Department of Dermatology, Inselspital, University Hospital Bern

Activity Report 2010

MINSELSPITAL

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 first activity report under the lead of Professor Luca Borradori. Since the change of the chairmanship in July 2008, the Department has undegone substantial changes in overall spirit, in the medical staf as well as in overall organization. Requisite changes positioned the Department in correctly to face the new challenges imposed by the new developments in the Swiss health cae system as well as by the current economic landscape. 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 pregraduate and postgraduate teaching. Efficient management with improvement of the various processes has emerged is indispensable to meet increasing budgetary constraint.

Prof. Luca Borradori
Director and Chairman

Therese Zürcher Chief nurse





Staff and collaborators (as for 31. 12. 2010)

Director and Chairman Professor L. Borradori
Vice-Chairman Professor Th. Hunziker

Chief Nurse Th. Zürcher

Faculty and Chiefs Professor R. Hunger

Professor N. Yawalkar

Chief secretary M. Schenk
Head of secretaries J. Sprecher
Research & development Dr B. Favre
Chief physician clinical ward
Dermatopathology sector Dr H. Beltraminelli

PD Dr I. Hegyi

Attending physicians Dr L. Parmentier,

Dr Th. Schneiter, Professor D. Simon

Consultants and lectors Dr M. Adatto (Laser), Dr P. de Viragh

(Trichology), Dr K. Fritz (Laser), Professor E. Haneke (Nail diseases), Dr H. Nievergelt (Histopathology), Dr A.-A. Ramelet (Phlebology), Dr A. Skaria (Mohs-Surgery)

Residents C. Blazek, Dr M. Corti, R. Della Torre,

Dr N. Irla, Dr D. Perruchoud,

Dr Z. Spanou, M. Stieger, Dr A. Surovy

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 cae center 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 center 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 22 beds, an out-patient section with several specialized clinics, a day hospital for management of complex cases with emphasis on chonic wounds, a phototherapy unit, a surgical unit, a laser platform, as well as a dermatopathology unit.
- The medical staff consists of 10 senior physicians and 8 junior physicians. There are currently one Professor, four associate Professors and one senior lecturer. Furthermore, there are 7 part-time board-certified consultants and lectors. The Department egularly hosts a number of guest physicians in training and 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. The nursing activity for the in-patients wad and distinct out-patient activities has earned an ISO acceditation attesting a high level of quality of the standards of the provided nursing practice.

Specialized nursing team

The nursing team is headed by Mrs TZürcher, member of the department's directorate. The nursing team constitutes the lagest 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 (Mr M. Held, Mrs B. Zurbuchen, Mrs TGross, Mrs B. Nydegger) 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 wark, an increased number of out-patient surgical cases related amongst others, to the introduction of the micrographic Moh's 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 in-patients is approximately 550 per year. There are up to 20 000 out-patient consultations per year 3 500 patients are cared for at the wound care clinic, up to 5 500 phototherapy teatments and 2 000 surgical procedures are routinely performed. The dermatohistopathology sector processes and analyses 18 000 skin biopsy specimens per year and is one of the lagest dermatopathology units in Switzerland.

Objectives

The main goals of the Department of Dermatology ae

- 1. to provide *high quality medical care and service*by offering a spectrum of specialized ambulant consultations as well as appropriate evaluation and management of patients requiring hospitalization. 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 postgraduate students in medicine and biomedical sciences, esidents, physicians and specialists of dermatology and venereology, as well as other specializations.

Overall, the Department is very enthusiastic and highly motivated to share experiences in clinical evaluation, management and teatment of dermatological patients through interface with other partners as well asto develop clinically oriented and basic investigative esearch projects in collaboration with other researchers or with pharmaceutical companies.

Current challenges

The structure of the Swiss health system is undegoing a substantial reorganization. The Swiss health system is one of the most expensive in the world. Measures are being taken in an efort to reduce expenditures 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.

Activity and areas of expertise

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

- Skin cancers including clinical evaluation, management and systematic follow up of melanoma and non-melanoma skin cancer patients using video-microscopy and digital imaging devises
- 2. Dermatosurgery, including Mohs' micrographic surgery
- 3. Chronic wound care with use of tissue-engineered skin equivalents and novel wound dressings
- 4. Pigmentation disorders with development of melanocyte transplantation approaches and of other treatments such Excimer laser
- 5. Inflammatory skin diseases, such as psoriasis and atopic dermatitis as well as autoimmune blistering skin disoders
- 6. Congenital vascular malformation, blistering and fragility syndomes of the skin
- 7. Acne and hidradenitis suppurativa
- 8. Chronic venous disorders
- 9. Nail disorders with specific conservative and surgical treatments
- 10. Dermatopathology

Detailed clinical services

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

Melanoma and pigmented lesion clinic

(responsible: Professor R. Hunger)

The incidence of malignant melanoma is rapidly gowing. The current incidence rate in Switzerland is 22 new cases per 100 000 inhabitants followed by over 200 melanoma elated deaths each year. While early stages can be cured by surgical excision, late stages have a poor pogno-

sis. To best follow up patients with malignant melanoma and to eco gnize these tumours at an early stage two specialized 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 egular 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 nevi and other patients at high risk for melanoma ae 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 clinic

(responsible: Dr L. Parmentier)

Non-melanoma skin cancers (NMSC) such as basal cell cacinoma and squamous cell carcinoma represent a medical and epidemiological challenge in Western countries. This is lelated first to the significant increase of skin cancers (4-8 % in Euope per year) as a consequence of the current life style (sun exposure) as well as the ageing of the populati on. In this context, there is a growing need and demand for skin sugical approaches ensuring good aesthetic results. Switzerland has the highest incidence of NMSC. Since the Inselspital is one of the Swisserferral centers 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 stong commitment to management of skin tumours of peculiar complexity A close collaboration with the Department of Plastic and Reconstructive Sugery (Chair: Professor A. Banic) exists.

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

- Tumour board: Interdisciplinary evaluation of patients with complex cutanoeus cancers together with the Department of Plastic and Reconstructive Surgery.
- 2. Dermatologic surgery, with particular focus on Mohs' micographic surgery.
- Non-invasive therapeutic approaches, such as photodynamic therapy (PDT), cryosurgery, and non-invasive topical immunomodulatory therapies.

Dermatosurgery clinic and micrographic surgery

(responsible: Dr L. Parmentier, Dr A. Skaria)

Micrographic surgery is a technique, which combines the sugical procedure with an immediate intraoperative histopathological assess ment of the excised tumour Its goal is twofold: first, to diminish the rate of recurrence of epidermal tumours from up to 20% in classical sugery down to 1-4% using Mohs' surgery; second, to improve the cosmetic result. The majority of treated tumours are mostly NMSC. Nevertheless, a modified technique called slow-Mohs' surgery also allows the treatment of certain forms of sacomas and malignant melanomas. So far these techniques represent the golden standard of treatment in the USA.

Our Department is one of the few centers in Switzerland, which provides Mohs' surgery. In Bern this approach has been introduced by Dr A.M. Skaria, who is currently the chairman of the dermatosurgery committee of the Swiss Society of Dermatology and Venereology.

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 pathome chanisms 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 tageted therapies with biologic treatments.

In our specialized 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 necosis factor inhibitors (etanercepts, 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 exclusive opportunity in Switzerland
- clinical research studies aimed at testing novel biologic teatments 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 characterization of the immune and inflammatory response in psoriasis (see research part).

Autoimmune skin diseases clinic

(responsible: Professor L. Borradori, Professor T. Hunziker)

Our Department has a specific interest and expertise in the evaluation, diagnosis and management of patients with sevee autoimmune blistering diseases of the skin and mucosa, such as bullous pemphigoid, epidermolysis bullosa, pemphigus and cicatricial pemphigoid, and gestational pemphigoid which is unique in Switzerland. Furthermoe, 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 center for patients from the Canton of Bern and from all over the country.
- Besides the clinical management of patients with autoimmune diseases, we are directly involved 1) in clinical multicenter Euopean studies aimed to characterize the clinical course, severity and pognostic 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- pecipitation techniques using recombinant proteins. Finally, we have contributed to the development of several different novel diagnostic ELISA tests.

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 afects more than 10% of children between the ages of 6 to 7 years. Irritant and allegic contact dermatitides as well as occupational eczemas ae common in adults. These groups of cutaneous diseases are characterized 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 aer of medical as well as socioeconomic importance.

This specialized 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 installa-

tion of adequate anti-inflammatory topical and systemic therapies, skin care and skin protection teaching courses, 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.

Paediatric dermatology clinic

(responsible: Dr K. Kernland Lang)

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

There are two major areas of interest and expertise:

- 1. Vascular malformations evaluated in the context of an intedisciplinary haemangioma board (together with paediatricians, angiologists and paediatric surgeons). The board takes advantage of the fact that the Department of Paediatric Surgery (chair: Professor Z. Zachariou) is the reference center in Switzerland for lage haemangioma and interstitial laser therapy. Vascular lesions involving the skin ae 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 specialized and comprehensive interdisciplinary evaluation of affected patients by the EB network consisting of paediatricians, gastoenterologists, dentists, plastic surgeons, and dieticians/nutritionists. Furthermore, molecular diagnosis for a variety of congenital diseases is povided in close

collaboration with various leading European laboratories. We have a specialized team ensuring appropriate wound dressing care and physiotherapy of affected EB patients. Finally, we also provide information and support to people living with these disoders as well as their family members and friends.

Laser clinic

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

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 diectly been involved in the development of laser devices in collaboration with various American and European companies.

Our laser center is equipped with state of the art laser devices (e.g. Cynergy Lasers). A close collaboration with specialists form 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, inflammatory skin conditions, and acne. Furthermore, we are also involved in studies aimed at assessing the impact of laser wavelengths on tissue eaction, safety aspects, as well as aesthetic issues.
- With regard to clinical research, we are currently analyzing the effect
 of distinct lasers on pigmentation disorders (Excimer, IPL), rosacea,
 psoriasis (Excimer and pulsed dye laser), atopic eczema (light vaccination, multicenter trial with Optomed), actinic keratoses (laser PDT)
 and acne (blue and red light laser sources).
- The clinical staff consists of Dr M. Adatto, past-Pesident and Honorary Member of the European Society of Laser Dermatology as well as medical director of Skinpulse Dermatology and Laser center Geneva,

Dr U. Büttiker, co-founding member of the Swiss goup of esthetic dermatology and skin care, Dr K. Fritz, specialist in laser dermatology and current President of the European Society of Laser Dermatology (ESLD), Dr N. Dietrich, dermatologist with specific interest for lasers.

Trichology clinic

(responsible: Dr P. de Viragh, Dr N. Pelivani)

We provide a specialized evaluation and cae of patients with complex and severe diseases of the scalp and hair Expert evaluation and individualized therapy are mandatory in cases of hair loss, hair structue alteration, and scalp inflammation or scarring.

To properly evaluate patients, the following exams ae 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 teatment efficacy objectively
- dermoscopic scalp evaluation (trichoscopy)
- scalp biopsies for examination by light micoscopy and immunohistochemistry studies.

The scientific experience in the field of hair physiology and diseases of the pilosebaceus follicle is attested by numeous presentations at international meetings and publications by the involved staf, 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 diagnosis 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 ofer both conservative and sugical management for a variety of inflammatory, infectious, tumoral and congenital nail diseases. Our clinic provides a unique expertise in nail sugery throughout Europe.

Phlebology clinic

(responsible: Dr A.A. Ramelet, Dr U. Büttiker Professor T. Hunziker)

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, occurs in up to 10% of the people. CVD is responsible for and may lead to acute and/or chronic eczematous diseases, pigmentation problems, leg oedema, dermatoliposclerosis, and leg ulcers, resulting in high morbidity and health costs.

Our Department is specialized in the clinical evaluation, clinical investigation (plethysmography, cw-Doppler and colour duplex) as well as in both the conservative (compession, 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 compensive and multidisciplinary evaluation of patients.

Chronic wound care center

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

The management of chronic wounds, severe venous or lymphatic disorders is organized in close collaboration with the chonic wound care center. Our Department has a large out-patient day clinic specifically dealing with evaluation and management of ecalcitrant skin wounds of venous, arterial, neuropathic, tumoral and/or of inflammatory origin. The running of the clinic and patients' management are critically supported by specialized nurses. Here we provide the entire spectrum of medical services, such as conservative (e.g. use of novel wound dessings, use of skin equivalents) and sugical treatments (conventional skin grafting, and complex grafting procedures).

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

Dermatopathology unit

(responsible: PD Dr I. Hegyi, Dr H. Beltraminelli, Dr H. Nievegelt)

The Dermatopathology sector deals with the pocessing 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 entile diagnostic spectrum of inflammatory, autoimmune and neoplastic skin diseases using conventional histological investigation, immunohistochemistry 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 postgraduate 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.
- Our dermatopathology sector has been officially recognized as training centre in dermatopathology by the International Committee for Dermatopathology (www.icdermpath.org).

Service

Consultations	2009	2010
Out-patient unit		
Number of consultations		
Out-patient unit (including private consultations)	16 340	17 320
Day care clinic	3 166	3 407
Surgery sector	1 799	2 154
Phototherapy sector	4 410	4 068
Corrective cosmetic procedures	689	721
Number of patients		
Out-patient sector	7 445	8 108
Private consultations	994	1 013
Day care clinic	376	355
Surgery sector	811	1 008
Physical treatment unit, Phototherapy sector	422	421
Activity of the hospital In-patient unit		
Number of hospitalized patients	532	573
Total of hospital days	4 403	3 962
Number of day care patients	106	131
Hospital average length of stay	8.1	6.7
Activity of the dermato-allergology laboratory		
Patch tests (number)	6 579	7 537
Activity of the dermatopathology sector		
Processed external biopsy specimens	10 806	11 477

Research and development projects

1. Autoimmune blistering diseases: bullous pemphigoid and pemphigus

Our group is implicated in studies aimed at understanding the patho-physiologic 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) characterizing the humoral and autoreactive T cell response to BP180 and BP230 in the disease course of the pemphigoids; 2) identifying labor atory markers predicting disease activity and outcome; 3) developing innovative diagnostic tools such as ELISAs and micoarrays 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 fluctious as an extracellular, broad range protease inhibitor.

Our current project represents a joined effort of seven European groups promoted by the European Framework programme VII with the following goals: 1) to better define the immune pathogenesis of pemphigus utilizing two in vivo models of pemphigus with emphasis on autoaggerssive T cells and their collaboration with autoantibody secreting B cells; 2) analysis of the autoantibody-driven effector phase frequently involving «epitope spreading»; 3) characterization of the molecular events leading to intraepidermal blistering; 4) analysis of the impact of therapeutic strategies such as the monoclonal antibody anti-CD20 (rituximab) on the cellular and humoral autoimmune esponse in pemphigus, and 5) definition and establishment of clinical parameters as valid measurements for the extent and activity of the disease and life quality assess ment in pemphigus.

2. Characterization of the interactions between spectraplakins and IF proteins

The group is primarily implicated in basic investigative studies aimed at characterizing 1) the association of plakin family members, plectin, desmoplakin and BPAG1e, with various intermediate filaments in epithelia and striated muscle cells; 2) the egulation of these interactions by posttranslational modifications (such as phosphorylation), and 3) the contribution of the plakins to the overall oganization of the cytoskeleton by linking intermediate filaments to the two other components of the cytoskeleton, the microfilaments and the microtubules, and to 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, BPAG1e, and intermediate filaments cause a variety of devastating human diseases, attesting to the importance of these poteins for tissue integrity.

3. Psoriasis research

Our studies are aimed at investigating basic immunological mechanisms, e.g. cytokines and chemokines and their egulation 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 [product EpiDex®]
- allogeneic, two-cell-type (fibroblasts and keratinocytes) wound stimulation [Allox®] - ORS-derived autologous melanocyte transplantation for skin depigmentation diseases, such as vitiligo.

Professor Thomas Hunziker has spent many years in the esearch field of tissue engineering with development of new approaches devoted to the treatment of skin defects. In independent and collaborative studies, his team developed tested and introduced respectively onto the market two tissue engineered products, EpiDex® and Allox®.

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 Allegology (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 analyzing 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 characterization 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 chonic inflammatory disorder of the apocrine gland-bearing skin. The clinical course can be devastating. End-stage hidradenits suppurativa is disabling and has a profound impact on the quality of life. At pesent, the pathophysiology of this condition is still poorly understood. To better understand its mechanisms we are performing the following studies: 1) analysis of the expression of Toll-like receptor 2 (TLR2) in lesional tissue, which seems to play an important role in maintaining the chronic inflammation; 2) characterization of the role of different subsets of macrophages (M1 and M2 subsets) and T cells (Th1 and Th2 cells) in the immuneesponse. To this end, we have established a novel method to isolate the infiltrating cells from the lesions to perform flow cytometric analysis.

8. Non-melanoma skin cancers

The research is focused on skin and oral squamous cell carinomas. Our study aims to identify clinically suitable molecular markers for metastatic properties, tumour development and tumour ecurrence potential by combining proteomic (tissue microarray, immune- histochemistry, in situ hybridisation, FISH) and genomic (cDNA array RT-PCR) techniques. 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 taget genes for novel pharmacological intervention.

We are currently establishing cohorts of patients with NMSC in the local population:

- to collect epidemiological data of the population at high risk for NMSC:
- to characterize genetic factors conferring a high risk for developing skin tumours. Bern and the adjacent egions show a relatively strong genetic homogeneity;
- to identify specific epigenetic factors: alimentation and other potential toxic exposure (e.g. arsenic) that may critically afect the development of NMSC besides sun exposure. As a matter of fact, some patients develop tumours in sun-protected areas.

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), a leukemic variant, are the most common types. Transformed T cells in CTCL are typically memory CD45RO+CD4+T cells, produce Th2 cytokines, and display skin homing eceptors such as cutaneous lymphocyte antigen (CLA) and CCR4. These cells have increased skin homing potential, explaining in part the high affinity of these cells for the skin. We have previously analyzed the frequency and distribution of dendritic cells (DC) in lesions of CTCL. Furthermore, we have recently performed a vaccination study with a human telomera se specific peptide (hTERT) in CTCL patients. The enzyme telomerase is critically involved in tumour cell immortalization. Further studies are aimed at investigating the role of T regs in CTCL.

Postgraduate teaching courses

14.01.2010	Probleme der alten Haut Guests: Professor C.U. Brand, Luzern, Dr G. Kaya, Genève, Professor R. Panizzon, Lausanne
25.02.2010	Häufige und seltene Haut- und Schleimhautmanifestationen bei Vaskulitiden, Kollagenosen und Autoimmunerkrankungen Guests: Professor C. Frances, Paris, Professor J. Samson, Genève
24.03.2010	Klinisch-immunologische Konferenz, BIC : Atopic der matitis Guests: Professor T. Bieber, Bonn, Professor S. Weidinger, München
15.04.2010	Hautveränderungen der Vulva: oft eine Herausforderung für Dermatologen und Gynäkologen
27.05.2010	latrogen bedingte und autoimmune Reaktionen der Haut: ein Update <i>Guest: Professor S. Aractingi, Paris</i>
11.11.2010	Handekzeme: neue berufsdermatologische und therapeutische Aspekte Guest: Dr H.P. Rast, SUVA Luzern
02.12.2010	Borreliosen: neues in der Klinik, Diagnostik und Therapie Guests: Dr P. Oliver, Sion, Professor B. Zelger, Innsbruck

Publications 2010

Original papers (peer-reviewed)

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Honors and prizes

Dr K. Fritz: Associate University Professor (invited), Universität für Medizin Pharmazie Carol Davila Bukarest. Anerkennung dieses Titels durch das Ministerium für Kultur und Wissenschaft des Bundeslandes Rheinland-Pfalz in Mainz (D), 28.09.2010

Dr K. Fritz: Ernennung zum Visiting Professor, Universität Sofia, 8.12.2010

Dr H. Beltraminelli: Prix international Jean Civatte, Journeés Dermatolo giques de Paris, Paris, 7.-11.12.2010

Dr C. Schlapbach: Posterpreis: «NK cells and cytotoxic T cells expess granulysin in multiple cutaneous drug reactions». Jahresversammlung der Schweizerischen Gesellschaft für Allegologie und Immunologie, St. Gallen, 15.-16.04.2010

Dr K. Kernland: Posterpreis Schweizerische Gesellschaft für Dermatologie und Venereologie, Zürich, 26.-27.08.2010

Dr I. Schepens: Berner Immunology Club Price for the best article in 2010: Schepens I, Jaunin F, Begre N, Läderach U, Marcus K, Hashimoto T, Favre B, Borradori L. PLoS One. 2010 Aug 18;5:e12250

Grants

Professor D. Simon: DNA-containing extracellular structures in eosinophilic diseases. S.T. Johnson Stiftung Bern

Professor N. Yawalkar: Characterization of the in situ inflammatory infiltrate in palmo-plantar psoriasis treated with alitretinoin. Basilea

Guest doctors

Savas Yayli, MD, Assistant Professor, Karadeniz Technikal University, Department of Dermatologie, Trabzon, Türkei (2 Monate)

Haur Yueh Lee, MD, Registrar, Dermatology Unit, Singapore General Hospital / National Skin Centre, Singapore (6 Monate)

Chanitwan Treewittayapoom, MD, Aesthetics Center, Kasemrad General Hospital, Bangkok, Thailand Bangladesh (1 Woche)

Daniela Gutierrez, MD, Department of Surgical Dermatology, Hospital General «Dr Manuel Gea González», Mexico

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Universitätsklinik für Dermatologie CH-3010 Bern Tel. +41 (0)31 632 22 88 www.insel.ch www. dermatologie.insel.ch



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