allergy.

Autoimmune skin diseases clinic

(responsible: Professor L. Borradori)

– Our Department has a specific interest and expertise in the evaluation, diagnosis and management of patients with severe autoimmune blistering diseases of the skin and mucosa, such as bullous pemphigoid, cicatricial pemphigoid, epidermolysis bullosa, pemphigus and cicatricial pemphigoid, pemphigoid which is unique in Switzerland. Furthermore, we are interested in the evaluation and management of patients with cutaneous manifestations of systemic diseases, such as systemic lupus erythematosus, dermatomyositis, scleroderma, vasculitis and Adamiantades-Behçet disease. In this context, our clinic is involved as tertiary referral centre for patients from the Canton of Bern as well as from all over the country.

- Besides the clinical management of patients with autoimmune diseases, we are directly involved 1) in clinical multicentre European studies aimed to characterise the clinical course, severity and prognostic markers in affected patients; 2) in the development of diagnostic tools such as ELISA for improved diagnosis and better follow-up; 3) in basic investigative studies to assess the immunological humoral and cellular response in affected patients (see research part).
- For correct evaluation of patients and classification of autoimmune diseases, we provide the required immunopathological analyses, such as direct and indirect immunofluorescence microscopy techniques (with various substrates), as well as immunoblot and immune-precipitation techniques using recombinant proteins. These immunopathological studies are carried out in close collaboration with the Institute of Immunology (immunopathology laboratory supervised by Dr Michael Horn). Finally, we have contributed to the development of several different novel diagnostic ELISA tests.

Paediatric dermatology clinic

(responsible: Dr K. Kernland Lang)

Dr K. Kernland Lang, consultant in dermatopaediatrics, ensures evaluation and management of children and adolescents with skin diseases. In particular, she is specialised in the evaluation of children with genetic, infectious, and endocrine diseases. Patients are evaluated in close collaborations with University Children's Hospital of Bern.

There are two major areas of interest and expertise:

- 1. *Vascular malformations* evaluated in the context of an interdisciplinary haemangioma board (together with paediatricians, angiologists and paediatric surgeons). The board takes advantage of the fact that the Department of Paediatric Surgery (Chair: Dr S. Berger) is the reference centre in Switzerland for large haemangioma and interstitial laser therapy. Vascular lesions involving the skin are however primarily managed by our laser team.
- 2. Diagnosis and management of patients with inherited skin blistering disorders such as *epidermolysis bullosa (EB)*. We offer a specialised and comprehensive interdisciplinary evaluation of affected patients by the EB network consisting of paediatricians, gastroenterologists, dentists, plastic surgeons, and dieticians/ nutritionists. Furthermore, molecular diagnosis for a variety of congenital diseases is provided in close collaboration with various leading European laboratories. We have a specialised team ensuring appropriate wound dressing care and physiotherapy of affected EB patients. Finally, we also provide information and support to people living with these disorders as well as their family members and friends.

Laser clinic

(responsible: Dr N. Dietrich, Dr N. Irla, Dr K. Fritz, Dr M. Adatto)

The laser clinic manages both in- and out-patients by using various laser types and light sources. Established and innovative therapies are provided under the supervision of experienced laser specialists to provide high clinical care. Dr Adatto and Dr Fritz have been directly involved in the development of laser devices in collaboration with various American and European companies.

Our laser centre is equipped with state of the art laser devices (e.g. vascular, ablative fractional, pigmented, excimer). A close collaboration with specialists from other Departments (angiology, paediatrics, and paediatric surgery) allows interdisciplinary clinical management.

- Efforts are made to improve therapy algorithms by the use of lasers for a number of skin disorders, such vascular malformations, pigmentary disorders and vitiligo, psoriasis, eczema, and inflammatory skin conditions. Furthermore, we are also involved in studies aimed at assessing the impact of laser wavelengths on tissue reaction, safety aspects, as well as aesthetic issues.
- With regard to clinical research, we are currently analysing the effect of distinct lasers on pigmentation disorders (Excimer, IPL), rosacea, psoriasis (Excimer and pulsed dye laser), atopic eczema (light vaccination, multicenter trial with Opto med), and actinic keratoses (laser PDT). The clinical staff consists of Dr M. Adatto, past-President and Honorary Member of the European Society of Laser Dermatology as well as founder and medical director of Skinpulse Dermatology and Laser Centre Geneva, Dr U. Büttiker, co-founding member of the Swiss group of aesthetic dermatology and skin care, Dr K. Fritz, specialist in laser dermatology and past-President of the European Society of Laser Dermatology (ESLD), Dr N. Dietrich and Dr N. Irla, dermatologists, with specific interest in lasers.

Skin ageing and pigmentation disorders (responsible: Dr N. Dietrich, Professor T. Hunziker)

After years of research and development, outer root sheath cell transplantation is now transferred to clinical application, whereby melanocyte precursor cells are transplanted in depigmentation disorders such as vitiligo and scars while keratinocyte precursor cells are used for skin rejuvenation. Transepidermal cell delivery is performed by micro needling using a dermaroller system. Taken together, the whole approach is minimally invasive (hair plugin and dermaroller application), which dramatically reduces the risk of adverse events and avoids relevant downtime. This novel treatment is an out-patient procedure, which lasts one to two hours.

Trichology clinic

(responsible: Dr P. de Viragh)

We provide a specialised evaluation and care of patients with complex and severe diseases of the scalp and hair. Expert evaluation and individualised therapy are mandatory in cases of hair loss, hair structure alteration, and scalp inflammation or scarring.

- To properly evaluate patients, the following exams are carried out:
- microscopical analysis of hair samples (trichogram) to assess structural abnormalities, establish the rate of hair loss, or identify genetic influences
- scanning electron microscopy for definitive diagnosis of hereditary hair abnormalities
- stereotactic photography and computer-assisted digital imaging (trichoscan) is used to evaluate treatment efficacy objectively
- dermoscopic scalp evaluation (trichoscopy)
- scalp biopsies for examination by light microscopy and immunohistochemistry studies.

The scientific experience in the field of hair physiology and diseases of the pilosebaceus follicle is attested by numerous presentations at international meetings and publications by the involved staff, as well as by the ongoing research activities such as treatment protocols for alopecia areata, therapy of chemotherapy-induced hair loss.

Nail disease clinic

(responsible: Professor E. Haneke)

In a dermatological practice, up to 15% of the patients present with nail disorders. The current knowledge in this area is not always satisfactory and management of many nail diseases has been limited due to lack of specific and effective therapeutic modalities. For example, onychomycoses that affect up to a third of the elderly still represent a problem with a complete cure rate remaining below 50%. Furthermore, treatment of nail psoriasis is still challenging despite the availability of systemic biological treatments. Evaluation of nail diseases and their diagnoses are further hampered by the fact that few dermatopathologists and pathologists have the required experience with the interpretation of nail biopsies. Most physicians are reluctant to biopsy the nail organ. Finally, some nail diseases require a specific surgical approach, and few experts are familiar with nail surgery.

In our Nail Clinic we offer both conservative and surgical management for a variety of inflammatory, infectious, tumoral and congenital nail diseases. Our clinic provides a unique expertise in nail surgery and nail pathology throughout Europe.

Phlebology clinic

(responsible: Dr Dr A.A. Ramelet, Dr U. Büttiker)

More than 50% of the adult population in Western countries suffers from chronic venous disorders (CVD). Besides varicose veins, the most severe form of CVD, chronic venous insufficiency (CVI), occurs in up to 10% of people. CVI is responsible for and may lead to acute and/or chronic eczematous diseases, pigmentation, leg oedema, dermatoliposclerosis, atrophie blanche, and leg ulcers, resulting in high morbidity and health costs.

– Our Department is specialised in the clinical evaluation, clinical investigation (cw-Doppler and colour duplex) as well as in both the conservative (compression, venoactive drugs, physiotherapy) and surgical (sclerotherapy, echo-guided sclerotherapy, surgery) treatment of CVD. There is a tight collaboration with the Department of Angiology in Bern (Professor I. Baumgartner, Dr T. Willenberg), which is of fundamental importance for comprehensive and multidisciplinary evaluation of patients Management of chronic wounds comprises special therapeutic procedures, which are provided by nurses specifically trained in wound care

Chronic wound care centre

(responsible: Professor T. Hunziker, Dr N. Pelivani)

The management of chronic skin wounds is organised in close collaboration with the chronic wound care centre. Our Department has a large out-patient day clinic specifically dealing with evaluation and management of recalcitrant skin wounds of vascular, neuropathic, tumoral and/or of inflammatory origin. The running of the clinic and patients' management are critically supported by specialised nurses. Here we provide the entire spectrum of medical services, such as conservative (e.g. use of novel wound dressings and matrix products) and surgical treatments (conventional skin grafting, complex grafting procedures).

For the management of recalcitrant chronic wounds our team frequently takes advantage of tissue-engineered skin equivalents. Specifically, our centre has developed a technique enabling the generation of autologous stratified epidermal equivalents using hair directly taken from affected patients (EpiDex®, see research part). The latter approach has been shown to be useful and cost-effective for the management of hard-to-heal chronic venous and mixed venous-arterial leg ulcers. The costs for the application of these autologous epidermal equivalents are now covered by Swiss health insurances.

Dermatopathology unit

(responsible: Dr H. Beltraminelli, Dr R. Blum, Dr H. Nievergelt, Professor E. Haneke)

- The Dermatopathology sector deals with the processing and evaluation of 15,000 to 18,000 tissue samples per year (with 50,000 slides). Biopsy specimens are referred from our Department (30%) of the university hospital and from dermatologists from all over the country (70%).
- The diagnostics cover the whole spectrum of dermatopathology, especially inflammatory, autoimmune and neoplastic skin diseases. For the most cases we use conventional histological investigations, when necessary immunohistochemistry (we have a large panel of stainings covering more than 90% of dermatopathology diagnoses) and molecular technologies (in collaboration with the Institute of Pathology, University of Bern). Our interest is specifically focused on the diagnosis of cutaneous lymphomas, melanocytic tumours and inflammatory diseases.
- The team of dermatopathologists is actively implicated in post-graduate teaching courses in dermatopathology. Furthermore, it provides weekly the clinical-pathological correlation during the meetings of our clinical staff.

International activities in the field of dermatopathology

- Since 2009 there is an intense collaboration with the Regional Dermatology Training Centre (RDTC) in Moshi, Tanzania. We provide human and technical support for the development of the local dermatopathology unit and supported fellowship of African specialists.
- Our dermatopathology sector has been officially recognised as training centre in dermatopathology by the International Committee for Dermatopathology (www. icdermpath.org). Since 2009 we have hosted several guest physicians from many countries: China, Egypt, India, Kenya, Saudi Arabia, Turkey.
- Since 2010 we participate to the Groupe Francais pour l'Étude des Lymphomes Cutanés (GFELC) as active members, discussing all skin lymphomas seen at our clinic.

Service

Consultations	2011	2012
Out-patient unit		
Number of consultations		
Out-patient unit (including private consultations)	19 126	21 791
Out-patient day clinic	3 322	3 609
Surgery sector	2 281	2 299
Phototherapy sector	4 836	5 298
Corrective cosmetic procedures	1 050	695
Activity of the hospital In-patient unit		
Number of hospitalized patients	504	538
Total of hospital days	3 068	2 866
Number of day care patients		
Hospital average length of stay (days)	6.09	5.33
Activity of the dermato-allergology laboratory		
Patch tests (number)	1 234	1 818
Activity of the dermatopathology sector		
Processed external biopsy specimens	11 739	12 079

Research and development projects

1. Autoimmune blistering diseases: bullous pemphigoid and pemphigus

Our group is implicated in studies aimed at understanding the pathophysiologic mechanisms of pemphigoids and pemphigus, a group of severe autoimmune blistering diseases of the skin and mucosae. These diseases run a chronic course, are frequently difficult to treat and are associated with a significant morbidity and mortality. Overall, understanding the etiopathogenesis of pemphigus and pemphigoid may provide crucial additional insights into basic mechanisms of autoimmunity and may help to design more specific therapeutic strategies.

The **pemphigoids** include bullous pemphigoid, gestational pemphigoid and cicatricial pemphigoid. They are a relatively common group of autoimmune blistering disorders associated with autoantibodies directed against two proteins of the cutaneous basement membrane zone, BP180 and BP230. The current project is aimed at: 1) characterising the humoral and autoreactive T cell response to BP180 and BP230 in the disease course of the pemphigoids; 2) identifying laboratory markers predicting disease activity and outcome; 3) developing innovative diagnostic tools such as ELISAs and microarrays for the detection of patients' autoantibodies with high sensitivity and specificity.

Pemphigus is another severe autoimmune blistering disease of the skin and mucous membranes. There are two major types of pemphigus: pemphigus foliaceus and pemphigus vulgaris. There is a related disease called paraneoplastic pemphigus sharing some overlap with pemphigus. They are caused by the production of IgG autoantibodies directed against cell-cell adhesion complexes, called desmosomes. Specifically, two transmembrane desmosomal proteins are characteristically targeted by patients' autoantibodies, desmoglein 1 and desmoglein 3. Paraneoplastic pemphigus autoantibodies target several intracellular linkers of the cytoskeleton, a family termed plakins, and a novel protein identified in our laboratory, called alpha-2 macroglobulin-like 1 protein, which is an extracellular, broad range protease inhibitor.

Our ongoing project represents a joined effort of several European groups with the following long term goals: 1) analysis of the autoantibody-driven effector phase frequently involving «epitope spreading»; 2) characterisation of the molecular

events leading to intraepidermal blistering; 3) analysis of the impact of therapeutic strategies such as the monoclonal antibody anti-CD20 (rituximab) on the cellular and humoral autoimmune response in pemphigus, and 4) definition and establishment of clinical parametres as valid measurements for the extent and activity of the disease and life quality assessment in pemphigus.

2. Characterisation of the interactions between plakins and the cytoskeleton

Our group is primarily implicated in basic investigative studies aimed at characterising 1) the association of plakin family members, plectin, desmoplakin and bullous pemphigoid antigen 1 (BPAG1), with the cytoskeleton in epithelia and striated muscle cells; 2) the regulation of these interactions by posttranslational modifications (such as phosphorylation), and 3) the contribution of the plakins to the overall organisation of the cytoskeleton since plakins can usually interact with at least two components of the cytoskeleton, the microfilaments, the microtubules and/or the intermediate filaments, and specifically anchor these structural networks to various membrane complexes. All these connections are critical for the maintenance of the cell architecture and tissue resilience to mechanical forces. In fact, mutations in the genes coding for plectin, desmoplakin, BPAG1, and intermediate filaments cause a variety of devastating human diseases, attesting to the importance of these proteins for tissue integrity.

3. Psoriasis research

Our studies are aimed at investigating basic immunological mechanisms, e.g. cytokines and chemokines and their regulation through therapeutic interventions in psoriasis. As control, findings are compared to those obtained in different forms of eczema. These investigations may help to identify new targets for future therapeutic intervention.

4. Translational medicine: cell therapies for chronic wounds and pigmentation disorders

Our clinic provides various approaches involving tissue engineering for skin wound treatment. Specifically, we offer

 autologous ORS (= outer root sheath of plucked anagen scalp hair follicles)derived keratinocyte transplantation for recalcitrant skin wounds [product EpiDex®]

- autologous ORS-derived melanocyte precursor cell transplantation for skin depigmentation disorders, such as vitiligo and leucoderma
- autologous ORS cell transplantation for skin rejuvenation.

Professor Thomas Hunziker has spent many years in the research field of tissue engineering with development of new approaches devoted to the treatment of skin defects. In independent and collaborative studies, his team developed, clinically tested and introduced onto the market two tissue engineered products, EpiDex® and Allox (allogeneic, two-cell-type [fibroblasts and keratinocytes] wound stimulation).

5. Cutaneous drug reactions

The main research goals are 1) to improve the understanding of the molecular interactions of drugs/chemicals with immune cells, i.e. T cells, dendritic cells and 2) to dissect the mechanisms by which these interactions stimulate and affect the immune system. These studies are planned to pave the way for improved methods to diagnose adverse drug reaction and to improve risk assessment of chemicals/ drugs. These studies are performed in close collaboration with the Division of Allergology (Professor W. Pichler) of the Inselspital in Bern.

6. Atopic eczema and contact dermatitis

Pathogenic mechanisms of chronic inflammatory skin diseases including eczema represent an important research area in our Department. By analysing the skin infiltrating cells and cytokines as well as their regulation, we aim to better understand the pathophysiologic mechanisms of eczema. Within this research frame, our interest is specifically focused on the function of eosinophilic granulocytes. Better characterisation of their pathogenic role in eosinophilic skin diseases is expected to help the development of new therapeutic strategies.

7. Hidradenitis suppurativa

Hidradenits suppurativa (also called acne inversa) is a chronic inflammatory disorder of the apocrine gland-bearing skin. The clinical course can be devastating. Endstage hidradenitis suppurativa is disabling and has a profound impact on the quality of life. At present, the pathophysiology of this condition is still poorly understood. To better understand its mechanisms we are currently performing studies using immunohistochemical and molecular biology methods to better comprehend the mechanisms leading to chronic inflammation. To better help these patients we have a special hidradenitis suppurativa clinic (responsible: Professor R. Hunger) at our department. At present we can offer these patients many different therapeutic options including the participation in clinical studies (i.e. Humira, laser treatment, extracorporal shock wave).

8. Non-melanoma skin cancers

Our research is focused on epidemiologically studies on NMSC.

- We are collecting UV-exposure behavioural data of the general population
- We aim to identify patients that are at high risk for developing NMSC (and melanoma) in the setting of immune suppression e.g. due to organ transplantation. Our collaborations with the different departments of the Transplant Board of the Inselspital are constantly developing.

Another field of expertise are the clinical trials with new therapeutic agents. Sonic hedgehog inhibitors are administered to otherwise untreatable basal cell carcinoma, and Resiquimod is being applied on actinic keratosis.

Future projects involve the genomic, proteomic and metabolomic characterisation of highly aggressive and recurrent NMSC in heavily sun-damaged non-immunosuppressed patients and in organ transplant recipients. This kind of research will involve a collaboration with the Department of Clinical Laboratory (Chair: Professor G. Fiedler). These studies are expected 1) to be useful for the selection of high-risk patients who may benefit from more aggressive treatment and follow-up protocols and 2) to identify targets for novel pharmacological intervention.

9. Cutaneous T cell lymphoma

Primary cutaneous T-cell lymphomas (CTCL) represent a heterogeneous group of extranodal non-Hodgkin lymphomas. Mycosis fungoides (MF) and Sézary syndrome (SS) are the most common types. Our specialists are well-connected internationally, especially with the Groupe Francais pour l'Étude des Lymphomes Cutanés (GFELC) and with the Dermatology clinic in Graz, where we studied the characteristics of rare cutaneous CD4+ pleomorphic skin lymphomas and related diseases.

10. Histological characteristics of microneedle treatment and laser on treated skin

We compared characteristics of the microscopic treatment zones (MTZ) induced by ablative fractional CO2 laser and by microneedle treatment in ex vivo human breast skin. Both technologies are able to create small epidermal defects, microneedle treatment bearing the advantage to lack devitalized tissue.

11. Bullous autoimmune diseases

We tested immunohistochemical stainings for bullous pemphigoid showing that sensitivity is much lower than with immunofluorescence methods.

Postgraduate teaching courses

19.01.2011	Phlebologie
	Guest: Dr Dr A.A. Ramelet, Lausanne
28.01.2011	Trichologie I
	Guest: Dr P. de Viragh, Zürich
17.02.2011	Was ist Ihre Diagnose?
	Prof N. Yawalkar, Bern
25.02.2011	Trichologie II
	Guest: Dr P. de Viragh, Zürich
19.05.2011	Stomatologie für Dermatologen und Zahnärzte
	Guests: PD Dr dent M. Bornstein, Bern, Dr J. Kamarachev, Zürich,
	Prof P. Itin, Basel
09.06.2011	Erkrankungen der Haare und Nägel
	Guests: Dr P. Reygagne, Paris, Dr B. Noecker, Darmstadt

22.09.2011	Dermatoallergologie 2011
	Guests: Dr K. Scherer, Bern, Dr P. Piletta, Genève, Dr T. Lipkow,
	Luzern, Dr I. Lehmann, Leipzig, Prof K. Bork, Mainz, Prof F.
	Spertini, Lausanne, Prof A. Straumann, Olten, Prof B. Ballmer-
	Weber, Zürich
13.10.2011	35 Jahre Dermatologie Bern – mein Rück- und Ausblick.
	Abschiedsveranstaltung von Professor Thomas Hunziker
	Prof R. Hunger. Prof N. Yawalkar. Dr R. della Torre. Dr N.
	Dietrich. Dr M. Stieger. Bern
01.12.2011	Neues zur Therapie von aktinischen Keratosen. Spinaliomen und
	Basaliomen
	Guests: Prof U.R. Hengge, Düsseldorf, Prof E. Stockfleth, Berlin
23.02.2012	Immundefekte
	Guests: Dr M. Rybojad, Paris, Dr M. Hoernes, Zürich
26.04.2012	Was ist Ihre Diagnose?
	Dr P. Oberholzer, Prof N. Yawalkar, Bern
10.05.2012	Haut und Umwelt; Fokus Hautbarriere
	Guests: Prof A. Hovnanian, Paris, Dr H.P. Rast, Luzern,
	Prof S.M. John, Osnabrück, Prof R. Fölster-Holst, Kiel
20.09.2012	Dermatochirurgie: Chirurgie in der Klinik und in der Praxis.
	Guests: Dr A. Skaria, Vevey, Dr E. Hübscher, Biel, PD Dr M.
	Constantinescu, Bern
15.11.2012	Haare und Nägel
	Guests: Dr P. de Viragh, Zürich, Prof E. Haneke, Freiburg (D)

Publications 2011

Peer-reviewed Articles

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Honors and Prizes

Dr H. Beltraminelli

International Affairs, Universität Basel, Grant: "Development of Dermatopathology Routine and Research in Africa", 11'100 CHF

Dr A.-A. Ramelet

Emeritus Fellow of the Australasian College of Phlebology

Ehrenmitglied, Deutsche Gesellschaft für Phlebologie

Australasian College of Phlebology, Award of Excellence for Pioneering Innovations in Phlebology

Dissertations

B. Cortes Sanchez: Mortality of bullous pemphigoid in Switzerland: a prospective study (Prof L. Borradori)

Cirus Schahab: Evaluation of the predictive and therapeutic impact of sentinel node biopsy in truncal malignant melanoma (Prof R. Hunger)

Publications 2012

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Honors and Prizes

Dr H. Beltraminelli

D. Steigleder Preis 2012 für eine herausragende Publikation in der Dermatopathologie: Beltraminelli H, Leinweber B, Kerl H, Cerroni L.

Primary cutaneous CD4+ small-/medium-sized pleomorphic T-cell lymphoma: a cutaneous nodular proliferation of pleomorphic T lymphocytes of undetermined significance? A study of 136 cases. Am J Dermatopathol 2009;31:317-322

Dr Dr A.A. Ramelet

Die Medizinische Fakultät verleiht die Würde eines Doctor medicinae honoris causa (Bern 1.12.2012)

- für seine langjährige intensive Tätigkeit als niedergelassener Spezialist, der beigetragen hat, die Phlebologie als medizinisches Fach und Spezialität national und international zu fördern und bekannt zu machen.
- für seine unermüdliche T\u00e4tigkeit als Autor und Verfasser von einer Vielzahl von erfolgreichen
 Lehrb\u00fcchern und Ver\u00f6ffentlichungen im Gebiet der Phlebologie, die internationale Anerkennung
 bekommen haben und als Standardwerke gelten.
- für seinen begeisterten Einsatz als Tutor und die Förderung einer Vielzahl von Schweizer und ausländischen Aerzten im Werdegang zum Fachspezialist im Gebiet der Angiologe, die er in seiner Praxis aufgenommen und empfangen hat.
- für sein unermüdliches Mitwirken als geschätzter und glänzender Speaker im Gebiet der Phlebologie in der Schweiz und in allen Ecken der Welt.

- für seinen langjährigen standespolitischen Einsatz im Gebiet der Dermatologie und Angiologie, der dazu beigetragen hat, dass die Phlebologie ein integrierender Bestandteil des Weiterbildungsprogramms zum Facharzt ist.
- für sein ständiges Interesse, seine Neugierde auf operative und medizinische Geräte und seine Beiträge zu deren Verbesserung bzw. zur Erleichterung von phlebologischen Eingriffen.

Dissertations

Della Torre Rocco: Clinical presentation and diagnostic delay in bullous pemphigoid: a prospective nationwide cohort. (Dr C. Combescure, Dr B. Cortés, Dr G. Marazza, Dr H. Beltraminelli, Prof L. Naldi, Prof L. Borradori)

Fiechter Sabine: Facial basal cell carcinomas recurring after photodynamic therapy: a retrospective analysis of histological subtypes (Dr A. Skaria, Dr H. Nievergelt, Dr R. Anex, Prof L. Borradori, Dr L. Parmentier)

Schneiter Thomas: Immunohistochemical analysis of Langerhans cells in psoriasis (Prof N. Yawalkar)

Guest doctors

Alhowaish Alauldin Khalef Mohamed aus Saudi Arabien vom 01.02.2011 bis 31.01.2012

Erdemoglu Yeliz aus der Türkei vom 11.06.2012 bis 10.12.2012

Kiprono Samson Kimaiyo aus Kenya vom 07.03.2011 bis 06.05.2011

Lee Haur Yueh aus Singapur vom 01.10.2010 bis 31.03.2011

Sallam Mohammed Abdel Azeem Shahwan aus Aegypten vom 16.09.2011 bis 15.06.2013

Tambe Swagata Arvind aus Indien vom 01.10.2012 bis 31.10.2012 (ISD Mentorship)

Tang Min Moon aus Malaysia vom 01.11.2011 bis 30.04.2012

Tu Honggang aus Shanghai vom 16.09.2011 bis 15.12.2012

Zuriel Daniel aus Kenya vom 05.12.2011 bis 03.01.2012

Grants

Swiss National Foundation, Analysis of molecular and cellular mechanisms in immune-mediated tissue damage of the skin: Hidradenitis suppurativa as a model disease, Robert Hunger, Nikhil Yawalkar, CHF 70'000.–

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Dr Dr A.A. Ramelet

(Phlebology)

Dr U. Büttiker (Phlebology)



Dr K. Fritz

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