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A Comparative Analysis of Quality of Life for Adolescents Versus Adults Affected by Alopecia Areata

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Adolescents' perceptions of disease often differ from those of children and adults. Research is needed to investigate adolescents' unique perceptions and experiences of disease so that health care and genetic counseling services can be better tailored to meet their needs. In the present study, data were obtained for 43 adolescents with Alopecia Areata (modal age = 15 yrs.) who are part of the National Alopecia Areata (AA) Registry. Data included: demographic and disease data from the National AA Registry and responses to the National AA Registry Quality of Life Questionnaire, a measure of five dimensions of functioning. Their data were compared to those of a sample of 45 adults with AA (modal age = 45 yrs.) selected randomly from the Registry. With the exception of age, there were no significant between-group differences for demographics or AA history. Adolescents scored significantly higher than adults ($p < .01$) on general functioning, spiritual functioning, physical functioning, and emotional functioning, and significantly lower on social and family functioning. Multiple regression analyses indicated that developmental status (adolescent vs adult) was the only significant predictor of scores for 3 of the 5 quality of life dimensions (general, physical, and social/family functioning). The results suggest that although AA potentially impacts the functioning of all individuals with the disease, adolescents' perceived quality of life is not a subset of adult functioning. Adolescents have a functioning style specific to their disease and developmental stage. Services need to be tailored specifically for adolescents struggling with AA.

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Cytokine mRNA Expression in the Skin and Lymphoid Organs of the C3h/Hej Mouse Model For Alopecia Areata

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Alopecia areata (AA) is a chronic hair loss disease involving peri- and intra-follicular infiltration by mononuclear cells. Several studies suggest immunomodulatory cytokines expressed by the inflammatory infiltrate not only act as mediators of immunity and inflammation but also regulate cell proliferation and differentiation and, as such, may play an important part in regulating hair growth and AA development. We examined in vivo levels of mRNA of 13 cytokines and chemokines in the skin, draining lymph nodes, spleen, and thymus of C3H/HeJ mice with AA and normal haired littermates using quantitative RT-PCR techniques. The levels of IFN-g and IL10 were statistically significantly higher in the skin and lymph nodes of AA-affected mice than in healthy controls while that of IL18 was lower. No statistically significant changes were found for the mRNA expression levels of IL17, IL21 and GM-CSF. Three main subfamilies of chemokines studied were CC chemokines, including RANTES, macrophage inflammatory proteins a and b (MIP-1 a and b), CXC chemokines, including CXCL1 and CXCL10, and CX3C chemokines represented by CX3CL1; all of which were found highly expressed in skin draining lymph nodes and/or the skin of mice with AA. Chemokines are involved in chemoattraction and activation of leukocytes to the site of inflammation and in the induction of cytokine production and are thus key determinants of inflammatory reactions and immunity. The fact that all the studied chemokines were expressed at significantly higher levels in AA-affected mice than in controls suggests they may play an important role in AA pathogenesis.

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finasteride for Treatment of Iatrogenic Androgenetic Alopecia In Woman

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finasteride, a type II 5-alpha-reductase inhibitor, has long been proposed to treat female pattern hair loss. Although female pattern hair loss associated with hyperandrogenism can respond to finasteride,there has been no report on its efficacy for rare cases of androgenetic alopecia that develops in women undergoing androgen therapy. In this work, we describe the efficacy of medium-high doses of finasteride (2.5 mg daily) in the treatment of Hamilton type hair loss associated with exogenous androgen supplementation. Despite the continuation of androgen supplementation, by 10 months of treatment, noticeable improvement of hair coverage on the scalp was observed. The symptoms assiciated hyperandrogenism inculding hirsutism and a lower pitch of the voice were also improved under the finasterid treatment. In summary, Hamilton type hair loss can develop on female patients under androgen

treatment and the hair loss can be effectively treated with medium-high doses of finasteride (2.5 mg daily) despite the continued androgen supplementation.

P-104

Prostaglandin Metabolism in Hair Follicle: PGE_2 and PGF_2alpha Synthesis and Interconversion

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Prostaglandins regulate a wide number of physiological functions. Recently PGF_2a ananalogue such as latanoprost was shown to have a real impact on hair regrowth. The aim of this study was to investigate and describe the expression profile in human hair follicle of prostaglandin (PG) metabolism key enzymes, i.e. Carbonyl reductase-1 (CBR1), microsomal Prostaglandin E synthase-1 (mPGES-1) and microsomal Prostaglandin E synthase-2 (mPGES-2), cytosolic Prostaglandin E synthase (cPGES), the aldoketoreductase AKR1C1 and the Prostaglandin F synthase AKR1C3. Quantitative RT-PCR evidenced i) the expression of all these enzymes in plucked hair follicles and ii) a higher expression of mPGES-2 and AKR1C3 in female hair follicles. Using Western blot, PGE2 and PGF2 ELISA assays and immunohistochemistry, we observed that most of hair follicle cell types were able to produce PGE_2 and/or PGF_2a and synthesized all PG metabolism enzymes. Moreover, a specific distribution in hair follicle was noted for each of these enzymes. These results demonstrated that an active but intricate prostaglandin metabolism could take place in human hair follicle, mainly oriented towards PGE_2 synthesis and concentrated in the bulb, including dermal papilla, matrix and keratogenous area. Local production of PGF_2a might equally rely on PGE_2 conversion and direct synthesis through AKR1C3/PGFS.

P-105

Comparative Evaluation of Patchy Alopecia Areata Response to Oral Therapy With Either Zinc Sulfate or Vit.B6

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Background and Aims: Alopecia areata is a relatively common problem as it may affect nearly 1% of world population until the age of fifty.The peak incidence will be in adolescence and young adults.Because of large socio-psychiatric impacts on the patients and its unknown etiology ,it deserves a significant consideration from therapeutic point of view .Until now, no effective and safe treatment can eradicate the illness,so it is worthy to study the subject.

Methods: 34 patients with patchy alopecia areata ,referred to educational skin centers in Isfahan university were recruited and randomized into two treatment groups, provided that they have the inclusion criteria (not to be pregnant ,or under any other treatment, not becoming progressive toward totalis or universalis types,over 7 year old)of the study.In case group we tried oral zinc sulfate (1 mg/kg/day),up to 3 months and in controls oral Vit. B6 tablets(2 mg/kg/day)in the same duration .They were followed exactly for responses in the terms of regrowing hair, subjective satisfaction from the treatment and side effects.

Results: After analyzing the data with the aid of chi-square test,in the case group,we got 11.7% complete response,76.6%partal and 11.7% no response or failure. In the second group(Vit.B6)we reached consecutively to 5.8% complete,58.9% partial and 35.3% no response.

Conclusion: With regard to the results of statistical analysis in our trial,the response rates of thw two study groups have no significant differences from statistical point of view,though the efficacy of treatment with oral zinc sulfate appears to be higher in alopecia areata subjects, with regards to the extracted data.

Key words: Alopecia areata ,Zinc sulfate,Oral treatment,Vit B6(pyridoxine)

P-106

Alopecia Areata: a Comparison Among Diverse Therapies

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Alopecia Areata is a common autoimmune hair disease, caused by an abnormal cell-mediated response against one or more antigens of the distal part of the hair follicle (lower segment).

A polymorphic cellular infiltration in the deep dermis, composed predominantly of T lymphocytes and Langherans' cells in the peribulbar region is usually detected.

The disease can be determined by a lot of diverse factors which cause hair loss in the anagen phase.

Both CD4/CD8 ratio increase and circulating CD8 decrease is demonstrated, always in association with other autoimmune diseases.

Alopecia areata can be treated with a lot of diverse therapies : Antraline, CyA, topical, intralesional and

systemic Corticosteroids, Phototherapy (U.V.B 311 nm), Minoxidil, Psychotherapy, PUVA, SADBE.

During a four years study, 146 patients affected with Alopecia Areata involving at least the 75% of scalp were treated. Efficacy of diverse therapies was evaluated both individually and in association. According to other authors we suppose that Alopecia Areata needs a multidisciplinary approach and that a therapy suiting for all the patients doesn't exist. In fact a lot of factors can variously influence the course of the disease.

P-107

Methotrexate in Patients with Chronic Severe Alopecia Areata of the Scalp

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Common features between psoriasis and alopecia areata, including immunologic and therapeutic aspects, suggest that methotrexate (MTX) may have therapeutic value in alopecia areata (AA).

We report an open, single-center, investigator-initiated pilot study to examine the efficacy of methotrexate in subjects with chronic, severe scalp AA. Study enrollees received weekly oral administration of 15 mg of MTX for 24 weeks. Outcome parameters included the Severity of Alopecia Tool (SALT) score as well as investigator and patient assessment of regrowth.

Four eligible patients with 91-95% scalp hair loss due to AA, of a duration from 2- 10 years were included. After 24 weeks, one of them had minimal regrowth, with a 2.1% lower SALT score. The second patient had no change of her condition, except for some regrowth of body hair. The third and fourth patient dropped out of the study after 4 months. In the third patient, the SALT score had decreased from 91% to 76.5%, and he noticed minimally improved scalp coverage. In the fourth patient, there was no regrowth. The treatment was generally well tolerated.

We could not show sufficient efficacy of oral, medium dose MTX in severe, longstanding AA in this small pilot study. However, another recently published study suggests some therapeutic value of MTX, especially in combination with oral corticosteroids. A large, controlled study with longer treatment intervals, different administration routes or higher doses may be needed to finally define the role of MTX in the treatment of AA.

P-108

Study of Apoptosis Regulation Process in Alopecia Areata

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To determine the level of apoptosis and proliferative activity of hair follicles (HF) cells in patients with alopecia areata (AA).

Ten scalp skin biopsy samples have been examined: 8 samples with AA and 2 samples from healthy controls.

With a method of immunohistochemical testing using monoclonal antibodies against DDF, bcl-2, p53, Fas, fas-l and Ki67, we have studied cells at the stage of complete apoptosis and the levels of expression of key apoptosis regulator molecules; also, proliferative activity of HF cells has been studied.

Results: A method of immunohistochemical testing with the use of antibodies against single-stranded DNA has revealed the presence of cells at the stage of complete apoptosis among HF keratinocytes, lymphocytes and endothelial cells in biopsy specimens obtained from donors with AA. Apoptotic cells were not found in controls.

At the skin biopsy with AA in matrix cells and in cells of HF inner root sheath (IRS) was identified protein p53; bcl-2-positive cells were revealed in the matrix of HF bulbs. p53 and bcl-2-positive cells were not found in controls.

In the studied skin samples of patients with AA, large amounts of fas-l were revealed in the basal layer of keratinocytes of outer epidermal sheath of the root (OESR) and in the cytoplasm of lymphocytes. In controls fas-l was present in the region of OESR in small amounts and was completely absent in lymphocytes.

Initiator molecule Fas was absent in biopsy specimens of both AA patients and controls.

Examination of proliferative activity of HF cells at the skin biopsy with AA revealed the presence of individual Ki67-positive cells in the IRS.

Conclusion. Disorder of apoptosis regulation has been revealed in patients with AA.

Changes in interactions between apoptosis promoters and inhibitors lead to development of pathologic telogen and a decrease in proliferative activity of HF cells.

P-109

Aging Processes In Human Hair Follicles

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To guarantee the growth of strong and healthy hair various specialized cell types in the follicle interact accordantly to a complex set of molecular signals. Biological alterations due to intrinsic or extrinsic stimuli can destabilise this well balanced system, thus effecting hair growth or metabolism. Also aging could be characterised as a disturbance in this perfectly organised machinery.

Albeit the predominant symptom of hair aging, greying, is addressed in a plurality of research activities, age related changes beyond loss of pigmentation remain obscure. It has been reported that hair follicle density, growth rate and hair diameter decline in age, but the molecular events underlying this macroscopic alterations are still poorly understood. Therefore we characterised hair follicles of two volunteer panels (below 25 years, above 50 years) on the molecular level. In this study we show that concordantly to other biological systems the hair follicle undergoes an aging process associated amongst others with a decline in structural proteins such as several keratins or a shift of apoptotic parameters. Those modifications might be aetiological for the reported alterations and providing bioactives fighting these age related changes is a challenge for cosmetic science.

P-110

Evaluation of Free Oxygen Radical and Antioxidant Capacity in Alopecia Areata

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Objectives: The pathophysiology of alopecia areata (AA) has not been clearly defined. We tried to analyze the differences of free radical status and antioxidant capacity in the blood between AA patients and normal control.

Approach: Sixteen patients with AA and 16 age- and sex-matched healthy controls were enrolled in this study. We analyzed serum levels of reactive oxygen metabolites (ROMs, mainly hydroperoxides, ROOH) using d-ROMs test (FRAS 4, H&D s.r.l., Italy) which represents the level of oxidative stress in the blood. BAP (biological antioxidant power) test (FRAS 4, H&D s.r.l., Italy) was also performed to assess the antioxidant power of the plasma as a measure of the ability to reduce ferric (Fe3+) ions to ferrous (Fe2+) ions.

Results: The mean levels of ROMs in serum of patients with AA (357.69±88.46 CARR U, Carratelli Units; normal value, 250-300 CARR U) were significantly higher than those of controls (287.81±20.22 CARR U, $p<0.01$). The antioxidant capacity (2063.44±132.67 mmol/l; normal value, 2200-4000 mmol/l) in the serum of patients with AA was significantly lower than that of control (2267.44±135.18 mmol/l, $p<0.01$).

Conclusions: We could find ROMs were increased and antioxidant capacity was decreased in AA patient. This could support the role of alteration of oxidant-antioxidant enzymatic system in the pathogenesis of AA.

P-111

Intralesional Injection of Cyclosporine A on Patches of Alopecia Areata

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Objectives: Alopecia areata (AA) infrequently manifests a refractory course and we often face difficulties in its treatment. Currently, triamcinolone (TA) intralesional injections (ILI) are regarded as standard treatment option for patch alopecia areata, but continuous ILI of TA may result in skin atrophy. Cyclosporine A (CsA) is an immunosuppressant originally applied in organ recipients, but it is widely used in dermatologic fields including alopecia areata, atopic dermatitis, and psoriasis. We would like to try the CsA ILI treatment for AA, instead of TA-ILI.

Approach: Injectable CsA ample (CIPOL Inj., Chong Kun Dang Pharm., Seoul, Korea) was diluted to 2.5 mg/cc with 5% dextrose solution. Those who have patch AA were selected. And, diluted CsA was injected to the AA lesion every two weeks. Several lesions were treated with TA as a control.

Results: Successful regrowth of hairs could be seen on CsA ILI site without any side effect like skin atrophy. But, the time consumed to induce new vellus hair was quite longer when it compared with that in classical TA-ILI.

Conclusions: We could find CsA ILI also effective treatment for AA patients. And no side effects like skin atrophy can be seen.

P-112

High Dose Methylprednisolone Therapy on Acute Diffuse Alopecia Areata

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Acute diffuse alopecia areata is a unique type of hair loss that mimics anagen effluvium, or in which the initial hair loss is diffuse and followed by total denudation of scalp within several weeks or months. Despite its peculiar clinical feature, the characterization and/or treatment of acute diffuse alopecia areata are very limited currently. In this study, we evaluated the characteristic clinical findings of acute diffuse alopecia areata, and confirmed the effect of high dose methylprednisolone therapy. The medical records of 13 patients with acute diffuse alopecia areata between January 2002 and April 2006 at the Department of Dermatology, Chungnam National University Hospital were reviewed. All patients were treated with high dose methylprednisolone therapy. Of the 13 patients who completed the study, 8 patients (61.5%) were male and 5 (38.5%) were female. The mean age was 29.6 years old. The progression of hair loss was stopped in 2.4 weeks on average from the initial treatment, and newly emerging hairs were recognized in 4.1 weeks on average from the initial treatment. At the end of observation, 84.6% (11/13) of patients showed terminal hair growth and 46.2% (6/13) of patients completely responded to methylprednisolone therapy. In conclusion, we found that acute diffuse alopecia areata can be occurred in male as well as female, and high dose methylprednisolone therapy is the effective method to treat those patients.

P-113

The Cell Infiltration in Alopecia Areata Lesion Is Induced By Th1 Chemokine

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The current idea towards that alopecia areata (AA) is one of an organ-specific autoimmune disease. Inflammatory cells surround hair follicles in the lesion of acute phase AA, and these cells are constituted by 60-80% $CD4^+$ T cells and 20-40% $CD8^+$ T cells. Th1 cytokine, such as IFN-g, has been dominantly detected in AA-lesion that implicates AA is Th1 disease. Although the phenomenon of cell accumulation in AA-lesion is known very well, the mechanisms of chemotaxis around the HFs has been largely ignored. Therefore, we investigated how the cells accumulate around the HFs in acute AA-lesions. Firstly, the expression of chemokine receptors and chemokines were immunohistochemically investigated. In normal human scalp skin, $CXCR3^+$ and $CCR4^+$ cells were rarely detected, and the number of $CCR4^+$ cells is slightly higher than that of $CXCR3^+$ cells. In contrast, $CXCR3^+$ cells were dominantly accumulated compared to $CCR4^+$ cells in the lesion of AA. In addition, IP-10 was very strongly expressed in and around the hair follicles in AA lesion compared to normal control. Next, in order to investigate the lymphocyte-chemotaxis functionally in AA patients, we used EZ-TAXIScan™ that can show real-time chemotaxis directly under a microscope. PBMC from AA patients showed the strong tendency of chemotaxis to IP-10 compared to TARC. Taken together, it is suggested that increased production of IP-10 may induce accumulation of $CXCR3^+$ T cells in acute AA lesions that results in hair loss.

P-114

Possible Role of p63 and Alpha-6 Integrin in the Hair Loss

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Objectives: Recent evidence has suggested that p63 plays an important regulator of hair follicle development and increased expression is seen in the outer root sheath. Integrins have a crucial function in the attachment of cells to the extracellular matrix and as important transducers of signals from the extracellular matrix to the matrix cells of the hair follicle. The aim of the current study was to investigate the possibility that p63 and alpha-6 integrin may involved in the pathogenesis of various conditions of hair loss.

Approach: Full thickness skin biopsies were obtained from the scalp in each of 15 persons with male pattern androgenic alopecia(MPAA), female pattern alopecia(FPA), alopecia areata(AA), female telogen effluvium(FTE). The control group consisted of 14 persons not having hair loss and any other systemic disease. Immunohitochemical techniques were used to assess p63 and alpha-6 integrin localization. In each section, the percentage of positive cells and the localization of expression were evaluated.

Results: In control group, p63 expression was seen in the epidermis and outer root sheath of hair follicles. P63 staining revealed a different pattern in the various conditions of hair loss. In MPAA and FPA, there were weak immunoreactivity in the follicle epithelial structure. In contrast, there were only minor changes of p63 expression in AA and FTE. Among the four hair loss groups, MPAA and AA showed more decreased immunoreactivity

of alpha-6 integrin in the basal sides of follicle epithelium. In control group, all epithelial structure were 100% positive to alph-6 integrin.

Conclusion: These expression data suggest a different role of p63 and alpha-6 integrin in the development of hair loss. Since both p63 and alpha-6 integrin are necessary for the hair follicle growth, it is worthwhile to take more concern in this proteins.

P-115

Results of Complex Treatment of Alopecia Areata

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In dermatologic practice Alopecia areata is one of the least studied diseases; it is also of great interest for investigation. We have singled out one quite interesting case of Alopecia areata from our practice: a female patient, 36 years of age, turned to us in June 2006 with complaints of gradual loss of hair on the head (as focuses), in the groin and the axillary region, on arms and legs, which started in April 2006.

The following examinations were carried out:

- trihogramma
- scalp skin biopsy
- complete blood count;
- coprogramma.
- The diagnosis made:
- Alopecia areata. Lichen planopilaris.
- The treatment given:
- immunomodulators (sol. Cicloferoni i/m)
- Bio-Selenium, Anacap;
- preventive antifungal therapy (tab. Lamizili);
- external procedures using the infrared laser according to a definite scheme.

Results: In 2 months after the beginning of treatment hair growth in the focuses of hair loss has been observed. In 5 months a complete recovery of scalp hair (the hair have become thicker than before) and hair growth in the groin, the auxiliary region, on arms and legs has been marked.

Conclusion: The given case from our practice once again proves the necessity of a more explicit approach to examination of Alopecia areata. It also proves the necessity of use of the complex therapy rather than only the external one.

P-116

Pulse Corticosteroid Therapy For Alopecia Areata: Study of 139 Patients

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Background/Aim: Recent reports of pulse corticosteroid therapy for alopecia areata (AA) show its efficacy for patients with a history of one year or less, but not for recalcitrant cases or alopecia totalis/universalis. The purpose of this study was to evaluate the efficacy and safety of pulse corticosteroid therapy for recent-onset AA patients.

Method: 139 severe AA patients aged over 15 were included in this study. The duration from the onset of active hair loss was within 12 months for 125 (89.9%) of those patients.

Results: 72.7% patients had hair loss on more than 50% of their scalp area. Among the recent-onset (duration of AA ≤6 months) group, 59.4% were good responders (over 75% regrowth of alopecia lesions), while 15.8% with more than 6 months duration showed a good response. Recent-onset AA patients with less severe disease (≤50% hair loss) responded at a rate of 88.0%, but only 21.4% of recent-onset patients with 100% hair loss responded. No serious adverse effects were observed.

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Treatment of Severe Alopecia Areata

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Many treatment modalities have been proposed to treat alopecia areata(AA). Of these, systemic corticosteroids and cyclosporine A (CyA) are effective in treatment of severe AA. However, their side effects and high relapse rates have discouraged us from using them in AA. Therefore, combination therapy is required to get adequate efficacy with acceptable toxicity. As CyA and steroids act through different mechanisms, combination therapy with them may produce synergistic effect.

We treated 25 cases of severe AA with combination therapy with systemic corticosteroid (methylprednisolone 16-24mg/day) and CyA (2.5-3mg/kg/day) for 24weeks. In all, 7 patients with alopecia universalis, 6 with alopecia totalis/universalis, 11 with AA involving more than 50% of the scalp and 1 with ophiasis were involved in this regimen. The efficacy of the combination therapy was evaluated at 12 and 24 weeks. We checked peripheral blood concentration of CyA to determine the therapeutic range of CyA with little or no side effects. Satisfactory hair

growth (terminal hair growth occurring more than 50%) was achieved in 68% (n=17), and cosmetically acceptable hair growth (terminal hair growth more than 75%) was in 44% (n=11). In a group which showed satisfactory hair growth, peripheral concentration of CyA was ranged from 30 to 140ng/ml.

Adverse reactions of therapy were elevated blood pressure in 1 patient, elevated serum cholesterol in 1 patient, which were controlled by medical treatment without cessation of therapy. In these patients, the side effects appeared when the concentration of CyA was elevated more than 200ng/ml.

This study shows that combination therapy with CyA and low dose corticosteroids would be effective and safe treatment for severe AA, and presents an effective concentration of CyA in peripheral blood.

P-118

Therapeutic Effect of Systemic Cyclosporine in the Patients with Alopecia Areta

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Objective: Cyclosporine is an immunosuppressive agent that has provided new approaches in the treatment of autoimmune disease. The theory of autoimmune pathogenesis of alopecia areata suggests a potential therapeutic effect of cyclosporine. We evaluated the therapeutic effect of oral cyclosporine combined with other modalities in severe and refractory alopecia areata patients.

Approaches: 38 patients (8 patch type alopecia areata, 6 alopecia totalis, and 24 alopecia universalis) were treated with oral cyclosporine 100-200mg/day with PUVA, DPCP, cryotherapy, intralesional steroid injection, topical steroid and minoxidil solution at least 6 months. Blood pressure, CBC, liver function test, BUN/Cr, electolyte, and urinalysis were checked to avoid any untoward effects.

Results: Of the 38 patients 23 patients(60.5%) showed new hair growth. 15 patients(39.6%) did not respond to therapy. Mean time until new hair growth was 13.8 weeks. Untoward effects occurred in 9 patients(23.7%), and they were as follows: 5 patients with gastrointestinal discomfort, 2 patients with hypertrichosis, 1 patients with headache and 1 pateints with hypertension.

Conclusion: Oral cyclosporine therapy with combined other modalities is recommended in severe and refractory alopecia areata patients.

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A Clinical Study on Alopecia Areata (2001-2006)

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Objective: We performed a study on alopecia areata in order to evaluate the clinical manifestation and compare the efficacies of treatment with intralesional injection of triamcinolone, imunotherapy with diphenylcyclopropenone(DPCP), topical PUVA, cryotherapy and oral cyclosporine.

Approaches: Total 444 patients with alopecia areata including 14 cases of alopecia totalis and 47 cases of alopecia universalis was performed for 6 years from March, 2001 to December, 2006 who visited to the Alopecia Clinic at the Department of Dermatology, College of Medicine, Chung Ang University.

Results: 1) The age distribution showed a peak incidence in the third decade (27.9%) and the mean age was 28.9 years, and 57 cases (12.8%) showed alopecia areata in patients below 10 years old. 2) The most common site was occipital region in both male and female patients; 157 cases (70.0%) and 145 cases(65.9%), respectively. 3) Previous episode of alopecia were observed in 97 (21.8%) and 44 cases (9.9%) had family history. 4) Associated diseases are seborrheic dermatitis (35 cases), atopic dermatitis (22 cases), thyroid disease (14 cases), hypertension (13 cases), diabetes mellitus (8 cases), etc. 5) The efficacies of the various modalities had no statistical differences.

Conclusion: These findings suggest that alopecia areata prominently develops in the thirds decade and the efficacies of the various modalities had no statistical differences.

P-120

Expression of Myc/Mad1 in The Human Hair Follicle During Hair Cycle and Alopecia Areata

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Objectives: Precise molecular mechanisms associated with transient growth/differentiation of follicular keratinocyte have not been fully elucidated in the hair cycle. Recent observations have suggested that proto-oncogene c-myc plays a pivotal role in the regulation of both apoptosis and growth in the epitherial cells. Mad1 is a Myc antagonist that functions as a transcriptional repressor. Inhibition of proliferative activity subsequent to Mad1 overexpression has been demonstrated in a variety of cell types, including

keratinocytes. However, little is known about the Myc/Mad1 expression in follicular keratinocyte. To elucidate whether c-Myc/Mad1 proto-oncogenes could be involves in normal human hair cycle and alopecia areata, in situ expression of Myc/ Mad1 was investigated.

Methods: Immunohistochemical analysis were performed for the specimens taken from surgery of patients and from patients of alopecia areata. Antibodies against PCNA (Proliferating Cell Nuclear Antigen), ki67, c-Myc and Mad1 were used.

Results: Immunoreactivity for ki67 was observed in the bottom portion of inner root sheath in human anagen hair follicle. In contrast, c-Myc-positive cells were visible in outer root sheath cells of bulge area. We compared expression of c-Myc/ Mad1 in normal human hair follicles during hair cycle and hair follicles of alopecia areata.

Conclusions: c-myc and mad overexpression might be related with switching to the hair cycle. These findings suggest that c-myc has been implicated not only in the cell proliferation, but also in the terminal differentiation and mad has been implicated in the cell differentiation in hair cycle.

P-121

Anthralin For Alopecia Areata: a Half-Side Comparison

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Objectives: Anthralin application is an option for topical immunosuppressant treatment of alopecia areata (AA). No controlled trials have been done. We report the successful treatment of AA by anthralin as demonstrated by half-side comparison.

Approach: Seven patients, 5 female, 2 male, aged 12 to 52 years (median 36 years) suffering from almost total AA or AA totalis for at least 2 years were treated daily with 1 or 3% anthralin cream on one half of the scalp only. In addition, 5% minoxidil solution was applied to the entire scalp twice daily. Skin biopsies for pathohistology were compared from anthralin-treated and non-treated sites. Scalp photographs were also taken.

Results: In the 7 patients treated, hair growth on the anthralin-treated half of the scalp set in around 5 months and continued to increase up to 18 months. After definite hair growth on the treated side, anthralin was also applied to the other half of the scalp. No side effects other than slight burning and brownish discoloration were noted. In scalp biopsies from treated areas exhibiting regrowth of hair, the lymphocytic infiltrates surrounding hair follicles tended to vanish, and the scalp tissue normalized, there were no signs of allergic contact dermatitis.

Conclusion: Our results indicate that topical immunosuppressant treatment of alopecia areata for 5 to 18 months with anthralin combined with topical minoxidil is a safe and efficacious treatment associated with normalization of scalp tissue.

P-122

Acute Diffuse and Total Alopecia

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Alopecia areata (AA) commonly starts with ovoid patches of hair loss and then presents several different clinical forms. The prognosis of AA is unpredictable. Indicators of a poor prognosis are long duration, family history of alopecia, and extensive hair loss. Alopecia totalis is well known to have a poor prognosis, so it is commonly resistant to several treatments and frequently recurs. We studied 23 patients(21 female and 2 male) with AA who showed extensive hair loss. But they present cosmetically acceptable hair regrowth within 6 months. Most of them were treated with DPCP, but some of them didn't have any treatment. They had a very acute course of total hair loss within two months. They don't have a history of systemic disease, or previous history of alopecia areata. Most patients were female in around thirty. The histopathology of the lesion revealed an infiltration of mononuclear cells around the hair follicles. These above findings indicate that these cases should be categorized as a subtype of AA, "acute diffuse and total alopecia", which shows favorable prognosis.

P-123

Perinevoid Alopecia – a Distinct Entity or Variant of Alopecia Areata?

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Alopecia occuring around a naevocellular nevus or Perinevoid alopecia, since its original description in the german literature in 1958 has rarely been reported subsequently. The senior author Prof. Patrick Yesudian published 3 cases in 1976 and also suggested that perinevoid alopecia is a distinct entity and not merely a variant of alopecia areata.

We report 6 further cases of perinevoid alopecia. In all these cases a central nevocellular nevus of varying duration was surrounded by an area of alopecia which was the presenting complaint. The excised central mole showed histopathologically intense lymphocytic infiltrate pervading nevus cells of varying numbers. Mucin depostion in the

dermis was demonstrated with special alcian blue stain. No regrowth of hairs was seen in the patch of alopecia after removal of the central on several months follow-up.

We present these cases for their rarity and review the meagre literature on this entity.

P-124

Analytical Versus Empirical Drug Screening Approaches For Alopecia Areata

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While numerous drugs continue to be used to treat patients with alopecia areata (AA) most patients are disappointed with the results. Treatments continue to be devised empirically and tested in small trials. The C3H/HeJ mouse skin graft or spontaneous models for AA provide tools for screening individual and combinations of drugs for efficacy and safety. More importantly, we can now move from an empirical to an analytical approach. Using the Affymetrix(r) gene expression tools (GeneChip Mouse Genome 430 2.0 Array) with the Ingenuity Pathways Analysis(r) software we evaluated mice at 5, 10, 15, and 20 weeks after skin grafting and mice with spontaneous AA compared to age and gender matched controls. Gene networks were identified but more importantly, FDA-approved drug targets for dysregulated gene products were defined. These data provide tools to both prioritize drug treatment options and test them for efficacy and safety. C3H/HeJ mice with AA can be treated by topical, local, systemic, or oral routes with a comprehensive analysis done to validate efficacy. Information on accessing the models for setting up drug studies can be found at http://jaxmice.jax.org/services/alopecia_areata.html and http://jaxmice.jax.org/library/notes/504/504b.html.

P-125

Funding Opportunities for Alopecia Areata Research Through the National Alopecia Areata Foundation

Kalabokes, Victoria;[1] Norris, David;[2] Shapiro, Jerry;[3] Bystryn, Jean-claude;[4] Christiano, Angela;[5] Duvic, Madeleine;[6] Gordon, Gary;[7] McMichael, Amy;[8] King, Lloyd E.;[9] Sundberg, John P.;[10]

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For the past 20 years, the National Alopecia Areata Foundation (NAAF) funded over 135 broad based research projects ranging from epidemiology, clinical trials, fundamental immunology, animal models, to genetics. These pilot and feasibility projects help investigators generate preliminary data necessary to apply for and obtain funding from major granting agencies. This year NAAF awarded 7 new research grants. These one year research grants are awarded for up to $50,000 (USD) and can be reapplied for in subsequent years. Numerous publications are the direct result of these grants which focused and propelled research in this area forward. This year we initiated a fellowship for 2 years to support a postdoctoral investigator to help them build a career in alopecia areata research. Future requests for applications will give priority to projects dealing with immunology of alopecia areata. Details on these grant opportunities and access to applications and instructions can be found at http://www.naaf.org/research/research-grantapplication2006-2007.asp.

P-126

Large Scale Immune Response Gene Expression Analysis Defines Alopecia Mouse Models

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Identifying the correct mouse model for psoriasis, alopecia areata, cicatricial alopecia, and other inflammatory and noninflammatory skin and hair diseases is a constant debate. Integrating large scale quantitative real time RT PCR (qPCR), histopathologic, and cytologic approaches, we evaluated spontaneous alopecia areata in C3H/HeJ mice, a form of psoriasiform dermatitis in chronic proliferative dermatitis (cpdm/cpdm) mutant mice, and a form of cicatrical alopecia in C57BL/6J mice. Our 384 qPCR set of immunoregulatory genes rapidly provided an easily interpretable profile for each model that was unique. The alopecia areata model results confirmed many of our previous studies indicating this is a T cell (primarily CD8+) driven disease. A longitudinal Affymetrix array experiment using the alopecia areata graft induced model not only confirmed these results but demonstrated a progressive and significant increase in expression of Cd8a

but also a series of genes in the canonical pathway. By contrast, chronic proliferative dermatitis is an inflammatory proliferative skin disease with a predominant eosinophil component. Changes were unique and reflected the pathogenesis of the mutant inflammatory skin disease phenotype. Early stage cicatrical alopecia had minor expression changes indicative of a nonimmunologic pathogenesis. Expression changes were consistent with histopathology and immunofluoresence results. This proof of concept approach provides the prototype for large-scale implementation to carefully define immunological mechanisms of skin diseases in mouse models and through translation, new molecular tools to accurately define human inflammatory skin diseases.

P-127

Deficiencies in the Paracrine Signalling System of Stem Cell Factor (Scf) and Its Receptor, C-Kit, Occur in Human Hair Greying

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Loss of hair pigmentation is a poorly understood aging phenomenon. Stem cell factor (SCF) regulates rodent pigmentation via c-kit. We showed previously that cultured human dermal papilla cells secrete SCF suggesting dermal papillae as local SCF sources. To determine whether alterations in the SCF/c-kit signalling system are involved in human greying, we investigated the expression of scf and c-kit genes in pigmented and non-pigmented hair follicles using semi-quantitative RT-PCR and located melanocyte antigens and c-kit by immunohistochemistry of cryosections.

Lower parts of anagen follicles were microdissected from human scalp samples treated with RNAlater to inhibit mRNA degradation. Total and poly(A)RNA were isolated, cDNA prepared and RT-PCR carried out in a dose responsive manner using primers for c-kit, SCF and control ß-actin.

Pigmented follicles (n=5) expressed c-kit and both soluble and membrane-bound scf. Immunohistochemistry located melanocytes exhibiting c-kit and melanocyte antigens in the hair bulb and outer root sheath. In non-pigmented follicles (n=5) expression of all three genes and melanocyte numbers in the bulb were significantly reduced.

The expression of scf and c-kit within human follicles and the presence of c-kit on melanocytes strongly support a paracrine role for this signalling system in human hair pigmentation. Soluble SCF would correspond to that secreted by dermal papilla cells,presumably influencing bulb melanocytes; membrane-bound scf may be involved in melanocyte migration. The reduced expression of scf and c-kit implies that failure of this system causes human greying. This may lead to new treatments; as cells still express c-kit, exogenous SCF may facilitate re-pigmentation.

P-128

A Retrospective Clinical Study of Alopecia Areata in Canada (2001-2004)

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Objectives: To evaluate the clinical manifestations and treatment of AA in a mixed ethnic population.

Approach: Alopecia Areata (AA) is a common disease of patchy non-scarring hair loss. There are 400-700 patients with AA in our study. Up to this point, we have tabulated the results of 100 patients.

Results: The ratio of males to females was 1:1.38 with 63 Caucasians, 19 Orientals, 9 East Indian, 8 Middle Eastern and 1 African-Canadian. The mean age on initial visit was 42.27 years. The family history was contributory in 12 cases. The majority of patients had AA of 3-12 months duration. The relapse rate was 15%. The most common site of predilection was the occipital area. Associated with diseases were: atopy, vitiligo, psoriasis and thyroid problems., The success rates of intralesional corticosteroid was 90% in limited AA, and DPCP immunotherapy for patients with alopecia totalis, universalis and ophiasis was with success rates of 78%.

Conclusion: For limited AA, intralesional corticosteroid was the first line treatment, as well as DPCP immunotherapy was the best option for patients with alopecia totalis, universalis and ophiasis.

P-129

Topical Immunotherapy With Diphenylcyclopropenone For Treatment of Alopecia Areata in Taiwan

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Background: The response rate of topical immunotherapy with diphenylcyclopropenone (DPCP) in the treatment of alopecia areata (AA) varied from 4-85% in the literature. This study was aimed to evaluate its efficacy in local Taiwanese patients.

Methods: Twenty patients with extensive AA were enrolled in this study, including 6 males and 14 females (age range 6-52 years, mean age 21.4) with disease duration between 6 months and 40 years (mean 10.3 years). DPCP was applied at 2-week interval and hair regrowth was evaluated after 6-month therapy.

Results: Twelve of 20 patients have completed 6-month therapy, while five are still undergoing treatment and two are dropped out due to intolerance. Hair regrowth more than 50% was observed in six patients (50%), in whom three had complete response (90-100% terminal hair regrowth) and the other three had partial response (50-90% terminal hair regrowth). The remaining six patients (50%) had no significant hair regrowth. There was no correlation between the response and the age of onset or disease duration (P=0.4 and 0.2, respectively). Two patients with pitting nails were not responsive to DPCP treatment. Side effects included pruritus 85% (17/20), blistering 50% (10/20), auto-sensitization 40% (8/20), occipital lymphadenopathy 20% (4/20) and hyperpigmentation 10% (2/20). Partial recurrence was observed in 33% (2/6) of responders in 2-26 months of follow-up after cessation of treatment. Among eight patients with AA totalis/ universalis, five (62.5%) presented hair regrowth more than 50%.

Conclusion: DPCP topical immunotherapy seems to be effective for extensive AA patients, especially those with AA totalis/ universalis . The most common side effect is pruritus. Recurrence after hair regrowth still poses a problem.

P-130

Alopecia Totalis With a Good Prognosis In a Patient Receiving Transient Clomifene

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Objectives: Alopecia areata is an autoimmune hair loss disorder characterized by peribulber infiltrate of T cells and hair cycle shift. Estrogen is well-known to modify immunological states and extend the anagen phase. To elucidate alopecia areata etiology,

Approach: Description of the clinical and histological findings in a patient with alopecia totalis. A 34-year-old woman with second infertility undergoing oral clomifene developed sudden total hair loss 3-weeks after first interval of taking clomifene. A biopsy of the scalp was transversely and horizontally sectioned.

Results: Transverse sections showed peribulbar infiltrate, consistent with the diagnosis as alopecia areata. Horizontal section showed a decreased number of anagen hair follicles and a increased number of regressing hair follicles. Soon after the hair shedding, terminal hair regrowth occurred.

Conclusion: Our patient developed alopecia totalis with a good prognosis after transient estrogen blockade by clomifene, which may suggest the hormonal role in the etiology of alopecia areata. Sudden estrogen blockade may have effect on hair cycles or immunological states or both, which might lead to trigger the onset of alopecia areata.

P-131

Lipodystrophia Centrifugalis of the Scalp Presenting With Arch-Form Alopecia: A 9-Year Follow-Up Observation

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A 2.5-year-old boy developed slightly depressed lesions with light erythemotous border on the right side of the neck and chin measuring 45mmx70mm and 35mmx38mm, respectively. SS-A/SS-B related erythema, LE profundus, and erythema annulare centrifugum were suspected, but no lines of evidence supporting the diagnosis were obtained. When he was 5.5 years old, at second visit, right chin lesion had disappeared but right neck lesion had extended centrifugally partly into the scalp, and linear arch-form alopecia was apparent on the right temporal region along with the edge of erythema. Hair regrowth was seen inside of the slightly depressed lesion. Two pea-sized regional lymphnodes were palpable. Biopsies taken at the alopecia showed non specific, non pilotropic lymphocytic inflammation in the subcutaneous fat. MRI findings revealed loss of subcutaneous fat inside of the lesion and helped to make diagnosis of the case as lipodystrophia centrifugalis developed on the neck and scalp. The alopecia continupously extended until he became 11 years old resulting in large arch-form alopecia Thereafter, expansion ceased and hair regrowth occurred in the linear alopecia. The 9-year follow-up of this case clearly demonstrates that centrifugal lipodystrophy might involve the scalp and cause linear arch-form alopecia.

P-132

Unusual Forms of Scarring Alopecia in Women – Peripheral Centripedal Scarring Alopecia?

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We experienced several cases of unusual forms of scarring alopecia in women. Case 1 was 45-year-old woman. Seven years ago, hair loss started in left temporal area and then spreaded to all the marginal areas of scalp. Her hairs in eyebrow were intact and there were no

evidence of hyperandrogenemia. Case 2 was 24-year-old female. Hair loss began in the frontal area at the age of 12, and then nearly all the margins of scalp became involved. She had regular menstruation and no evidence of hyperandrogenemia. Her eyebrow hairs were very sparse. Case 3 was 64-year-old woman. Six months ago, hair loss was observed in the both frontal areas. She was postmenopause and had no evidence of hyperandrogenemia. Her brow hairs were intact. In the histopathologic examinations of these cases, no evidence of alopecia areata or lichenoid inflammation were noted. They were compatible with burn-out alopecia. With only clinical finding of these patient, many diseases should be considered as possible diagnoses. In non-scarring alopecia, alopecia areata and female pattern hair loss (Hamilton type) were possible candidates. In Scarring alopecia, there were fibrosing alopecia in patterned distribution, pseudopelade and frontal fibrosing alopecia. But, our cases were not compatible with these in clinical and histopathological features. And so, we think these cases can be a new disease entity of scarring alopecia and propose 'peripheral centripetal scarring alopecia in women' for these cases. We expect more cases to be collected and analysed for the validification of this new entity.

P-133

Hair Loss in African American Women with Focus on Central Centrifugal Cicatricial Alopecia

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Central centrifugal cicatricial alopecia (CCCA) is the term given to the destructive hair loss over the central scalp seen primarily in African American women. It is the most common type of hair loss in African American women and usually presents to dermatologists when scarring is obvious and little can be done to reverse the hair loss.

In an attempt to better understand the prevalence of this condition and the factors that may be involved in the initiation or accentuation of the process, members of the North American Hair Research Society (NAHRS), with the support of Procter and Gamble, have developed a photographic scale to rate the degree of hair loss in CCCA and have begun a project to assess the level of agreement between patient and dermatologist in using this scale. In addition, the team has piloted and begun the validation process of a questionnaire assessing multiple familial, environmental, hair grooming and medical factors that could be implicated in this condition. Results from our first screening of ~150 women will be presented.

P-134

2 Cases of Folliculitis Decalvans after Hair Restoration Surgery

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Objectives: We report 2 cases of folliculitis decalvans in patients who underwent hair restoration surgery.

Case 1: 43 year old male patient developed severe pain, itching, papules, pustules, crusts and follicular tufting in the area of the grafts, 22 years after his hair transplant surgery.

Case 2: 47 year old patient with MPHL showed a hairless patch on the crown in 1992. The biopsy confirmed MPHL and showed no signs of inflammation or scarring. The patient underwent hair transplant surgery in January 1993 for the restoration of his hair line. 8 weeks after the procedure the patient showed erythematous papules and pustules around the hairless area on the crown.

Approach: A 4 mm punch biopsy was taken from the affected area.

Results: The pathology results showed folliculitis decalvans in both cases.

Case 1: Treatment: Minocin 100 mg twice daily and topical fucidic acid and Hydrocortisone (Fucidin H(r) cream). The lesion improved greatly after 4 weeks.

Case 2: Treatment: Cloxacillin 500 mg 4 times a day for 2 weeks, topical fucidic acid (Fucidin(r) ointment). The condition improved and the patient underwent a second session of hair transplant surgery in 1996. 2 years after the second surgery he showed signs of active folliculitis decalvans. Treatment: Minocin 100 mg twice daily and Fucidin(r) cream. The lesion stabilized over the following 2 years.

Conclusion: Folliculitis decalvans can be aggravated by surgical procedures such as hair transplantation. A thorough scalp examination and discussion of risks is crucial before surgical scalp procedures are performed.

P-135

Lupus Erythematosus Associated Alopecia-Cleveland Clinic Experience on Diagnosis, Evaluation and Treatment

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Background: Alopecia is a common feature of discoid lupus erythematosus. There is currently few data in literature that delineates the varied presentations of hair loss in lupus erythematosus.

Objective: To evaluate the clinico-pathological correlation of lupus erythematosus and its associated alopecia in attempts to standardize the diagnosis and effective treatment of the disease.

Methods: We reviewed the medical records and biopsy results of 19 patients with lupus erythematosus and alopecia that were seen in the Cleveland Clinic Department of Dermatology between 2003 and 2006.

Results: The most common clinical presentation was multiple patchy plaques due to lupus erythematosus. Disease progression was halted and improvement of active lesions was seen in patients on Plaquenil (anti-malarial) and intralesional Kenalog (steroid).

Limitations: This study was limited by being retrospective in nature.

Conclusion: Clinical presentation of hair loss due to lupus erythematosus varies with degree of disease involvement and disease state at time of clinical presentation. The most common clinical finding was the presence of multiple plaques in the scalp. The most frequent histopathological finding was lymphocytic infiltrate. While previous data has showed that anti-inflammatories are efficacious in the treatment of lupus associated alopecia, our incidental and anecdotal finding supports the combined use of steroids and anti-malarials.

P-136

A Case Report of Hair Regrowth in Central Centrifugal Cicatricial Alopecia With Topical Tacrolimus 0.1% Ointment

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Background: Central centrifugal cicatricial alopecia (CCCA) is an insidious form of primary lymphocytic scarring alopecia of the crown that occurs predominantly in adult black women. Most attribute the condition to the repeated use of traumatic hair grooming practices. Current recommendations for management are the cessation of this behavior, the adoption of natural coiffures, and treatment with topical and/or intralesional corticosteroids, and tetracycline adjunctively. In the authors' estimation, results are often disappointing. Camouflage remains the best option.

Objective: To determine if topical tacrolimus, a modulator of T-lymphocyte activation with trichogenic properties in some humans and in rodent models, has therapeutic value in CCCA.

Approach: Two subjects with advancing disease and limited to no response to conventional treatment were prescribed 0.1% topical tacrolimus ointment twice daily. Treatment response was based on subject and dual clinician global assessment of hair regrowth and scalp coverage, and was followed with serial photography.

Results: Two female black subjects, ages 54 and 73 years, with progressive longstanding disease, were treated for 36 and 25 months, respectively. By all measurements, one subject demonstrated hair regrowth after 6 months of treatment, with noticeably improved scalp coverage over the ensuing years of treatment. The other subject reported hair regrowth between months 4 to 18, with stabilization thereafter; this finding was not substantiated by clinical or photograph review.

Conclusion: Topical tacrolimus holds great promise in the management of some subjects with CCCA. In-depth characterization of treatment response determinants along with a formal, half-head study of adequate sample size are needed to further explore and quantify this therapeutic potential.

P-137

Cicatricial Pemphigoid Involves the Scalp With Scarring Alopecia

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Objectives: To discuss scalp involvement in cicatricial pemphigoid.

Approach: A 56 year old female presented with scalp and oral findings for one year. Her scalp was extremely itchy, burning and painful. She also presented with pain in the mouth. There is also a history of joint pain and general malaise. There were some eye symptoms. Physical

examination revealed scarring hair loss with erosions. Erosions were also present in the oral cavity. But there was no abnormality on eyes.

Results: Histopathology and immunohistopathology was consistent with cicatricial pemphigoid. Patient was treated successfully after 3 months of dapsone and topical superpotent corticosteroid ointment. Symptoms and physical findings improved markedly.

Conclusion: Cicatricial pemphigoid may present as a secondary scarring alopecia and can be treated successfully with oral dapsone and superpotent topical corticosteroids.

P-138

Monilethrix In Tasmania

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Monilethrix is a rare autosomal dominant hair shaft dysplasia that results in beaded hair fibres that are fragile. Affected individuals may present with alopecia, keratosis pilaris and rarely nail dystrophy. Clinically, the monilethrix phenotype is variable although penetrance is usually complete. To date, eleven mutations in three type II hair cortex keratins have been identified as responsible for dominant monilethrix. Recently, mutations in desmoglein 4 (a desmosomal cadherin) have been found to cause rare cases of recessive monilethrix.

We identified a large multigenerational Tasmanian kindred that demonstrates autosomal dominant monilethrix with variable penetrance. We undertook a clinical-genetic study of this family, comparing clinical findings with hair microscopy and hair fibre tensile strength.

We contacted 330 family members. We examined 119, and obtained 3 hair samples (from different scalp sites) from each. There were 18 affected individuals and 101 unaffected. Of those affected: 5 individuals were severe, 8 were moderate and 5 were mildly affected. Of those clinically unaffected: 3 provided a history of childhood monilethrix and 15 were obligate carriers, having transmitted the disorder to their children.

There was a wide spectrum of hair microscopic findings, which could not be consistently related to clinical severity. At this stage, hair fibre tensile strength studies do not show a consistent relationship with clinical severity. There were significant intra-patient differences on hair microscopic examination.

Our study describes a large monilethrix family displaying incomplete penetrance and a wide spectrum of clinical severity with discordant microscopic findings.

P-139

Familial Clouston Syndrome

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Brother and sister presented with total hair loss, affecting the scalp and eyebrows, dating since birth. A second brother presented with scanty scalp hair. Father was similarly affected. There was no history of parent consanguinity. Grandmother and cousins had only scanty scalp hair.

The cases presented also with peculiar papular pebbling on the ventral and dorsal aspects of the fingers. On the palmer side, the papules were arranged along the finger print lines. On the dorsal surface, the involvement of the nail bed led to near complete destruction of the nail plates. The younger sister presented with peculiar notching along the biting edge of the incisors, simulating the pebbling on the surface of the skin.

P-140

Hypotrichosis Simplex – A South Indian Variant?

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In our tropical hair clinic at Chennai formerly Madras cosiderable number of patients present with congenital hypotrichosis. There is no other congenital abnormality apart from hypotrichosis. It does not fit in any of the prviously listed congenital hypotrichoses. We present few of this mysterious hypotrichosis which could be sproadic mutations.

Patients of all ages varying from 2 years to 35 years present with hypotrichosis of the scalp hair often existing from birth or after the first tonsure. The other appendages are normal except for trivial dental abnormalities. The hair is thin, dry, brittle, lustreless and fragile. The light microscopy does not reveal any abnormality. We lack facilities to do electron microscopic studies. Majority of the cases are sproadic and lack family history. Most of them are born to consanguinous parents.

It is very difficult to classify and type the congenital alopecia without genetic studies.There is some response to topical minoxidil.

It appears that thease cases could represent a particular south indian variant of Hypotrichosis simplex. We seek help from the sophisticated centres for genetic study

P-141

Genomic Analyses of Two Japanese Pedigrees with Monilethrix

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Monilethrix is an autosomal dominant hair disorder characterized by the beaded appearance of the hair due to periodic thinning of the shaft. This disorder is reportedly caused by mutations in the helix termination motif of two type II cortex keratins, hHb1 and hHb6. We analyzed the genomic sequences of these keratins for two independent Japanese pedigrees with Monilethrix, a 32-year-old mother and her 3-year-old daughter, and a 27-year-old woman and her 5-year-old son. We detected a heterozygous point mutation of E413K (change of GAG to AAG at codon 413) in exon 7 of the hHb6 gene in both pedigrees. Scanning electron microscopy revealed a constricted internodal alternating pattern in the hair samples of these patients. Topical application of minoxidil and careful treatment of the hair were effective treatments in these cases. Genotype/phenotype correlation was not obvious in our cases or in the previously reported cases harboring this mutation.

P-142

Successful Treatment of Temporal Triangular Alopecia By Hair Transplantation

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Objectives: To determine if hair transplantation is a viable treatment for temporal triangular alopecia (TTA).

Approach: Temporal triangular alopecia is a form of non-scarring alopecia on the temporal scalp. It occurs very rarely and appears usually in children at birth up to 6 years of age. It is often unresponsive to any medical treatment. We present a case of a 17-year-old boy with a 3.5 X 2 cm patch of TTA since birth on the left temporal portion of the scalp. Hair transplantation was performed by removing a 3.5 X 1.05 cm strip from the occipital donor area and subdivided into 325 follicular units. These were placed with dense packing into the recipient area of TTA.

Results: A cosmetically successful result was seen 16 month post-operatively.

Conclusion: Hair transplantation is a successful option for patients with TTA.

P-143

Epilatory Effect of Glycyrrhizic Acid

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Hypertrichosis, hirsutism and giant hairy nevus are well known examples of abnormal hair growth with some risk of a significant negative impact on the psychosocial development of affected people. So far, all known methods for hair removal are more or less effective and show partly considerable side effects like pain, skin irritation, contact eczema, folliculitis, and hyper-pigmentation. In co-operation with a study group of Turkmenistan we found a new principle of painless and rapid hair removal based on liquorice, a commonly used herbal extract of the traditional Asian medicine. In the meantime we defined the liquorice compound glycyrrhizic acid to be responsible for the epilatory effect. We dissolved 15% glycyrrhizic acid in an aqueous solution containing 10% urea and 20% ethanol and treated wistar rats in the neck region twice a day. After 3 days first indications for hair loss became visible. After 6-12 days the treated skin was nearly free of hairs without any sign of skin irritation. Even after a periodically long term treatment over one year no abnormality of the skin surface was visible, but a permanent reduction in re-growing hair quantity by more than 50%. Based on these findings Glycyrrhizic acid is a candidate molecule for the development of a powerful agent for painless and permanent hair removal.

P-144

Dandruff Is Characterized By Increased Cytokines in the Stratum Corneum

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Dandruff is a condition that is characterized by the presence of flakes on the scalp and/or itch. This condition is known to be associated with decreased levels of scalp skin ceramides, similar to those found in dry skin.

In this study, we investigated the levels of inflammatory markers in the scalp skin of Asian panelists. Panelists were recruited and segmented into healthy (no visual flakes) and dandruff (flakes adhering to scalp skin) groups. Stratum

corneum samples were collected and extracted. These samples were analyzed for cytokines by ELISA and total protein by Bradford assay. Extractable protein increased in the dandruff group compared with healthy subjects, most likely as a result of the increase in adherent flakes. Cytokines were expressed as pg cytokine/ug protein. The ratio of interleukin-1a receptor antagonist protein (IL-1RA) to IL-1a was found to increase dramatically from 20:1 in healthy scalp panelists to over 100:1 in those with dandruff ($P < 0.01$). Likewise, IL-18 was also found to increase dramatically from 0 to ~500 pg/ug protein in the two groups respectively ($P < 0.01$). Prostaglandin E2 was detected, but no changes were seen between groups. Tumor necrosis factor-a, IL-1b, IL-6, and IL-8 were not detectable in the samples.

These data demonstrate that dandruff is associated with perturbations in inflammatory markers in scalp skin stratum corneum. This confirms previous hypotheses suggesting that dandruff is driven by a number of factors, including the quality of the stratum corneum and its interaction with Malassezia.

P-146

The D.H.I.® Technique – A Smart Quality Control System – -A New Method of Hair Restoration

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1. DHI International Medical Group, Athens, Greece;
2. Skinterface and IntHairNet (Brussels), Tournai, Belgium

The D.H.I.® (Direct Hair Implantation) technique, is a minimally invasive method of hair transplantation which avoids the need for a strip of donor skin to be removed from the back of the head. Therefore no scalpels or stitching are required at any point during the procedure.Single hair follicles are extracted one by one from the donor area (back of the head) and re-implanted with the unique patented device, the DHI Implanter.

The method Direct Hair Implantation(r) guarantees 100% natural results and maximum survival of implanted hair follicles through a minimally invasive procedure with no visible scars. The DHI Medical Group developed a new Protocol to overcome the negative aspects of the strip procedure, such as: scarring, patients' fear of surgery, donor area follicle destruction, uncontrolled placement that created unnatural results and poor growth.DHI comprises the largest international medical and research medical team exclusively involved in the treatment of scalp and hair disorders. DHI developed and patented the new method that have gained the recognition of the world medical community. The crowning achievement of our life time commitment is the direct hair implantation medical procedure, also knowing as simply the D.H.I.® Technique.

The D.H.I. Technique has now been in existence for over 37 years and thousands from around the globe enjoy the amazing results.

DHI is simply the best solution to all scalp and hair disorders.

P-148

A Comparative Clinical Trial of Evaluation of the Efficacy of Oral Terbinafine (Lamisil) and Prednisolon in Patients With Seborrhoeic Dermatitis

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Background: Previous trials have suggested that oral terbinafine, , could be useful in the treatment of seborrhoeic dermatitis.

Objectives: To investigate the clinical efficacy of oral terbinafine , in patients with moderate to severe seborrhoeic dermatitis.

Methods: fifty outpatients (19 men and 31 women) with moderate to severe seborrhoeic dermatitis were enrolled in the study. After a 2-week wash-out period, patients were randomized to either oral terbinafine (n = 25 or prednisolon (n = 25) daily for 4 weeks . Patients were followed up for an additional 8 weeks .They were evaluated at weeks 0, 2, 4 and 12 . The end-point of the study was clinical evaluation of erythema, scaling and itching, on a 0-3 scale. A global clinical score, was also calculated.

Results: At baseline, the mean ± SD global clinical score was 6.68 ± 1.8 in the prednisolon group and 6.56 ± 1.89 in the terbinafine-group. At weeks 1 the mean ± SD global clinical score in the prednisolon group was 3.36 ± 1.75 and 4.56 ± 1.73. At weeks 4 the mean ± SD global clinical score in the prednisolon group was 2.48 ± 1.53 and 3.18 ± 2.35, At week 8 the mean ± SD global clinical score in the prednisolon group was 2.64 ± 1.73 and 4.28 ± 2.41,respectively, which was significantly different from baseline. As compared with baseline values and the prednisolon group, terbinafine treatment ($P = 0.82$, T-test) reduced the mean ± SD global clinical score. No serious adverse events were recorded in either group.

Conclusions: This is the first trial to show oral terbinafine being effective in the treatment of moderate to severe seborrhoeic dermatitis.

P-149

Ebastine, a Second-Generation Antihistamine, as a Supportive Medication For Alopecia Areata

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Despite our accelerated understanding of the pathophysiology of alopecia areata (AA), evidence-based remedies for AA are still limited. Thus, there are clear demands on new therapeutic approaches. A couple of clinical studies in the Japanese literature reported favorable effects of second-generation antihistamines, including ebastine, for the treatment of AA. In addition, we also experienced promoted hair regrowth in some AA patients after oral administration of ebastine. To objectively assess the efficacy of ebastine for the treatment of AA, we performed open-labeled study using C3H/HeJ AA model mice. Seven pairs of C3H/HeJ littermate mice with similar extent of AA lesions were prepared. One of each pair of mice orally received ebastine (1.5mg/head/day) daily for 4 weeks, while another mouse was given control solution. About 2 weeks after the initiation of the trial, apparent hair regrowth in AA lesions was observed in 3 out of 7 ebastine-treated mice. In contrast, no improvement of AA lesions was noticed in placebo-treated mice. Histopathological investigation of AA affected sites of placebo-control mice revealed intensive inflammatory cell infiltration around anagen hair follicles and moderate cell infiltration within subcutaneous fat layer beneath telogen hair follicles, while such cell infiltration was noticeably reduced in AA sites of ebastine-treated mice, irrespective of phenotypical improvement of hair loss. Further investigation is necessary to definitively address the effect of ebastine in human AA, however, these findings, together with our clinical observation, suggested that ebastine could be a useful supportive medication for AA.

P-150

The Efficacy and Safety of AP-FHG0604T on Female Pattern Hair Loss

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Background: Many anti-androgen drugs, mineral supplements and topical minoxidil have been used for the treatment of female pattern hair loss (FPHL). However they do not always achieve the successful results and there is still much desire for more effective therapy.

Objectives: The purpose of this 18-week, double-blind, placebo-controlled, randomized clinical trial was to investigate the efficacy and safety of a new topical agent, AP-FHG0604T in the treatment of FPHL.

Approach: A total of 33 women (mean age: 33.4 years old) with FPHL applied topical AP-FHG0604T solution (n = 17), or placebo (vehicle for AP-FHG0604T solution; n = 16) twice daily. Efficacy was evaluated by phototrichogram, investigator's photographic and patient's subjective assessments. All adverse effects during the study were reported.

Results: After 18 weeks of therapy, topical AP-FHG0604T treatment showed significant improvement compared with baseline values in total hair count, non-vellus hair count, and linear hair growth rate. In the placebo group, non-vellus hair count and ratio of anagen hair significantly decreased. The change rates of total hair count and non-vellus hair count in AP-FHG0604T group were significantly higher than those in the placebo group. Neither investigator's photographic assessments nor patient's subjective assessments of hair growth showed statistically significant differences between AP-FHG0604T group and placebo group. Some patients who used AP-FHG0604T complained of local irritation during the study, but the irritation was so mild that they did not need any treatments for it.

Conclusions: We conclude that AP-FHG0604T is a safe and efficient topical agent that can be another treatment of choice for FPHL, as shown by objective assessment with phototrichogram.

P-151

How Does Minoxidil Stimulate Hair Growth? – A Mechanism Via Potassium Channels in Human Hair Follicles

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How minoxidil acts is currently unclear, despite widespread topical use for hair loss. Suggested mechanisms include vasculature stimulation. Other potassium channel opening drugs (PCOs) also stimulate hair growth implicating ATP-sensitive potassium (K_{ATP}) channels. We recently demonstrated that minoxidil and other PCOs stimulated deer follicle growth in vitro (Davies et al., 2005), but human studies are inconclusive.

To investigate whether K_{ATP} channels are present in human follicles, we used organ culture and molecular biological approaches. Scalp follicles were incubated in media ± minoxidil, tolbutamide (potassium channel closer) or a combination and measured for 9 days. Gene expression

of the 2 types of K_{ATP} channel components, regulatory sulfonylurea receptors (SUR) and pore-forming units (Kir) were investigated by RT-PCR.

Follicle growth rate was inhibited by tolbutamide (1mM) and high concentrations of minoxidil (1mM); combined treatment increased inhibition. Only tolbutamide decreased anagen follicle number. Scalp follicles expressed genes for SUR1, SUR2B, Kir6.1 and Kir6.2.

This first report of human follicle inhibition by tolbutamide indicates a biological response to potassium channel closers in vitro; anagen shortening is the opposite of PCO's anagen prolongation in vivo. Minoxidil's reported contradictory effects in vitro may be due to culture conditions opening channels. Two forms of K_{ATP} channels are expressed in human hair follicles; only SUR2B channels respond to minoxidil. These results suggest: minoxidil acts directly on human follicles via K_{ATP} channels; novel drugs acting via SUR1 channels alone, or with drugs acting via SUR2B channels, could stimulate greater hair growth; tolbutamide may have applications in suppressing hair growth.

P-152

Dermal Trichophytic Granuloma

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The fungi causing tinea capitis, rarely in the immunocompromized state invade the dermis causing granulomatous reaction. Two cases of dermal trichophytic granuloma that invaded the deep dermis and extended to the regional lymph nodes are presented. The cases followed the prolonged faulty use of systemic and local steroids. The presentation, diagnosis and management of the case was real dilemma. Complete recovery followed the stoppage of use of steroids and initiation of systemic antifungal treatment.

P-153

A Tool From the Nature to Treat Diffuse Alopecia

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A natural product made from organically cultivated pure essantial oils helps to activate dormant hair follicles and revive hair growth. It is a gel containing natural plant sources in an essantial oil blend. A study was conducted in our center to evaluate the efficacy of this product in the management of diffuse alopecia.

25 women and 25 men with diffuse hair loss of various causes participated in the study. An assessment of hair loss was done before and after using the gel by questionarre, serial photographs, clinical examination, dermatoscope and trichogram. Patients were asked to massage the gel over the scalp for 15minutes at every night for a period of 6 months and wash the scalp next morning with a mild shampoo. Periodical assessment of hair loss and hair growth was done every month. No concomitant medications were administered.

Noticeable improvement was seen within 30 days in all the patients. There was 60% reduction in the number of hairs falling. Seborrhoea and scalp itching reduced considerably. At the end of 2 months there was 90% reduction in the number of hairs falling. 30% of the patients felt that new hairs were growing. At the end of 3 months 60% of the patients had improved hair growth. 6 months follow up showed encouraging results.None of them experienced hypersensitivity or any adverse reaction. All patients revealed that the gel gave immense relaxation and a sense of well being in the scalp. Many felt that the gel provided natural sheen to the hair.

This novel preperation proves to be a very useful tool in the management of diffuse hair loss through its multiple therapeutic benefits such as decreasing DHT, regulating the hair cycle, increasing the microcirculation, decreasing dandruff and increasing nutritional support all in a natural way.

P-154

Treatment of Hirsutism with Topical Eflornithine: Our Experience

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Introduction: Hirsutism is caused by an excess production or action of androgens, usually by the ovaries or adrenal glands. The two most common causes of hirsutism are polycystic ovary syndrome (PCOS) and idiopathic hirsutism.

Eflornithine is a specific, irreversible inhibitor of the enzyme ornithine decarboxylase which is thought to slow hair growth by inhibiting this enzyme in hair follicles.

Objectives: the purpose of our study is to evaluate the effect of topical eflornithine for the treatment of hirsutism.

Approach: our treatment regimen was application of a thin film of eflornithine (as 11,5% cream) to the affected areas of the face twice daily for 12 weeks in a group of 20 patients and placebo cream in the other one, without any other topical, systemic or mechanical treatment. We also used a self-assessment questionnaire to assess the effects of treatment on patient well-being.

Results: after 12 weeks' treatment approximately 48% of women treated with eflornithine reported marked improvement in facial hirsutism, compared with 6% of women treated with a placebo cream. Besides, self-assessment questionnaire showed that eflornithine reduced the mean level of overall discomfort and bother. We had just one case of burning and erythema.

Conclusion: Improvement in facial hirsutism can be seen within 4 to 8 weeks after starting topical treatment with eflornithine. Hirsutism may return to pretreatment levels about 8 weeks after discontinuing the medication. Eflornithine is not a depilatory agent; rather, it retards hair growth and could be used in addition to the other hirsutism treatments.

P-155

Distinct Expression of Estrogen Receptor Alpha and Beta in Different Regions of the Human Hair Follicle of Male Versus Female

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Objectives: In this study, we investigated estrogen receptors (ER) expression and gene regulation of 1) male versus female, 2) frontotemporal versus occipital region and 3) human scalp skin versus hair to further explore gender, scalp location and hair follicle region dependence of estrogen (E2) effects on human hair follicles.

Methods: Skin samples obtained from patients undergoing plastic surgery were collected and either fresh frozen and used directly for RNA isolation or embedded and used for cryosections. Using Laser Microdissection and Pressure Catapulting (LMPC), we microdissected three different regions of the hair follicle (dermal papilla, hair matrix and bulge region) from cryosections of hair follicles from males and females, isolated total RNA from the samples, and then analyzed mRNA expression levels of ER by TaqMan. We also examined an additional 70 genes which are potential HF growth modulators. Immunohistochemistry was performed for ER-alpha and ER-beta protein expression.

Results: Contrary to previously published data, we found stronger ER-alpha mRNA expression than ER-beta mRNA expression in scalp skin samples. We also found that ER-beta mRNA expression in the hair follicles varied in the microdissected regions (dermal papilla, hair matrix, bulge region) and the distribution pattern was gender and scalp location dependent. ER-beta immunoreactivity differed between hair follicle regions, while ER-alpha protein was overall weakly expressed in skin and hair. Of 70 genes tested, several genes were expressed in a sex-dependent manner.

Recognition of the E2-dependent gene regulation will be crucial for the development of more effective gender-tailored management strategies for female versus male pattern balding.

P-156

The Effects of POMC Peptides on the Immune System of the Hair Follicle

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Background: Hair follicle is a widely available and instructive immune privilege(IP) mini organ in human body that it can be used for a model of studying the maintenance, collapse and restoration of IP. And there are various regulation factors acting on the generation, maintenance, and collapse of hair follicle IP. It is well known that neuropeptides originated from Proopiomelanocortin(POMC) are created in many organs including skin and display various immune regulation effects.

Objectives: To investigate the phenotypic effect of POMC peptides on the hair follicle IP.

Approach: first, we used a potent catagen inducer-interferon-g to make ectopic MHC class I expression hair follicle model in cultured human hair follicles, and then, we examined the effects of POMC peptides on the regulation of ectopic MHC class I expression in cultured human hair follicles using reverase transcriptase-polymerase chain reaction(RT-PCR) and immunohistochemical stain technique.

Results: we showed ectopic MHC class I expression in human anagen hair follicle can be normalized by treatment with adrenocorticotropic hormone(ACTH).

Conclusion: POMC peptides-ACTH are promising candidates for immune privilege restoration.

P-157

A Comparative Study on the Efficacy of Alexandrite and Diode Lasers For Hair Removal in Iranian Women

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Background: Hirsuties is a common problem in the middle east,especially Iran. As many epilatory methods lead to transient and unwanted effects like pseudofolliculitis,

advances in laser technology are admired by the patients demanding a relatively permanent method of hair removal. We aim to compare the clinical efficacy,and side effects of hair reduction of Diode (Nidek) and Alexandrite (Gentlelase) laser systems.

Methods: 105 women with fitzpatrick skin types 2-4 and terminal Facial hair were recruited into 2 separate groups who underwent 5 monthly laser-assisted hair removal sessions with either Gentlelase Alexandrite laser (755 nm, 2-msec pulse, 18 mm spot ,range of fluences used, 14-20 j /cm^2) or a Diode Nidek laser (785 nm, 25 msec,5 mm spot, range of fluences used 58-61.1 j /cm^2). Follow-up hair density counts and subjective satisfaction results of each area were obtained at each of the 5 treatment visits.

Results: After about 3 laser treatments, hair counts were reduced to the degree that no shaving or plucking process were required by most of the patients. At the end of 6 months follow up period a mean degree of, 60% improvement in hirsuties score was occurred in nearly equal amounts in both treatment groups. 2 months after the 5th and last treatment, mean degree of clinical hair reduction was observed to be about 60% with no significant differences between the laser systems and fluences used,the patient"s satisfaction score was high especially in Alexandrite group of treated patients

Conclusion: No significant differences were observed between alexandrite and a diode laser for hair removal with fortunately minimal adverse sequelae(1 keloid scarring which improved with intralesional triamcinolone injections). Long-term acceptable hair reduction can be obtained in most patients after a series of laser treatments.

P-158

Relationship Between IGF-I and Other Various Factors to Control Hair Follicle Growth

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Objectives: Insulin-like growth factor – I (IGF-I) share high degree of structural and functional homology with insulin and is a potent mitogen supporting cell growth and survival in many kinds of the tissues and cells. It also plays a role in some differentiation and anti-apoptotic function. IGF-I stimulate hair follicle growth, maintain anagen stage and postpone catagen stage. But exact mechanism of effect of IGF-I on hair follicle growth is not yet clearly proved. We investigated the relationship between IGF-I and other various factors (ex. apoptosis related molecules, pro-inflammatory cytokines, other growth factors, etc.) to control hair follicle growth.

Approach: We performed hair follicle organ culture with two experimental groups. One is IGF-I treated group and the other is control group. We also performed RT-PCR at 2,4,6,8 day of organ culture.

Results: We observed that IGF-I increased PDGF-A, PDGF-B and expression ratio of Bcl-2/Bax.

Conclusion: These results show that effect IGF-I on the hair growth is related with anti-apoptotic effect of IGF-I and up-regulation of PDGF-A and PDGF-B

P-159

Topographical Expression of Msx1 and Msx2 in Sheep Skin

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The size, density and growth duration of hair and wool follicles vary between body sites. In sheep, control of this topographic variation could lead to improved wool value and animal welfare. Two homeodomain-containing transcription factors, Msx1 and Msx2, have previously been linked to regional specification within the skin and also act as regulators of differentiation within the hair follicle matrix. We have characterised the expression patterns of Msx1 and -2 by real-time PCR in multiple body sites of adult sheep and in foetuses at the time of follicle primordia formation. In adult skin, both anterio-posterior ($P<0.01$) and dorso-ventral ($P<0.001$) gradients were observed in Msx1 expression across the trunk. However, mRNA of both Msx1 ($P<0.001$) and Msx2 ($P<0.001$) were four-fold lower on the face than the belly. Higher concentrations of Msx1 and -2 transcripts were present in adults than in foetuses, possibly reflecting additional roles in regulating the differentiation and growth of the hair shaft. In foetal skin of 70 days gestation, the expression of both Msx1 ($P<0.01$) and Msx2 ($P<0.01$) was greater on the belly than the midside. Msx1 expression was five-fold ($P<0.001$) and Msx2 two-fold ($P<0.001$) greater on the face than the belly. Thus, Msx expression was greatest in regions with more advanced follicle development, but lower eventual follicle density and fibre growth. These correlative data are consistent with the involvement of Msx1 and -2 in the development of skin regions, follicle growth, and anterio-posterior and dorso-ventral gradients of fibre growth characteristics in sheep.

P-160

Hair Follicle Melanocytes Do Not Constitutively Express MHC Ia or II Antigens

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The anagen hair bulb is one of the few sites of immune privilege (IP) in mammalian tissues. A collapse in hair follicle IP, with increased expression of major histocompatibility complex (MHC) class Ia and MHC class II, is thought to be the mechanism behind alopecia areata (AA) resulting in patches or widespread areas of alopecia. In contrast, the autoimmune attack seen in vitiligo results in depigmented skin. Despite a common autoimmune target, the melanocyte, these two diseases are infrequently co-expressed and rarely co-localised. As such, we hypothesized that there must be fundamental antigenic differences between melanocytes of the skin and those of the hair follicle. In order to examine ex-vivo expression of MHC antigens on melanocytes of the hair follicle and epidermis, we performed double immunofluorescent staining on scalp cryosections from normal subjects with either w6/32 or CR3/43 and NKI/beteb recognizing MHC-Ia or MHC-II expression and melanocytes respectively.

We found that anagen hair follicle melanocytes residing above the apex of the dermal papilla do not express MHC-Ia or MHC-II. Epidermal melanocytes however, do express MHC-II. Due to the strong staining with w6/32 by epidermal keratinocytes, NKI/beteb-labeled melanocytes could not be accurately identified through double-staining and their expression of MHC-Ia could not be conclusively determined. Our finding of a contrasting MHC expression pattern between these anatomically distinct melanocyte populations may further our understanding why hair follicle melanocytes are preferentially attacked in AA whereas epidermal melanocytes are the target in vitiligo.

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P-161

Adenosine Stimulates Fibroblast Growth Factor-7 Gene Expression in Dermal Papilla Cells and Its Contribution to Hair Elongation

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Adenosine is known to play various physiological functions through its receptors' mediated signal-transduction pathway, in various cell types including dermal papilla cells (DPCs) in hair follicle (1). We performed DNA microarray analyses of DPCs with or without adenosine, and found that adenosine stimulates fibroblast growth factor-7 (FGF-7) gene expression levels by greater than 2-fold. Elevations of the extracellular FGF-7 protein levels were also observed. These upregulations of FGF-7 both at mRNA and protein levels were inhibited by A2b adenosine receptor-specific antagonist, alloxazine, but not by antagonists for other subtypes. In addition, the intracellular cAMP levels were raised by adenosine in a dose-dependent manner. Moreover, an increase of intracellular cAMP augmented the FGF-7 upregulation. Taken together, these results show that adenosine treatment of DPCs upregulates FGF-7 expression via the A2b adenosine receptor and that cAMP acts as one of the second messengers in this pathway. Furthermore, treatment with FGF-7 at concentrations of 10 ng/ml or greater significantly stimulated hair fiber elongation in human scalp hair follicle organ cultures. These data imply that adenosine stimulates hair growth through FGF-7 upregulation in DPCs.

1) Li et al., J. Invest. Dermatol. 117, 1594-, 2001

P-162

Repeated Hair Depilation Does Not Alter the Hair Growth Cycles of C3H Mice

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The mouse is commonly used to investigate the hair cycle because of its predictable hair cycle and synchronized hair growth. The murine hair growth (anagen) can also be stimulated by depilation, a procedure that results in all telogen hair follicles entering the anagen stage at the same time. In the current study, we examined the effects of repeated depilation on the hair cycle in C3H mice. Male C3H mice, 46-60 days old in telogen phase, were depilated with a commercially available hair removal wax. Once

the hair follicles in the depilated area were in anagen VI (defined by the presence of grossly evident new hair shafts), a group of these mice were depilated a second time. Results were compared to the mice that had been depilated only once. Examination of the twice-depilated mice defined injury to the hair shafts and hair follicles; however, the injury was repaired over a 7 day period and the hair follicles remained in the identical stage as the single depilation mice. In spite of the hair follicle injury and regeneration, the twice-depilated mice entered the catagen phase at the same time as the mice that had only been depilated once. These findings demonstrate that the depilated anagen hair follicles can repair the injury caused by hair plucking and regenerate the follicles without immediately entering catagen or telogen. Depilation of the anagen hair does not alter the programmed hair cycle initiated by the first depilation.

P-163

Identification of Beta Catenin-Regulated Genes in Human Hair Outer Root Sheath Cells Cultured in Vitro

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The Wnt signaling induces various cellular responses, including cell proliferation, fate determination and terminal differentiation, through the stabilization and accumulation of b-catenin. Although b-catenin has been recognized to be a key molecule in the hair follicle formation and anagen induction, the down-stream effectors of b-catenin have not been clearly defined yet. To identify the b-catenin-regulated genes, we made a recombinant adenovirus harboring the expression cassette for b-catenin. After adenonviral transduction into the human hair outer root sheath (ORS) cells cultured in vitro, the increase of cellular b-catenin was confirmed by Western blot analysis. Then, we isolated total RNA and performed cDNA micrarray. We chose the genes that showed at least two-fold induction by b-catenin. The expression of selected genes was verified using RT-PCR. As a result, we identified several b-catenin-regulated genes in ORS cells, including keratin 15, 16 and 17. In addition, the expression of some histone deaceytylases, such as HADC1, 2, and 3, were significantly affected by the overexpression of b-catenin. The roles of b-catenin-regulated genes in ORS cells will be investigated further. Our results provide important clues, on which to base further investigations of hair growth modulation by b-catenin.

P-164

Expression of Ephrin-A and Epha Family in Hair Follicles and Effects of Ephrin-A-Epha Oversignaling on Hair Formation and Differentiation

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Objectives: We have already reported that ephrin-A3 was markedly down-regulated in dermal papilla cells from androgenetic alopecia patients. Although ephrins are known to regulate a variety of developmental processes, little is known of their role in hair development. So we investigated the expression of ephrin-As and whose receptors (EphAs) in hair follicles throughout the hair cycle. We also tried to clarify the role of ephrin-As – EphAs signaling on hair follicle formation and differentiation.

Approach: We studied the expression of ephrin-As and EphAs in C3H/He mice from the day of birth to the second hair cycle with qPCR and immunofluorescence methods. Next, ephrin-A3 was subcutaneously injected into neonatal mice and the effects of ephrin-A3-EphAs over-signaling on hair formation and differentiation were studied morphologically.

Results: ephrin-A1, A3, A5, and EphA4 were expressed synchronously with the hair cycle and were localized in outer root sheath at anagen phase and secondary hair germ at telogen-anagen transition phase. Subcutaneous injection of ephrin-A3 into neonatal mice markedly accelerated differentiation processes of hair follicles and increased the hair follicle number; this was not a transient phenomenon but was also conserved in the second hair cycle.

Conclusion: All findings of these studies revealed the characteristic spatiotemporal expression of ephrins and Ephs in hair follicles through the hair cycle, and also indicated that ephrin-A3 not only accelerates the hair follicle development, but also increases the density of hair follicles. Ephrin-A3 is the first molecule presumed to be involved in hair follicle differentiation and formation.

P-165

Whole-Mount Detection of Apoptosis and Proliferation in Human Hair Follicles by 2-Photon Laser Microscopy

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In recent studies, we have correlated cutaneous apoptosis and proliferation during hair follicle (HF) morphogenesis and cycling demonstrating the crucial role in sculpturing the HF structure in mice (Magerl et al., J Invest. Dermatol. 2001,116:947). Here we introduce a pioneering technique to overcome the limits of traditional two dimensional staining methods by using whole mount imaging of dissected human hair follicles visualized by deep penetrating two-photon laser microscopy.

With the novel whole-mount in situ technique, TUNEL and Ki67-immunoreactivity were combined to investigate the spatiotemporal patterns of apoptosis and proliferation within micro-dissected human hair follicles. In addition, we were capable to detect adjacent blood vessels as well as collagen an elastin fibres. These structures were co-visualized by second harmonic generation and auto fluorescence imaging. With this experimental setup, key stages of the human hair follicle cycle were analysed and three-dimensional maps were generated by software rendering.

Beside massive up-regulation of Ki67-positive keratinocytes seen in the proximal hair matrix of anagen HF, clusters of Ki67-immunoreactive cells were seen in the distal portion of the HF in close vicinity to the putative stem cell region. Consistent to previously described expression patterns in mice, bundles of strong TUNEL positive cells were seen in the trailing epithelial strand in human catagen HF.

Three dimensional follicular imaging has highlighted an unexpected degree of dynamics and turnover of growth and regression processes within the human HF as well as remodelling of connective tissue underlining the vital function in shaping HF topology.

P-166

The Immune Privilege of Human Hair Follicles Is Selective and May Not Include Resistance to Complement Activation

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The immunology of hair follicles and their role in the skin immune system has significant impact both biologically and clinically. The hair bulb part during anagen is believed to retain immune privilege (IP) characterized by very low expression level of MHC I, suppression of MHC II-dependent antigen presentation, and production of immunosuppressive agents. We generated a list of 19 immunoregulatory genes, and determined their differential expression in human hair follicles (HF) as compared to normal skin epithelium. We performed microdissection of HF from scalp biopsies of normal individuals, and further dissected the tissues into bulb (B) and shaft (S) parts. RNA synthesis was then conducted, followed by reverse transcription and, finally, real-time RT-PCR was conducted. Consistent with previous publications, the immunosuppressive gene a-MSH was significantly upregulated in both bulb and shaft (2.06 fold, and 4.26 fold respectively). Consistent with a lack of lymphocytes and antigen presentation in HF, CD80 (B: 5.30 fold; S: 3.99 fold) and CD86 (B: 4.09 fold; S: 1.60 fold) were downregulated. The apoptotic genes Fas (B: 2.46 fold) and FasL (B: 78.71 fold; S: 7.79 fold) were both downregulated significantly in our analysis. Also, we found that complement suppressive factors, such as CD 55 (B: 5.48 fold; S: 3.52 fold) and CD59 (B: 2.29 fold) were downregulated. These results reveal some putative candidates that participate in the IP of hair follicles, but HF IP is selective and, notably, the ability to blockade complement activation may actually be reduced as compared to normal skin epithelium.

P-167

Uneven Proteoglycan Distribution Along the Human Hair Follicle

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Background: Proteoglycans are known to play a key role in many cellular signaling pathways involved in hair follicle biology. Although proteoglycans were well described in rodents, they were incompletely studied in adult human hair follicle.

Objectives: To review and complete description of proteoglycans and glycosaminoglycans in human anagen hair follicle and for selected one during the hair cycle.

Approach: We used immunohistochemistry and immunohistofluorescence to revisit the expression pattern of glycosaminoglycan chains and core-proteins in human hair follicle. The studied epitopes included CD44v3, syndecan, perlecan, versican, aggrecan, heparan sulfates, chondroitin sulfates and keratan sulfate.

Results: Our results confirmed and extended the notion that both connective tissue sheath and dermal papilla contained high amounts of proteoglycans such as perlecan, versican, heparan sulfates or chondroitin sulfates. We also observed a varying distribution of these components along the hair follicle. Especially, we noted a proteoglycan impoverishment

at the very bottom of the bulb. During catagen, 4C3 and PG4 chondroitin sulfate epitopes disappeared in dermal papilla and connective tissue sheath respectively, confirming the arrest of extracellular matrix synthesis during this regression phase.

Conclusion: Uneven expression along the anagen follicle and remolding of some epitopes during hair cycle suggest that proteoglycans are involved in nutrient diffusion, cell proliferation and differentiation, and hair protection.

P-168

Activin A and Follistatin Influence Hair Follicle Development in Mice

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Members of the TGFb superfamily are known modulators of hair follicle development. In particular activins and follistatin are highly-expressed in the skin at critical phases of hair follicle formation. To ascertain if these molecules are causally related to hair follicle induction, we determined the effects of exogenous activin A and follistatin on the development of tylotrich and non-tylotrich hair follicles in embryonic mouse skin cultures. Changes in gene expression associated with treatment with activin A were also quantified by quantitative PCR of candidate genes involved in TGFb superfamily signalling in a subset of the animals.

Skin explants were collected from 13.5 and 15.5 days post coitus (dpc) mouse embryos and cultured for 3 days in the presence or absence of recombinant human activin A (rhActA) or follistatin (rhFS300). While there was no significant effect of rhActA on follicle density in 13.5dpc skin, there was a 10-17÷ decrease in follicle density of 15.5dpc skin cultured in rhActA compared to controls ($P<0.05$). However, there were no changes in the gene expression in rhActA-treated explants, when normalized against three housekeeping genes. While rhFS300 supplementation had no effect on follicle density, rhFS300 did reduce the extent of follicle downgrowth and delayed follicle maturation in the 13.5 dpc-derived explants.

These results suggest activin A is involved in follicle initiation of non-tylotrich hair follicles, most likely through post-translational modifications of components of the TGFb signalling pathways, rather than via gene expression. Follistatin appears to influence follicle maturation and downgrowth through mechanisms as yet unknown.

P-169

Expression of Pitx2 in Human Hair Outer Root Sheath Cells

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Pitx2, a bicoid-type homeodomain transcription factor, has been shown to play a central role in differentiation and development. In the human, four isoforms of Pitx transcripts has been isolated, wihich are named as Pitx2a, b, c and d. Pitx2a, Pitx2b, and Pitx2c are structurally related, differing only in their amino terminal region. Pitx2d shows somewhat different structure, and acts to repress the activity of the other Pitx2 isoforms. Among those, Pitx2c isoform was predominantly expressed in normal human epidermal keratinocyte cultured in vitro. In this study, we investigated the expression of Pitx2 in hair follicle using immunohistochemistry analysis. The expression of Pitx2 is detected predominantly in outer root sheath (ORS) of lower half of hair follicle. To investigate the role of Pitx2 in ORS cells, we made a recombinant adenovirus harboring the expression cassette for GFP-Pitx2c fusion protein. Primary cultured ORS cells were transduced with recombinant adenovirus and then Pitx2 expression was detected in the nucleus. To identify the Pitx2-regulated genes, we performed RT-PCR and Western blot analysis for several intermediate filament proteins and cell cycle-related proteins. Interestingly, overexpression of Pitx2c in ORS led to the upregulation of keratin 6. In addition, overexpression of Pitx2 resulted in the change of several cell cycle-related protein levels such as p21. These results implicate the potential importance of Pitx2 in the regulation of hair growth.

P-170

Substance P Receptor Expression in Human Hair Follicles

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Background: Among the constituents of skin, hair follicle is an organ which has the highest density of nerve fibers distribution. It has been reported that neuropeptides which are secreted by nerve fibers have important roles in the hair growth and hair cycle change. Substance P (SP), as a neuropeptide distributed over the wide human skin that displays its effect through combining with special receptor. In the previous study conducted by us, we showed

that SP had a positive effect on the hair growth and especially prolonged the anagen phase in culture of human hair follicles.

Objectives: To investigate the expression of substance P receptor (SPR) in human hair follicles, hair follicle cells and its expression change when treated with SP and SPR antagonist – spantide I.

Approach: Human hair follicles and hair follicle cells were cultured. The expression of SPR was examined by semiquantitative reverse transcriptase-polymerase chain reaction(RT-PCR) and immunohistochemical stain. The expression change of SPR in human hair follicles was detected by RT-PCR and Western-blotting analysis.

Results: SPR expressed in human hair follicles and hair follicle cells, SP upregulated the expression of NK-1R, SPR antagonist -spantide I can reduce the expression of NK-1R.

Conclusion: In culture of human hair follicles, SP, through combining with special receptor-SPR displays the effects of prolonging the duration of anagen phase.

P-171

EGF and FGF Signalling Have a Role in Mouse Hair Follicle Morphogenesis and Patterning

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Epidermal growth factor (EGF) has previously been shown to block hair follicle (HF) morphogenesis. However, the mechanism underpinning this phenomenon has not been investigated in detail, perhaps because EGF ligand is not endogeneously expressed in skin during early HF initiation and patterning. Keratinocyte growth factor (KGF) has also been shown to block follicle formation in organ culture in a manner not yet understood. In this study, we revisited the roles of the EGF and KGF signalling pathways in normal HF morphogenesis in mice.

first, semi-quantitive PCR was used to profile the expression of EGF and KGF ligands and receptors within separated epidermis and dermis of E12.5-15.5 mouse dorso-lateral skin. This analysis discovered endogenous expression of EGFR ligands, Heparin binding EGF and Amphiregulin, as well as the KGFR ligand KGF. Intriguingly, immunohistochemistry revealed a marked reduction in both EGFR and KGFR expression in developing placodes and subsequent hair germs. Functional studies using embryonic skin organ cultures identified that EGFR or KGFR activation within E13.5 skin (before placode formation) inhibited HF development in a dose dependent manner. This was confirmed by in situ hybridisation and immunological detection of molecular markers specific to developing HFs. Activation of either receptor within E14.5 skin (post placode formation) had no effect on hair follicle development.

We propose a role for EGF and KGF signalling in which receptor downregulation may be required for epidermal cells to escape ligand stimulation, thus permitting placodal cells to follow a follicular rather than an interfollicular differentiation pathway.

P-172

Endostatin Overexpression in the Skin Interferes With Hair Follicle Development

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Objectives: To study how overexpression of endostatin, the C-terminal domain of collagen XVIII, affects hair follicle morphogenesis. Collagen XVIII is a basement membrane (BM) proteoglycan, suggested to have a role in maintaining the structural integrity of BMs. Endostatin is also known to affect integrin- and VEGF-mediated signaling.

Approach: Mice overexpressing endostatin in the skin under the keratin-14 promoter (ES-tg) and control FVB/N mice were used in the experiment. Skin samples were collected from the neck region of control and ES-tg male mice (n=5 per group) at different timepoints after birth (1-32 days). HE- and immunofluorescence stainings were performed.

Results: At postnatal day 1 the hair follicles in both mouse lines were positively stained for collagen XVIII. However, in the ES-tg mice reduced intensity of the staining was detected with an antibody specific for the two longest variants of collagen XVIII. These include a variant with a cysteine-rich domain homologous to the frizzled-proteins which potentially binds to Wnt-proteins. At day 25 the hair follicles of control mice reached deep to the subcutis to the close vicinity of the panniculus carnosus. However, in the ES-tg mice the hair follicles were not found as deep in the subcutis, and the follicles also appeared thinner and fewer in number. The analyses from the other timepoints are currently ongoing.

Conclusion: Based on our results, we suggest that excess of endostatin leads to abnormal hair follicle development.

P-173

Morphological and Immunohistochemical Examinations of Human Hair Follicles: Special Reference to the Bulge Area

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We have focused the characterizations of the bulge areas of human hair follicles where follicular stem cells may be present. Serial transverse sections of human scalp skin were observed. In the terminal hair follicles of the human scalp we found apoptotic pocket-like structures in the outer root sheath of the bulge area at anagen, but not telogen phase. The size of these apoptotic pockets was variable, ranging from pin hole-like spaces to larger structures. Moreover, the distributions of Merkel cells, Langerhans cells and melanocytes within human hair follicles were immunohistochemically examined. Merkel cells were stained with CK20, while Langerhans cells were stained with CD1a. Melanocytes were also decorated with NKI/ beteb. We immunohistochemically confirmed the localization of Merkel cells, Langerhans cells and melanocytes within the bulge areas in normal human hair follicles. Using a double staining technique, it was clearly demonstrated that a small proportion of Merkel cells were closely contacted with Langerhans cells below the sebaceous gland level, presumably indicating the bulge area. Merkel cells and Langerhans cells connected directly or approached each dendrite within the basal layer of the outer root sheath. We demonstrated a close anatomical relationship between Merkel cells and Langerhans cells and pocket-like structures within the bulge area of human hair follicles.

P-174

Transforming Growth Factor-B Receptor II is Preferentially Expressed in the Companion Layer of the Human Anagen Hair Follicle

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Transforming growth factor beta (TGF-b) is a multifunctional growth factor with multiple roles in skin including hair follicle development and cycling, where it regulates cell proliferation, differentiation and apoptosis, as well as in wound healing. While TGF-b RI and TGF-b RII expression helps define early human hair follicle morphogenesis, expression in the adult human hair follicle remains to be established. The aim of this study was to assess TGF-b receptor expression in human scalp anagen hair follicles. Immunohistochemical and double immunofluorescence analysis of TGF-b RI and RII was conducted on frozen sections of haired human scalp obtained from 10 healthy individuals.

TGF-b RI expression was detected in the outer root sheath of anagen hair follicles while TGF-b RII was expressed almost exclusively in the companion layer of inner root sheath and less so in pre-medulla keratinocytes. Both receptors were co-localized in the companion layer of the proximal and mid follicle. The well-described role of TGF-b in keratinocyte apoptosis during catagen is likely to involve anagen-specific hair follicle components including the companion layer as this layer provides the slippage plane supporting the inner root sheath and hair shaft as they ascend to the skin surface. Results of this study suggest that the co-localization of TGF-b RI / RII complexes at the companion layer would facilitate TGF-b signalling at this site to regulate apoptosis of the companion layer keratinocytes, facilitating shrinkage/ contraction of this cell layer during hair follicle regression / catagen.

P-175

Leptin Is a Paracrine Regulator of Hair Cycle

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Leptin, one of adipokines secreted from adipocytes, is known to affects energy balance by interacting with hypothalamus. Recent studies have shown that non-adipose tissues also produce leptin. Leptin acts on target tissues via specific receptors (Ob-Rs), and activates STAT3. We have previously reported that the activation of STAT3 is indispensable for hair cycle progression. In this study, we examined whether leptin is physiologically involved in hair cycle progression using well-established diabetic model mice. Back skin of 5 wk old C57/BL6 mice showed late anagen phase, while the hair follicles of Ob-Rb deficient Db/Db mice were still in the first telogen phase, indicating the inhibition of the second hair cycle progression. Hair plucking of back skin induced the anagen phase in 7 wk old C57/BL6 mice, but Ob/Ob mice showed no hair growth 3 weeks after plucking. In Ob/Ob mice, the angen phase was induced 1week after plucking concomitant with local leptin injection. Moreover, anagen was induced in the injected site 3 weeks after local leptin injection in 7 wk old C57/BL6 mice. The production of leptin by cultured human dermal papilla cells were confirmed by RT-PCR and ELISA. Phosphorylations of ERK, JAK2, and STAT3 in cultured human keratinocytes were examined by western blot using specific antibodies for phosphorylation sites. All

of the molecules were phosphorylated by leptin treatment. These results indicate that leptin is physiologically involved in hair cycle progression, and suggest that the angen phase is induced by leptin from dermal papilla cells in a paracrine manner.

P-176

The Notch Signaling Pathway Is Involved in Wool Follicle Development

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Wool follicle development is initiated during fetal life through signals exchanged between the mesenchyme and epithelium. Follicle primordia are initially visible as condensations of dermal prepapilla cells associated with epithelial thickenings. Notch genes are expressed in fetal skin and the signal pathway is involved in cell fate specification.

This study investigates the role of Notch in specifying the papilla cell population, during initiation in the sheep, using in situ hybridization (ISH) and cell culture.

Ovine skin samples were collected from fine-wooled Merino and strong-wooled Tukidale fetuses (day 56 and 70 of gestation). ISH studies were conducted using a DIG-labelled riboprobe generated from a murine Delta-1 cDNA sequence. Counts of specifically labeled cells were analysed. Dermal papillae (DP) harvested from adult Merino whisker follicles were cultured in vitro. Cultures were treated with a g-secretase inhibitor (DAPT) that blocked Notch signaling to determine if it affected cell aggregation.

ISH results revealed the presence of Delta-1 transcripts prior to and during follicle initiation. Significant differences in the numbers of labeled cells were found during initiation. At this time, the percentage of labeled cells was 41.54 ± 1.60 in the Merino, compared to 46.22 ± 2.22 in the Tukidale. In vitro studies showed that DAPT inhibited DP cell aggregation, presumably through Notch signal blockade. We conclude that Notch pathway genes expressed in mesenchymal cells are involved in specifying prepapilla cell fate at follicle initiation.

P-177

Keratin Gene Expression Varies Between Sheep Breed, Primary and Secondary Wool Follicles and with Follicle Growth Status

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Mammalian fibres are predominantly comprised of keratins and their associated proteins, hence the expression and translation of the corresponding genes will underlie many fibre characteristics. Recent rapid progress in the understanding of the genomic structure of keratin genes and their expression in the human hair follicle have provided a basis to study the mechanisms of hair and wool fibre formation. Skin samples were collected from New Zealand Wiltshire, Romney and Merino sheep, and from wool follicles in synchronised stages across the hair cycle. The expression patterns of five intermediate filament and six keratin-associated protein (KAP) genes were investigated by qPCR, Northern blot and in situ hybridisation. Significant differences in expression between sheep breeds, follicle growth stages, and between primary and secondary follicles were found. While expression of the follicle-specific genes fell rapidly during catagen, only some keratin intermediate filaments (KRT27, KRT31 and KRT85) and KAPs (KRTAP6.1 and KRTAP8.1) appear to be involved in brush-end follicle formation. Localisation patterns for KRT31, KRT35, KRT38, KRT85, KRTAP4.3 and KRTAP6.1 differed between primary and secondary follicles, and qPCR showed higher levels of expression of these genes (apart from KRTAP6.1) in body sites with lower S:P ratios and lower follicle densities. Further studies are underway to link gene expression with wool protein composition and, in turn, to the control of fibre formation. An improved understanding of the regulation of all the major wool and hair keratins and KAPs will contribute to the development of novel fibres, new cosmetics and keratin-based industrial applications.

P-178

Gene Expression Pattern Similarity Between Hair Follicles and Basal Cell Carcinomas

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Hair follicles and BCCs can be regarded as ordered and disordered skin appendages respectively, and may utilize similar molecular mechanisms of growth. We wanted to examine the similarities and differences in gene expression patterns between BCCs and hair follicles to define common growth mechanisms and patterns that distinguish an

ordered skin appendage from a disordered skin growth. Nodular cystic BCCs (n= 8) and non-follicular skin epithelium (n=8) were obtained from previously untreated patients undergoing Mohs surgical resection. Scalp hair follicle epithelial root sheath was micro dissected from between the sebaceous gland duct and the lower one third of the hair follicle (n=7). Microarray analysis was performed using 21K sequence verified cDNA arrays and selected genes were validated using quantitative PCR. Two differentially expressed genes sets were identified by T-test and 1.5 fold changes filtering from BCC and hair follicle epithelium verses skin epithelium respectively. Based on these two lists, 1429 similarly expressed genes in hair follicles and BCCs were obtained and applied to multiple signaling pathways analysis. Analysis indicated that Notch signaling, apoptosis, hedgehog, WNT, and TGF beta pathways were involved in regulating formation of hair follicles and BCCs. In particular, Notch signaling, including Notch 1, Notch 2, DTX2 and DNER, showed selective differential activation in BCCs and hair follicles.Our data provides compelling evidence that "tumorgenic" growth signaling pathways are commonly expressed in both hair follicle epithelial progenitor regions and BCCs. However, in hair follicle 3 times the number of genes is differentially expressed as compared to BCCs.

P-179

Characterization of Wnt Ligands Important For Hair Follicle Development

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Multiple Wnt ligands are expressed in embryonic skin at the time of hair follicle placode initiation, and several of these are upregulated in placodes and in specific subsets of hair follicle cells at subsequent developmental stages. Analysis of transgenic mice expressing Wnt/β-catenin reporter genes has indicated that Wnt/β-catenin signaling is active at several stages of hair follicle development. Forced expression of the potent secreted Wnt/β-catenin pathway antagonist Dickkopf1 (Dkk1) prevents initiation of hair follicle placode development, demonstrating that Wnt/β-catenin signaling plays a critical role in this process. However, the specific Wnt ligands required for hair follicle development have not been identified. To begin to address this question we are analyzing skin and hair follicle development in mice carrying loss of function mutations in Wnt genes that are expressed in the embryonic skin and hair follicles. Analysis of mice lacking epithelial Wnt3, that is broadly expressed in the embryonic epidermis, revealed defects in limb development, but normal hair growth. Similarly, hair follicle development was grossly normal in mice lacking Wnt10b, the Wnt showing the earliest specific localization to developing placodes. As expression of Wnt10b overlaps with that of a related Wnt, Wnt10a, we have now generated mice lacking Wnt10a. Preliminary analysis suggests that mice lacking Wnt10a die during embryogenesis. We are currently determining the stage of lethality of Wnt10a-null mice, and analyzing the skin and hair follicle phenotypes of Wnt10b-/-; Wnt10a+/- mice.

P-180

No Association Between Serum Ferritin Levels and Hair Loss Activity in Otherwise Healthy Women

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Background: Hair loss is common in women. Female pattern hair loss (FPHL) and diffuse telogen effluvium (TE) account for most cases. Low iron stores are considered a possible contributing factor, and assessment of serum ferritin levels is recommended as part of routine investigation. However, contradictory data have failed to resolve whether an association exists between hair loss and low ferritin levels.

Objectives: To evaluate the relationship between serum ferritin levels and hair loss activity determined by trichogram in otherwise healthy women.

Approach: Retrospective case study of 413 consecutive women who presented at the Department of Dermatology, University Hospital of Zurich hair clinic between 2002 and 2005 for assessment of hair loss due to FPHL or TE. All underwent biochemical investigations and trichograms.

Results: After exclusion of patients with a history of disease, abnormal laboratory studies (except ferritin), or on drugs known to cause hair loss, 181 women remained. Of these, 112 (62 %) women had a serum ferritin > 30mg/L (lower reference limit of normal for children, men and non-menstruating women), 55 (30 %) between 10 – 30 mg/L, and 14 (8 %) < 10 mg/L (lower reference limit of normal for menstruating women). No correlation was found between serum ferritin levels and pathologic trichograms (telogen rate > 15%).

Conclusion: There is no relationship between serum ferritin levels and hair loss activity determined by trichogram. The usefulness of serum ferritin assessment for the purpose of therapeutic iron supplemation in women with FPHL or TE remains debatable.

P-181

Lipid Metabolism By Cutaneous Malassezia Yeasts and Its Implications For Scalp Condition and Dandruff

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Dandruff is a global consumer problem, characterised by flaking and scaling of the scalp, accompanied by itch and irritancy. However, despite much research, the aetiology of the condition remains poorly understood, although there is a strong consensus that yeasts of the genus Malassezia are a major contributory factor. Again, however, there is a paucity of understanding on how this commensal organism adopts a pathogenic phenotype. The objective of these studies was to investigate the metabolism of sebaceous lipids by Malassezia yeasts, a mechanism by which these organisms have previously been reported to generate scalp irritants that mediate dandruff. Assay systems were developed to study the metabolism of triacylglycerols and fatty acids by a representative selection of Malassezia isolates. Malassezia species exhibited lipase activity, hydrolysing triacylglycerols to free fatty acids, while the ability of these yeasts to utilise fatty acids as a source of carbon and energy was also demonstrated. Of particular note, Malassezia species were shown to partially catabolise structurally-unusual (e.g. methyl-branched) fatty acids to chain-shortened species. At face value, these volatile fatty acid (VFA) products may be seen as promoters of scalp itch and irritancy, and thus mediators of dandruff. However, this rather simplistic explanation ignores the many other sources of fatty acids, including VFAs, on scalp skin, as well as information emerging on the complex immunological interaction that exists between Malassezia and its host. Thus, the metabolism of sebaceous lipids by Malassezia yeasts, while of academic interest, is probably not a major aetiologic factor in dandruff.

P-182

The Role of Alimentary Integrators in a Trichologic Context: a Report of Italian Association of Women Dermatologists

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Recent evidence of literature have well established the important role for health of the alimentary integrators contained naturally in food such vitamins, minerals, fibers. The use of these molecules by dermatologists is individual and it doesn't follow specific guidelines. Usually patients assume these molecules by self prescription following hormonal changes of pregnancy and seasonal climatic changes.

It is demonstrated that the use of elementary integrators containing cysteine and sulphurated aminoacid as well as of vitamins, antioxidants mineral and free antiradicals like A, B5 vitamins and microelements can be very useful in some stress conditions.

To better understand the role of alimentary integrators in the regimen of patients the Italian Association Women Dermatologists conducted a questionnaire on 285 women investigated the knowledges and the employment of common integrators.

P-183

Iron Deficiency-Induced Hair Loss Due to Incorrect Dietetic Habits in Iran

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Background: Iron deficiency – induced hair loss is very common in Iran even in urban areas,although its incidence in rural regions will be much higher.Statistics show 80% of female Iranians in reproductive age have subclinical iron deficiency although this level would not necessarily cause anemia but would be sufficient to cause hair dryness, fragility and losses.

Discussion: A very common and cultural habit in our citizens is drinking strong tea especially immediately after lunch and dinner,so despite probably enough intake of iron in meat,eggs and similar foods ,this will lead to intestinal malabsorption of Iran. On the other hand in rural areas the red meat availability is limited due to its dear price and cultural or social habits of villagers shift them to eat rice, bread and "beans/vegetable" soup (instead of steak or kebabs made from meat) as main nutrition.

Conclusion: These facts are obtained in our research in detail.

Education and insight to the adverse effects such as hair loss, graying hair and hair shaft fragility which is very important to young Iranian females can possibly reverse such habits effectively and with a low cost.

Key words: Iron deficiency, hair loss, dietary habits, Iranian females

P-184

The Stimulatory Effects of Cepharanthine and Plant Worm on Hair Growth

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Objective: The purpose of this study is to analyze the effect of Cepharnthine (CE), a biscoclaurine alkaloid obtained from the plant, and Plant worm (Cordyceps sinensis) on hair growth stimulation in a C3H/HeN mouse system in vivo. The effect of CE on cell proliferation of dermal papilla cells (DPCs) and outer root sheath cells (ORSCs) in vitro was also analyzed.

Approach: For quantitative evaluation of hair growth in mice, 0.002% CE solution, 0.75% Plant worm solution and vehicle solution (75% alcohol) were applied to the dorsum of the 8 weeks old C3H/HeN mice once daily for three weeks, after clipping the dorsal hair in telogen. In vitro: DPCs and ORSCs were cultured with or without CE for 5 days, and then tested of cell proliferation by alamarBlue™ assay.

Result: Significant effect on hair growth of mice treated with CE and Plant Worm were seen compared with the vehicle treated group ($p<0.05$, $n=10$). In addition, 0.1μ/ml CE stimulated cell proliferation of cultured DPCs ($p<0.05$), but not that of cultured ORSCs.

Conclusion: These results confirmed that CE and Plant Worm were significantly effective in accelerating hair re-growth, otherwise CE might have an effect on DPCs directly.

P-185

Human Scalp Hair Growth Modulation By Dickkopf1

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Objectives: To investigate the effects of Dickkopf 1 (DKK-1) on human scalp hair growth.

Approach: Outer root sheath (ORS) keratinocytes and dermal papilla (DP) cells were cultivated from human scalp hair follicles and treated with recombinant human DKK-1 (rhDKK-1). Hair follicles were also cultured in vitro in the absence or presence of recombinant human DKK-1 (rhDKK-1) in William's E medium.

Results: rhDKK-1 inhibited the growth of outer root sheath (ORS) keratinocytes but not DP cells. rhDKK-1 also induced apoptotic cell death in ORS cells accompanied by Bax induction. In addition, rhDKK-1 inhibited elongation of hair shafts and caused apoptotic cell death of epithelial cells in cultured hair follicles.

Conclusion: Altogether, our data suggest that DKK-1 may inhibit the human scalp hair growth by triggering apoptosis in follicular keratinocytes.

P-186

Hair Growth Activity of Cosmetic Diaminopyrimidine-Oxide Compound in Vitro & in Murine Anagen Induction

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Many pyrimidine oxide derivatives were known to have the vasoactivity for hypertension and alopecia. But only minoxidil (6-(1-Piperidinyl)-2,4-pyrimidinediamine-3-oxide) was approved from FDA for topical drugs for alopecia.

We investigated the hair growth activity of 2,4-diamino-6-pyrrolidin-pyrimidine-3-oxide (Triaminodil, Proderma, Italy, Cas No. 55921-65-8), which was developed for cosmetic ingredient. We first observed the active effect of triaminodil & minoxidil on NIH3T3 fibroblast in ATP-sensitive potassium channel-dependent fashion and then anagen induction also was evaluated after topical administration on telogen phase murine dorsal area.

In vitro effects of established potassium channel opening were indirectly assessed on NIH3T3 fibroblast in the absence of aminoglycoside antibiotics, phenol red and 5% fetal bovine serum-supplemented medium. 2.5mM tolbutamide inhibited 40% proliferation of NH3T3 fibroblast as reported previously. When minoxidil & triaminodil were treated to the fibroblast with 2.5mM tolbutamide, growth inhibition of NIH3T3 fibroblast was suppressed 51.49% by 100uM minoxidil 58.7% by 100uM triaminodil, respectively. Two topical preparations of single dose (0.5%, w/v) of minoxidil and triaminodil were topically administered with vehicle (ethanol/ propylene glycol/ water= 3/ 2/ 5) on clipped dorsal area of female telogen phase C57bl/6. The grown hair weights of topical minoxidil preparation(52.17 ± 4.99mg, $P<0.001$) and topical triaminodil (59.27 ± 10.59mg, $P<0.001$) increased significantly than that of vehicle (14.26 ± 2.51mg). Cosmetic triaminodil compound will be easily used as an effective vasodilator for anti-hair loss cosmetics or quasi-drugs.

P-187

Importance of Reversible and Environmental Factors in Hair Loss in Developing Countries

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Receding hairlines and the arrival of the bald patch are feared by men and especially women around the globe. Not even the efforts of a few superstars to make baldness fashionable have succeeded in releasing men or women from this inherent terror.Bald women are not socially acceptable at all.

Hair may start to disappear from the temples and the crown of the head at any time. For some men this process starts as early as the later teenage, for most it happens in the later 20's and early 30's. Initially it may just be a little thinning that's noticed. Then, the absence of hair allows more of the scalp to become visible.

Some men are not troubled by this process at all. Others, however, suffer great emotional distress associated with a lack of self-confidence and sometimes depression and even suicidal attempts.

Not every hair follicle has the baldness gene which is why some hair falls out whilst other hair doesn't.

Other causes of hair-loss that are usually reversible include; iron deficiency anaemia especially in middle eastern countries and developing communities around the world,a statistical survey showed 85% of female college students in Isfahan have a ferritin level lower than 50 microg/ml ; hypothyroid state may be first present with hair thinning and increased loss ; fungal scalp infection (Favus in our country in rural -resident adult patients has been detected more than before; some prescribed medicines(Ocps in women in childbearing age is the most common birth control tool especially in resent industrialization and emotional stress in young adults due to financial problems in developing countries and after-war situations. An insight to reversible factors such as diet deficiencies and medications can encourage any hair loss control treatment effectively

P-188

Premature Graying Hair a Common Problem in Iranian Adolescent Students

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Background: Premature graying of scalp hair is exteremly feared by female adolescent people in our country. The hair and its beauty nowadays will be a preoccupation in the youngs .Hair may start to become gray from the temples of the head at any time depending on genetic background. For caucasians,this process may start as early as the early twenties. Most of it though,happens in the later 20's and early 30's. Initially it may not be a cosmetic disaster.As in our culture and even global culture whitemning or graying will be a strong sign for old age, it is hated by the youngs and as a statistical survey shows, causes great emotional distress associated with a lack of self-confidence .

Discussion: A few causes of graying hair are usually reversible which increase its incidence dramatically in recent years, including: iron deficiency anemia, folate and Vit B 12 deficiency especially in middle eastern countries and developing communities around the world, (a statistical survey showed 70% of female high school students in our city, Isfahan, have a ferritin level lower than 45 ng/ml; association with hypothyroid state is to be evaluated.Stress sufferers,near national exams for example show rapid and early manifestation in this regard,some prescribed medicines (anti malarials which are sometimes prescribed for a mild arthralgia, application of cedar leaf on hair during bathing) and crash diets taken for a slim-body (Barbie) fashion in causes protein malnutrition (i.e. methionine and tyrosine low intake).

All can be prohibited by an educational program in high schools.

Conclusion: An insight to reversible factors such as diet deficiencies and medications can encourage any hair graying control treatment effectively

Key words: Premature graying hair ,Iranian adolescent population, environmental factors

P-189

Oral Supplementation With Taurine in the Treatment of Women With Hair Fragility

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The aim of this study was to evaluate the efficacy of oral supplementation with daily Taurine 150 mg + Catechin 75 mg + Zinc 15 mg (Inneov Trico masse) in the treatment of women with fine hair, hair fragility and decreased hair thickness.

Materials and *Methods:* The study involved 20 women patients aged from 20 to 68 years (median age 45) who presented to us with fine hair and decreased hair thickness. These women had to take Inneov Trico masse tablets, twice a day, for 6 months.

Assessment was carried out using standardized global photograph of the scalp and measuring, with videodermoscopic images, hair diameter of a target area.

- Videodermoscopic images were acquired by computerized polarized-light videomicroscopy Dermoscope DDS(r) Dermascope 2.0 Software (for measuring hair diameter)

- The target area was a patch of ten hairs. During the first visit the researcher cut hair of the patch. The hair were collected and exanimate too at month 2, 4 and 6

Results: In 11/12 patients that have terminated the 6-month's study, the evaluation of the average of the hair diameter showed increase (from 0,040 to 0,045 µm). 6 other women have interrupted the study to 4 months, 4 patients showed a good increase of the hair diameter (from 0,040 to 0,043 µm).

Conclusions: Our study suggests that oral supplementation with Taurine in association with Catechin and Zinc may be helpful in the treatment of woman with hair fragility.

This work was sponsored by a grant from Inneov nutricosmetics Italy

P-190

Iron Deficiency and Alopecia

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Objectives: Iron deficiency (ID) is the world's most common nutritional deficiency and is associated with significant morbidity. Alopecia affects women and men of all ages and can have a significant impact on health and quality of life. We reviewed the literature on the relationship between ID and alopecia.

Approach: We used a MEDLINE search from 1965 to 2004 using the subject headings "alopecia" and "iron deficiency." In addition, we reviewed the relevant references that those articles cited. Studies that used human subjects with clinical endpoints were chosen.

Results: Eleven studies matched our criteria. All 11 studies examined females, while 2 examined males. The studies varied widely both in sample sizes and study types. Many suggest that ID may be related to alopecia areata, androgenetic alopecia, telogen effluvium, and diffuse hair loss, while others do not.

Conclusion: There may be a significant relationship between ID and alopecia areata, androgenetic alopecia, telogen effluvium, and diffuse hair loss. If ID is discovered, the cause of ID must be identified. ID can be treated safely with ferrous sulfate. Excessive iron supplementation may cause iron overload and should be avoided, especially in high-risk patients such as those with hereditary hemochromatosis. Patients who do not respond to iron replacement therapy should undergo additional testing to identify other underlying causes of ID.

P-191

finasteride Treatment for Female Pattern Hair Loss: Prospective Pilot Study

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finasteride is among the most effective FDA approved treatment male pattern hair loss. Unfortunately, it did not get the FDA approval for females because of the poor outcomes in the initial studies.

Objectives: To investigate for some of the reasons for poor response to finasteride in females with androgenetic alopecia through: 1, verifying the diagnosis; 2, assessment of serum level of androgens (free testosterone, DHEAS, 17 hydroxy progesterone) and 3, compliance of the patients to treatments.

Methods: the plan is to include 30 females with clinical diagnosis of androgenetic alopecia. Pre treatment measurements of the serum level of free testosterone, DHEAS, 17 hydroxy progesterone, standard photograph for the scalp and four mm biopsy are to be done for all patients. finasteride 1mg should be given for all patients for 24 weeks. Eight weeks post finasteride administration, serum androgen levels to be repeated with finasteride level. the later labs to be repeated after completion of 24 weeks of treatments in addition to photographs. In each patient, bimonthly counting for the given tablets are recorded.

Result: 14 patients have completed the 24 weeks treatment period. All of them were compliant with treatment. Scalp biopsy showed featured of androgenetic alopecia. Four patients showed good response to finasteride and another four were mildy improved. five of the 14 patients did not show any significant improvements and one got worse. Of the good responders, one found to have high androgens. There was no adverse effect in all patients.

Conclusion: Although not yet completed, this pilot study showed 8 of the 14 patients (57%) responded to finasteride. An amendment in the objectives was added to include the assessment of the efficacy of finasteride in female patients. By June 2007, 25 patients are expected to complete the study and we may able to show their outcomes.

P-192

The Role of the Androgen Receptor Gene CAG Repeat Polymorphism in the Development of Postmenopausal Facial Hirsutism and Body Hair Changes

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The human androgen receptor (AR) gene contains a variable number of CAG repeats. Shorter repeat length may result in augmented AR-receptor mediated sensitivity of the hair follicle and has been associated with early male balding1 and hirsutism2. We have assessed the relationship between the CAG polymorphism of the AR receptor gene and the pattern of X-inactivation of the X-chromosome in the development of postmenopausal facial hirsutism and body hair changes.

184 normal postmenopausal female of Northern European origin were examined by a single observer and assigned a facial and body hair score using a modified Ferriman and Gallwey score. Genomic DNA extracted from peripheral blood was analysed for the number of CAG repeats. X-inactivation pattern analysis was carried out by looking at the methylation status of each allele after DNA digestion with HpaII. Spearman rank correlation was used to analyse the relationship between CAG repeat length and facial and body hair scores.

Positive correlation was found between shorted CAG repeat length and facial hirsutism and skewing of X-inactivation toward the shorter allele. This was statistically significant ($p<0.05$) in the older postmenopausal females (age>65). No significant correlation was found with body hair.

These findings support a role for the CAG repeat polymorphism of the AR gene in the development of postmenopausal facial hirsutism. Further evaluation of this genetic predisposition may help identify those most at risk of developing unwanted hair changes and guide management, particularly in norm-androgenic postmenopausal females with facial hirsutism.

P-193

p16ink4a Mediated Premature Senescence of Balding Dermal Papilla Cells

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DP cells derived from frontal (balding) human scalp hair follicles (BDPC) have been used to study Androgenetic (AGA). In this study, we have investigated the growth of human DP cells isolated from balding (BDPC) and non-balding (NBDPC) male scalp. Our data confirmed previous reports that BDPC have much slower growth rates in vitro when compared to NBDPC. However, we observed that the slow growth of BDPC was associated with a large flattened morphology characteristic of senescent fibroblasts and was confirmed by demonstrating expression of senescence-associated beta-galactosidase. Premature senescence was specific to BDPC and not seen in NBDPC. Also, connective tissue sheath (CTS) fibroblasts from balding follicles did not undergo premature senescence indicating that this phenomena was specific to BDPC and not due to unhealthy follicles. The senescence of BDPC was associated with terminal growth arrest as demonstrated by decreased expression of PCNA antigen and increased expression of p16INK4a. BDPC also expressed a range of markers of oxidative stress and DNA damage including HSP27, Super Oxide Dismutase, Catalase and phospho-ATM. These results demonstrate that early onset of senescence in balding DP cells is associated with up-regulation of p16INK4a possibly resulting from oxidative stress and DNA damage. Moreover, we show this is a specific characteristic of BDPC and is not seen in CTS fibroblasts from balding follicles or NBDPC. These data identify novel mechanisms that may be responsible for aspects of AGA and may be associated with induction of TGF-b by DHT in BDPC and role of TGF-b in oxidative stress.

P-194

Comparison of the Efficacy and Safety of Topical Minoxidil and Alfatradiol in the Treatment of Androgenetic Alopecia in Women

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Two drugs which are approved for the treatment of androgenetic alopecia in women in Germany were compared with regard to their influence on hair growth.

Patients were randomised to group I (n = 52) using 2% minoxidil solution twice daily for 12 months or to group II (n = 51) using 0,025% alfatradiol solution once daily for 6 months and were then switched to 2% minoxidil solution for months 7-12. Changes in hair growth parameters were determined using TrichoScan.

Topical treatment with 2% minoxidil solution for 6 months resulted in a significant increase of cumulative hair thickness ($p < 0.0001$) and absolute hair density ($p \leq 0.0025$), whereas these parameters of hair growth remained nearly unchanged after 6 months of treatment with alfatradiol solution. Evaluation of the same parameters from month 7 to month 12 demonstrated that 12 months minoxidil treatment resulted in an increasing stabilisation (group I). After the Alfatradiol/Minoxidil switch in group II a significant increase in cumulative hair thickness and absolute hair density could be achieved. The results obtained almost equalled those achieved in group I with continuous minoxidil treatment. Both study medication were tolerated very well.

Treatment with minoxidil can induce an increase in hair density and hair thickness, whereas treatment with alfatradiol results in deceleration or stabilisation of hair loss.

P-195

finasteride Efficacy in Male Pattern Baldness in Iranian Men

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Background: Androgenetic alopecia (AGA) is one of the most common causes of hair loss in genetically predisposed men and women. We studied the therapeutic efficacy and safety of oral finasteride in male patients with AGA.

Materials and *Methods:* A total of 120 male AGA patients, 19-55 years of age, were enrolled in the study for a period of 12 months. Oral finasteride, 1mg/day, was started and the drug efficacy was assessed on the basis of pre- and post-treatment clinical photographs, trichogram, and hair pull test by the investigators. Routine biochemical investigations and a questionnaire related to sexual disturbances were carried out to assess the safety profile of the drug at each follow-up visit every 2 months.

Results: Improvement in hair growth was observed by comparing the paired pre- and post-treatment global photographs ($p < 0.05$), hair pull test evaluation ($p < 0.001$) and increase in anagen- telogen hair ratio ($p < 0.001$) with the trichogram, as early as 4 months of finasteride therapy with maximum benefit in the middle of scalp followed by vertex and frontal areas. No significant side effect related to the drug was observed except for a little decrease in libido in 2 men.

Conclusion: It is concluded that oral finasteride is a relatively safe, well tolerated and efficacious drug for AGA in males.

Key words: finasteride, Male pattern Baldness.

P-196

Trichodynia Is a Distinguishing Symptom of Telogen Effluvium

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Objectives: The prevalence of trichodynia is controversial. Controversy may stem from the diagnostic confusion between androgenetic alopecia (AGA), chronic telogen effluvium (CTE) and their association (AGA+CTE).

Approach: With the aid of the modified wash test (WT) (1), we surveyed10 men and 85 women complaining of hair loss. After 5-day-abstention from shampooing, they soaped and rinsed the hair in a basin and collected all hair remaining in a gauze covering the basin bottom. Hair were counted and divided into <3 cm hair (vellus hair) and into >3 cm hair. Patients with <100 total hair and >10% vellus hair were diagnosed as having AGA; those with >100 hair and <10% vellus hair were diagnosed as having CTE; those with >100 hair and >10% vellus hair as having AGA+TE and patients with >100 hair and <10% vellus hair as having CTE in remission.

Results: Trichodynia was reported by 22 patients: 17 had CTE, 2 AGA and 3 CTE+AGA. None has CTE in remission. The prevalence (51%) of trichodynia in patients with CTE and CTE+AGA was statistically highly significant ($c^2 = 20.077$, $p < 0.001$).

Conclusion: Trichodynia is almost exclusive of patients with CTE as it affects about one half of the them and may be a marker of activity of an inflammatory peripilar process.

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P-197

Variability in the Androgen Receptor Gene: Strong Association With Androgenetic Alopecia, Functional Implications and Indication For Positive Selection

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Androgenetic alopecia (AGA, male pattern baldness) is the most common form of hair loss. Its pathogenesis is androgen dependent, and genetic predisposition is the major requirement for the phenotype. We have recently demonstrated that genetic variability in the androgen receptor gene (AR) is the cardinal prerequisite for the development of early-onset AGA, with an etiological fraction estimated at 0.46. The investigation of a large number of genetic variants covering the AR locus suggests that a polyglycine encoding GGN repeat in exon one is a plausible candidate for conferring the functional effect. The polyglycine tract is located in the transactivating domain of the androgen receptor protein (AR), suggesting an effect of repeat length on receptor function. We compared the functional characteristics of the two most common alleles (23 and 24 repeats) and two extreme alleles (10 and 27 repeats) in a reporter gene assay in HeLa cells. Our data provide evidence of functional differences between the two most common alleles of the AR GGN repeat. The AR haplotype with the highest frequency (0.45) in the German population, which confers risk to AGA, seems to be evolutionarily recent, as indicated by the low sequence identity with the ancestral haplotype and larger extent of haplotype homozygosity. This implies that a variant at the AR locus may have experienced recent positive selection that led to an increase in frequency of the AGA susceptibility allele in the European population.

P-198

Quantitative Analysis of the Effect of finasteride in Korean Androgenic Alopecia Patient

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Objectives: finasteride (FNS) has been widely used to treat androgenetic alopecia (AGA) in males. Most precise data to evaluating the effect of FNS was phototrichogram, but there has been relatively lack of data in Asian people. We tried to observe the effect of FNS in Korean AGA patients by using phototrichogram.

Approach: Thirty two patients with AGA were enrolled in this study. All the patients were taken phototrichogram (Folliscope, Lead M Co., Korea) before and 6 months after treatment with oral FNS (Propecia, MSD Korea, Korea) 1mg/day. We measured hair density and hair diameter only without clipping of hairs, because of the cosmetic problems.

Results: The average densities of hairs in AGA patients (104.4±26.2 /cm^2) were significantly increased after 6 months treatment with FNS (120.8±25.0 /cm^2, $p<0.01$). The average diameters of hairs (60.8±13.8 mm) were also significantly increased after 6 months (68.5±14.7 mm, $p<0.01$).

Conclusions: We could find FNS is also effective in Asian AGA patients.

P-199

Efficacy of Adenosine on a Female Pattern Hair Loss

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Background: Adenosine up-regulates vascular endothelial growth factor and fibroblast growth factor-7 in cultured hair dermal papilla cells. We previously showed that in Japanese men, adenosine improved androgenetic alopecia due to thickening of thin hair generated by hair follicle miniaturization.

Approach: To investigate efficacy of adenosine against hair loss in women.

Approach: Thirty Japanese women with a female pattern hair loss were recruited in a double blind, randomized, placebo-controlled study. Volunteers topically used either 0.75% adenosine lotion or placebo lotion twice daily for 12 months. Data were obtained at 0, 6 and 12 months. Efficacy was evaluated by assessing global scalp coverage by dermatologists, and from a phototrichogram.

Results: After 12 months of human trial, it was shown that adenosine was significantly superior to placebo on global improvement from direct assessments by dermatologists and photograph based assessment by investigators. By phototrichogram results, adenosine lotion could show significant improvement based on the change of hair growing speed and change of thick hair rate compared to placebo. Adenosine also showed significant improvement by self-assessment results. No side effect was encountered during the trial.

Conclusions: Adenosine improved hair loss in Japanese women by stimulating hair growth and increasing thick hair. Adenosine is useful for treatments of androgenetic alopecia in men and a female pattern hair loss in women.

P-200

Interaction of Androgen Receptor With Wnt Signaling Axis in Dermal Papilla Cells

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Objective: Wnt and androgen are known to positively and negatively affect mammalian hair growth. We hypothesized that androgen reduces hair growth through the interaction with Wnt signaling system. The purpose of this study is to investigate the effect of androgen on Wnt signaling in dermal papilla cells (DPCs).

Approach: The effect of androgen and Wnt3a on keratinocytes (KCs) proliferation was measured using co-culture system of DPCs and KCs. Molecular mechanism of interaction of androgen and Wnt signals in DPCs was examined by analyzing the expression, intracellular localization and activities of androgen receptor (AR) and down-stream molecules of Wnt signaling. We also studied the expression level of TGF-beta in DPCs by real-time PCR analysis.

Results: Wnt3a stimulated the growth of KCs when co-cultured with DPCs. Wnt3a-dependent growth of KCs was suppressed by androgen in male-derived DPCs (MDPCs) co-culture, but not in female derived DPCs co-culture. Androgen treatment suppressed Wnt-mediated transcription and promoted the expression of TGF-beta in MDPCs. While both of male- and female-derived DPCs expressed AR, the expression level and the degree of nuclear translocation of AR were higher in MDPCs.

Conclusion: These results strongly suggest that the inhibitory action of androgen on KC proliferation in the co-culture is mediated through the suppression of Wnt signaling as well as TGF-beta production by AR in MDPCs.

P-202

Female Pattern Hair Loss Commonly Affects Sides and Back of Scalp

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Hair thinning in female pattern hair loss (FPHL) is typically most pronounced over the top and front of the scalp. However, some women show a more widespread distribution of scalp hair loss with involvement of the sides and a back of the scalp. In this study we have evaluated the frequency of hair thinning in different regions of the scalp in a cohort of women with FPHL

We studied 67 women with FPHL (grades 2-5 on the Sinclair scale). Using a method described by Olsen (J Am Acad Dermatol, 48;253-62; 2003) the scalp was divided into 9 regions (frontal, mid-scalp, vertex, temporal x2, lateral x2, occipital x2) and hair density was assessed in each region using a 7-point visual analogue scale).

Low hair density was most pronounced in the frontal region of the scalp, closely followed by mid-scalp and vertex. Thinning in the temporal regions was also common (70%) although none of the subjects showed deep recession of the frontal hair line. 49% of women were judged to have significant hair thinning affecting the sides of the scalp and 22% showed thinning in the occipital regions.

This study confirms the clinical impression that, unlike male balding, FPHL in women often affects the sides and back of the scalp as well as the top and frontal regions. This has implications for management of FPHL, particularly for surgical treatment, and raises further questions about the identity of the (patho)biology in pattern hair loss in men and women.

P-203

Androgenetic Alopecia: Concordance of Hair Loss in Twin Pairs

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Androgenetic alopecia is a common disorder that affects both men and women, but its mode of inheritance has been a contested topic. Our objective was to measure and compare hair loss in monozygotic and dizygotic twins and to determine concordance rates between pairs. In fraternal twins, expected concordance is 50% for a monogenetic simple Mendelian transmission and less than 50% for a polygenetic trait; 100% concordance is expected for monozygotic twins. Recruitment of twins took place at the 2004 National Twinsday Festival in Twinsburg, Ohio. Twins filled out hair questionnaires to determine demographics and exclusion criteria. Each participant had stereotactic frontal/vertex/occipital scalp photographs(Canfield Scientific). Buccal swabs were collected for zygosity testing and were perfomed by AnaGen Technologies, Inc. The photographs were evaluated in a blind manner by one of the investigators(VHP) for degree of alopecia and concordance/discordance amongst twin pairs. A total of 44 twin pairs were enrolled, 16 were excluded from the study. Of the 28 twin pairs evaluated, 2 of the 4 dizygotic twins were discordant(50%) and 3 of the 24 monozygotic twins were discordant(11%). This preliminary data shows an unexpected discordance rate of 11% amongst the monozygotic twin pairs suggesting that environment may have a greater influence on androgenetic alopecia than previously recognized. Ongoing enrollment of twins in the study will allow for larger sample size and improved power to further evaluate the inheritance pattern of androgenetic alopecia.

P-204

A Multicenter, Randomized, Placebo-Controlled Double-Blind Clinical Trial of a Novel Formulation of 5% Topical Minoxidil Foam vs. Placebo in the Treatment of Androgenetic Alopecia in Men

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Although 5% topical minoxidil solution is safe and effective, a vehicle that does not contain propylene glycol and is more aesthetically pleasing to the consumer, would be a distinct advantage to consumers for use in androgenetic alopecia (AGA).

Objective: To assess the efficacy and safety of 5% topical minoxidil when formulated in a new foam vehicle (TMF) for men with AGA.

Method: Two-phase study:

- Sixteen week double-blind placebo-controlled phase to evaluate the efficacy and safety of the 5% TMF. This phase was conducted on 352 men ages 20-49 with patterns IIIv, IV or V Hamilton Norwood with the primary efficacy endpoints of change between Baseline and Week 16 target area hair counts (TAHC) and Week 16 subject assessment of change in hair loss condition from Baseline.
- Open-label extension phase to collect 52 weeks of safety data with 5% TMF. One hundred forty-three subjects continued on this phase of the study. Safety was monitored by taking intercurrent history, vital signs and scalp irritation assessment by both investigator and subject.

Results:

- Statistically significant increase at Week 16 compared to Baseline in TAHC with the 5% TMF group (170.8 to 190.8 hairs) compared to placebo (168.9 to 174.4) ($p<0.0001$).
- Statistically significant subjective assessment of hair loss condition ($p<0.0001$) on 5% TMF (70.6% noted increased hair growth, including 47.8% moderate or marked hair growth) compared to placebo (42.4% noted increased hair growth, including 21.5% moderate or marked hair growth).
- No significant safety concerns were raised and the 5% TMF was well tolerated over a one year use period.

Conclusions: The 5% topical minoxidil product, formulated without propylene glycol and in a foam vehicle, is a safe and effective treatment for men with AGA.

P-205

A Clinical Study of Androgenetic Alopecia (2004 – 2006)

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Objective: The purpose of this study was to evaluate the family history, and clinical status of patients with androgenetic alopecia.

Approaches: 789 patients with androgenetic alopecia were assessed at the Alopecia Clinic, Department of Dermatology, College of Medicine, ChungAng University Hospital over a 3 year period from 2004 to 2006

Results: 1) Men (520 patients) are affected 1.9 times more than are women (269 patients). Most of them are twenties (male 223; 42.8%, female 85; 31.5%). 1.9:1.0. 2) In the 520 male patients, Norwood class IIIv was dominant (161 patients; 30.9%). In the 269 female patients, Ludwig class I was superior (218 patients; 81%). 3) 395 patitents (75.9%) of 520 male patients and 198 (73.6%) of 269 female patients had a family history. 4) The most common accompanying disorder was seborrheic dermatitis (male 407; 78.2%, female 155; 57.6%). And others include atopic dermatitis, hypertension, thyroid disease, etc. 5) Serum testosterone level were increased in 92 (17.6%) of 520 male patients and 36 (13.3%) of 269 female patients.

Conclusion: Most of these results are compatible with our previous study carried out in 2004. But, female andogenetic alopecia patients are nowadays increasing in number.

P-206

Men with Kennedy's Disease Have a Reduced Risk of Androgenetic Alopecia

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Background: Spinal and Bulbar Muscular Atrophy or Kennedy's disease (KD) is an X-linked recessive neuro-degenerative disease caused by a functional abnormality of the androgen receptor gene on chromosomal locus Xq11-q12. Expansion of a polymorphic tandem CAG repeat in the first exon is correlated with age of onset and disease severity. Androgenetic Alopecia (AGA) is a polygenic trait also associated with functional polymorphism of the androgen receptor gene. We sought to investigate whether partial loss of function in the androgen receptor gene associated with CAG polymorphism reduces the risk of androgenetic alopecia in affected men.

Methods: Members of the Kennedy disease patient support group were invited to participate in an online survey to determine the age related prevalence of AGA among men affected by KD. Data from 113 male respondents with Kennedy's Disease was compared to data from 332 white males of European descent in Maryborough, Australia.

Results: The mean AGA score for men with KD was 1.64, (95% confidence interval 1.41 – 1.87). The mean score for men in Maryborough was 2.82, (95% CI 2.71 – 2.93). Treating AGA score as a continuous variable we found age to be a highly significantly related to AGA score in men from Maryborough ($p < 0.001$) but not among men affected by KD ($p = 0.90$).

Conclusion: Men with KD have a reduced risk of AGA, possibly due to a functional alteration in the androgen receptor gene.

P-207

Female Pattern Hair Loss In Twins

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Background: Twin studies have demonstrated male pattern hair loss (MPHL) has a hereditability of around 80%, indicating that around 80% of the total variance in MPHL could be attributes to additive genetic effects. The heritability of female pattern hair loss (FPHL) is not known, nor is the hereditability of dandruff or greying of hair.

Objectives: To investigate the heritability of FPHL through twin concordance.

Methods: A pilot study was conducted among 100 twin pairs. All completed questionaires prior to attending scalp examination. Subsequently questionnaires were mailed to 1000 female twin pairs (2000 females), aged between 21 and 75. Twins recorded their own hair thickness and that of their sister as well as presence or history of dandruff, grey hair and cancer.

Results: 412 (=824 QN) questionnaires (response rate 41.2%) were returned, of which 249 were monozygotic (N=498) and 163 were dizygotic (N=326) twin pairs. Heritability for FPHL in the pilot study was 0.75. In the main study hereditability was ~0.69 in self-scored hair thickness and ~0.86 in twin rating hair-thickness.

Conclusion: There is a strong heritability for female pattern hair loss, under both conditions of self-rating of hair thickness, and twin rating of hair thickness. Additive genetic effects play a major role in the development of FPHL.

P-208

Uncommon Tropical Hair Disorders

Sundaram, Murugusundram; Yesudian, Patrick; Skin Hair & Nail Clinic, Chennai, India

Uncommon scalp disorders like pityriasis amiantacea and plica polonica are frequently seen in southern parts of India. We present ten such cases of cosmetic significance.

Many female patients and few male patients of ages varying from 20 to 50 presented with matting of hair and thick white scales adhered to the hair to our clinic. All were asymptomatic except for occassional itching. All were concerned about the unpleasent appearance of the matted hair.

Hair examination was done in all the cases to find out the pesence of parasitic infestations, fungal infections and casts. Scalp biopsy was done in a few unresponsive cases to rule out psoriasis. A detailed history was taken to reveal the hair grooming habits.

No cause was found in most of the cases. Majority of them showed pityrosporum folliculitis. One had psriasis. Two had parasites and fungus. Many of them responded to kartyol shampoo. We advise tonsuring of hair in a few. Psoriasis was treated with coal tar shampoo and topical steroids.

These disorders pose a significant cosmetic problem. They are mainly due to the tropical weather and humidity coupled with infrequent and inadequate hair cleaning habits. In certain parts of south India these are due to relgious practices among the head priests who grow long hair.

P-209

Peculiar Forms of Pressure Alopecia

Sundaram, Murugusundram; Yesudian, Patrick; Skin Hair & Nail Clinic, Chennai, India

Alopecia occurring at sites of constant pressure is common. We present a few peculiar rare forms of pressure alopecia.

Occipital pressure alopecia is very common in infants in south India because if the habit of sleeping on the floor. Pony tail alopecia common in female children is not very uncommon in the male children of south india because hair is grown lengthy in male children also till it is offered to God as a religeous custom. A form of pressure alopecia is common in male sikh children because if the tight hair style forced by the the sikh religeous custom. Pressure alopecia is also a common place affair in hindu priests who grow long hair and tie tightly a tuft if hair. Spectacle frame alopecia is common in young adults because of the tight spectacles frames worn in order to prevent the spectacles falling due to the slippery sweat common in the humid tropical weather. Hair pieces now being commonly used give raise to pressure alopecia due to the clips. Oil massage of the scalp which is very popular in various parts of south India advocates vigorous rubbing of hot oil over the scalp causing pressure alopecia sometimes irreversible.

These peculiar forms of pressure alopecia are unique and common in south India. This paper is to emphasize the cultural, social geographical, environmental and religeous influenzes in studying clinical hair disorders.

P-210

Posterior Parting: a Necessary Photo Control For Female Pattern Hair Loss Diagnosis and Evaluation

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Objectives: Evaluate "posterior parting" besides the anterior parting width as a complementary and effective method for Female Pattern Hair Loss (FPHL) diagnosis and documentation.

Approach: Dr. Elise Olsen has described the "frontal parting" as an effective photographic control for patients with FPHL. It is a useful technique, and we also consider the evaluation of the posterior parting for scalp documentation, helping with the differential diagnosis of chronic telogen effluvium and diffuse hair loss. In a photo studio, with a professional digital camera, we proceed the standard photos – frontal, both diagonal and top view, plus the frontal parting, with the patient forehead rested over a cephalo-static device. With a regular comb and clips we expose the posterior midline from top to bottom to perform the "posterior parting" photo.

Results: The main advantage of anterior parting is to estimate the amount of hair thinning and loss of density, which are not specific of FPHL. Comparing frontal to posterior parting we can: determinate the extension of hair thinning and realize if the process is more diffuse or localized (providing an idea of the original hair density). Medical treatment options for FPHL are limited and hair restoration surgery should be considered as a complement to hair treatments.

Posterior parting is an extremely valuable technique, allowing an estimative of donor area density (occipital) and its viability for performing a hair restoration.

Conclusion: Posterior parting photo control is an effective method not only for FPHL evaluation and diagnosis, but also helps estimating the donor area density for a possible hair restoration surgery.

P-211

Retrospective Study Into the Effect of finasteride on Hair Thickness in Male and Female Patients With Androgenetic Alopecia

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Between 2003 and 2006 over 2000 patients consulted the trichologists of a specialized Dutch clinic. finasteride was prescribed to men and women, diagnosed with androgenetic alopecia. Prescription of finasteride to women was restricted to Post-menopausal women and women who stated in writing that they were not pregnant at the time of prescription and would not become pregnant during the treatment. Individuals took 1,25 mg of finasteride daily and compliance was monitored by a count of the prescribed medication. At basline and at one and two years after baseline, reproducible images of the head and hair were made. In addition, detailed images of four predelection sites for androgenetic alopecia were analyzed for hair density and thickness. The effect measure for finasteride treatment consisted of the thin-to-thick (TT) ratios of four sites at the scalp. To determine a TT-ratio, the sum of the thickness of the three thinnest hairs was divided by that of the three thickest hairs.

876 compliant subjects were remeasured after one year, and 364 subject were measured two years after baseline. The overall TT-ratio's in all subjects at baseline for four sites at the midline (front, center, vertex and rear) was 0.25 (SD 0.05). In both the male and female subjects the TT-ratio was the same (0.25; SD 0.05). One year after baseline, the overall TT-ratio was 0.34 (SD 0.07). The ratios for male and female subjects were both 0.34 (SD 0.07). Two years after baseline, the overall TT-ratio was 0.37 (SD 0.07), whereas both ratio's for male and female subjects were 0.37 as well (SD 0.08).The TT-ratio's of male and female subjects, both one and two years after baseline, were not statistically significantly different (Student t-test; $P<0.01$).

The results of this study indicate that finasteride is effective in establishing thicker hair in men and women.

P-212

Estimation of finasteride Sensitivity of Male Pattern Baldness Patients By Determination of Triplet Repeat Number in Androgen Receptor Gene and Hormone/Cytokine in Serum

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Objectives: finasteride is effective on male pattern baldness (MPB) although there is a variation in the efficacy of this drug among the MPB patients. To know any factor, which correlates with the effectiveness of finasteride, the polymorphism of androgen receptor (AR) gene and serum levels of certain hormones and cytokines were analyzed.

Approach: After PCR of blood cell DNA, number of triplet repeats (CAG+GGC) in the first exon of AR gene was determined. Testosterone, dihydrotestosterone, IGF-1 and TGFb-1 were determined by immunological assays before and one month after the drug treatment. Symptoms, typed by photographic method before and 6 months after the drug treatment, were compared.

Results: When the number of the triplet repeats was plotted against the degree of symptom improvement after treatment, a broad correlation between these variables was observed. The smaller the repeat number, the higher the improvement. finasteride was more effective on the improvement of patient group with smaller repeat number in AR gene@($\leq$40) than that with larger one ($\geq$41). There was a unique tendency in initial level of hormone and cytokine in the smaller repeat number group. Furthermore, change in these factors after treatment with finasteride for one month was also characteristic. On the other hand, no such inclination was observed in larger repeat number group, who were poor responder to finasteride.

Conclusion: Effect of finasteride after a long-term (6M) treatment on individual patient is able to be estimated by determinations of AR gene polymorphism and survey of hormone/cytokine levels within a short-term (1M).

P-213

The Estrogen Receptor Beta Gene, ESR2, in Female Pattern Hair Loss

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Objectives: Female pattern hair loss (FPHL) is a complex polygenic trait with an unproven relationship with androgens. The genes involved in the pathogenesis of FPHL remain unknown, but are likely to include genes related to the androgen and estrogen pathways. The ESR2 gene is located on chromosome 14q22-24 and codes for the estrogen receptor beta (ER-b). Estrogens play a vital role in non-reproductive tissues in both sexes and are able to modify androgen metabolism in hair follicles. In contrast to ER-a, ER-b is the predominant subtype within the outer root sheath and epithelial matrix, making it likely that the ESR2 gene directly modulates the hair growth cycle. This study aims to evaluate the relationship between ESR2 gene variants and FPHL.

Approach: Allele and genotype frequencies of tag single nucleotide polymorphisms (tag SNPs) in the ESR2 gene were compared between 150 cases with FPHL (stage 3 or greater on the midline clinical grading scale), and 90 controls (aged >50 years with no hair loss conditions), using c^2-tests. Tag SNPs were chosen using the HapMap database, and are representative variants in a region of linkage disequilibrium, whereby their examination would be sufficient to capture the genotypic information of all known SNPs in that region.

Results: Three ESR2 tag SNPs that collectively capture 33 SNPs in the gene have been analysed and there were no significant differences in allele or genotype frequency between cases and controls ($p>0.1$).

Conclusion: By essentially examining 33 SNPs located in the ESR2 gene region, we have been unable to identify genetic association between ESR2 and FPHL. However, the association of this gene with FPHL cannot yet be discounted. We are currently analyzing the remaining tag SNPs necessary to capture all known SNPs in the gene region, and are recruiting an additional 275 cases and 400 controls through the Melbourne Collaborative Cohort Study to increase statistical power of this study.

P-214

Comparison of Microscopic Images of Animal Vibrissae Hair Shaft Using Hard X-Ray Microscopy

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Objectives: Recently, it was introduced that microscope using highly coherent, bright third generation x-ray could be an alternative way to visualized the ultrastructure of material. The hard x-ray from the third generation synchrotron light source has a higher energy with better penetration and there is no needs to sample preparation so it is more suitable for the biological samples(ex. hair) without processing artifacts or damage to samples.

Approach: We firstly investigated the ultrastructure of some mammalian vibrissae hair shafts, including dog, cat, rabbit, rat, mouse, and hamster with hard X-ray microscopy in Pohang Accelerator laboratory.

Results: Three distinct structures (medulla, cortex, and cuticular layer) of vibrissae hair shaft were clearly distinguished in all species except cat. We also could find that the detailed characters of each sample were different. Among them, the most distinct characteristics is the medullar structures.

Conclusion: We firstly visualize the integrated internal structures of various vibrissae hair shaft with this new technique.

P-215

A Rare Family Case of Moniletrix

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Moniletrix is a rare hair disease generally inherited with an autosomal dominant fashion.

Walter Smith in Dublin first described the disease in 1879 as "rare nodose condition of the hair." Successively, Radcliff Cocker named the disease moniletrix to define a clinical condition characterized by extreme fragility of the hair which appeared rosary beads shaped.

Hair shaft is beaded and shows elliptic nodes with a diameter ranging from 0,7mm to 1,0mm, separated by narrower internodes.

Hair easily breaks and is not able to achieve a normal length.

The Authors present a case of a family composed of six members. Four of them were affected with the rare disease. In particular, they reported the striking healing obtained by treating the youngest daughter with griseofulvin.

P-216

Hard x-Ray Microscope; New Investigative Tool For the Hair Morphology

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Objectives: Better visualization of morphologic details of hair fiber has great importance in the fields of cosmeceuticals, clinical diagnostics, and so on. Conventional methods to investigate hair morphology including light or electron microscope have limitations in terms of limited resolution and laborious sample processing.

Approach: Hard x-ray microscope uses bright, coherent and highly collimated x-ray from the 3rd generation synchrotron as a light source. X-ray from the synchrotron was attenuated by hair fiber and converted to visual light at the scintillator. To visualize hair fiber more clearly, phase contrast lens was applied. Resolution power was about 90nm. Sample hairs obtained from various races and body sites were just mounted without any processings.

Results: Images revealed natural characteristics of hair fibers. Detailed structure of cuticle, cortex and medulla was clearly visualized. Several overlapped cuticle, vertically oriented macrofibrils of the cortex was distinguished. Medulla showed amorphous granular structures.

Conclusion: Hard x-ray microscope is useful tool to investigate detailed natural morphologic characteristics of hair fiber.

P-217

Ultrastructure of Fine Merino Wool

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Merino wool is a fine high-curl fibre that is often used as a model system for understanding the behaviour of other mammalian fibres such as human hair. The structural elements of a single wool fibre that define its mechanical properties occur across a wide spatial scale. Both large-scale features, for example the distribution of multiple cells of different types, and small-scale features, for example the arrangement of intermediate filaments, are implicated in defining the wool fibre's structural integrity. We have constructed a series of scale illustrations at the whole-fibre, cellular and sub cellular scales for Merino wool which summarise the results of our recently completed survey of Merino wool ultrastructure, the most comprehensive to date.

P-218

Comparison of Hair Shaft Damages By Different Spectrums of Ultraviolet Light

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Objectives: Among the various causes of extrinsic hair damages, exposure to sunlight, especially ultraviolet light is inescapable in daily life. Interests about photoaging in skin have been increasing for many decades, but studies and concerns about the effects of ultraviolet light to hair have been emerging recently. Macroscopically, hairs exposed to ultraviolet light tend to be dry, course and stiff, and usually lose their strength, color and luster. In this study, we investigated the patterns of microscopic and chemical changes of photo-damaged hairs after irradiating different spectrums of ultraviolet light.

Approach: To observe the patterns of changes caused by different spectrums of ultraviolet light, scanning and transmission electron-microscopy, and protein analysis method to detect soluble hair protein were employed.

Results: Structural changes such as hair cuticle damages were induced mainly after UVB irradiation, while hair soluble protein changes were induced mainly after UVA irradiation. UVB and narrow UVB showed similar results.

Conclusion: Different spectrums of ultraviolet light may cause different patterns of damage to hair shaft.

P-219

The Form of Hair Follicle Determines the Shape of Hair

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Objective: In order to investigate the effects of the form of hair follicle on the decision on the shape of hair shaft we analyzed the correlation between the shape of hair shaft and those of hair follicle by grafting the isolated hair follicles from newborn rat vibrissa onto the back skin of severe combined immunodeficient (SCID) mouse.

Approach: The shape of regenerated hairs was observed. Some hairs were plucked to examine the shapes of the hair in the next hair cycle. HE staining was also proceeded to study the shape of hair follicles after regeneration.

Results: Almost all grafted hairs were regenerated on the back of SCID mice. About sixty percent of regenerated hairs showed straight shape and the rest of hairs became bent even though only straight hair follicles were grafted. Plucked hairs were discovered to keep the same hair shape. HE staining of regenerated hair follicles demonstrated that straight hair shape was derived from straight hair follicle and curved bulb region resulted in wavy hair shape. In addition, kinky hair shape was found to have remarkable bent hair follicle in total.

Conclusion: Taken together, these findings strongly suggest that changes of degree in bending hair follicles result in various shapes of hair in proportion, indicating a prominent correlation between the shape of hair shafts of those of hair follicles.

P-220

Implanted Hair Follicle Stem Cells Facilitate the Repair of Severed Peripheral Nerves and the Spinal Cord

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The hair follicle bulge area is an abundant, easily accessible source of actively growing, pluripotent adult stem cells. The fluorescent protein GFP was used to follow the follicle stem cell's fate. The pluripotent hair follicle stem cells are positive for the stem cell markers CD34 and nestin but are negative for the keratinocyte marker keratin 15, suggesting their relatively undifferentiated state. The hair follicle stem cells can differentiate into neurons, glia, keratinocytes, smooth muscle cells, and melanocytes in vitro. In vivo, the hair follicle stem cells greatly enhance the rate of nerve regeneration and the restoration of nerve function. After transplantation in the severed nerve in mice, the hair follicle cells transdifferentiate largely into Schwann cells, which are known to support neuron regrowth. Function of the rejoined sciatic nerve was measured by contraction of the gastrocnemius muscle upon electrical stimulation. After transplantion of GFP-expressing hair follicle stem cells between the severed thoracic region of the spinal cord of mice, the hair follicle stem cells also differentiated into Schwann cells and joined the severed spinal cord. The rejoined spinal cord improved hind-limb locomotor performance. Thus, hair follicle stem cells provide an effective accessible, autologous source of stem cells for treatment of peripheral nerve and spinal cord injury.

P-221

Towards Potential Markers For the Human Hair Follicle Stem Cell Niches

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Regeneration of wounded skin has been attributed to hair follicle stem cells (HFSC). To utilize HFSC as a source for the generation of human autologous skin transplants, explicit characterization of these cell populations and their particular niches is desperately required. The actual approach therefore aims in the definition of potential markers for the multipotent epithelial cell population of the human HF in correlation to complementary precursor cells of mesenchymal origin.

For this purpose, skin biopsies obtained from excess of surgeries were processed to cryo-sections with longitudinally orientated HF and stained by immunofluorescence.

Cytokeratin 15, recently identified as one preferential marker of the human epithelial HF stem cell region, was co-visualized with Vimentin, a marker for mesenchymal derived fibroblasts. Cytokeratin 15 immunoreactivity (IR) was expressed in keratinocytes of the distal and central outer root sheath (ORS) including the bulge region, adjacent to isolated Vimentin IR fibroblasts of the connective tissue sheath. In addition, isolated fibroblasts of the upper proximal HF as well as clusters of fibroblasts in the lower bulb and the HF dermal papilla were Vimentin IR.

Tenascin C and further candidate marker Collagen IV, showed IR along the peripheral connected tissue, demonstrating their usefulness in demarcating stem cell compartments. Other tested markers such as Desmin and Collagen XVIII did not show designated IR expression.

These results suggest a crosstalk between epithelial and mesenchymal precursor cells and demonstrate an increasing significance in defining the HF stem cell niches by simultaneous co-visualization techniques.

P-222

Immunohistological Demarcation of the Human Hair Follicle Bulge Region: Indications of Immune Privilege, and Expression of Potential Stem Cell-Niche Elements

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This immunohistological study aimed at obtaining evidence on whether or not the bulge region of the outer root sheath (ORS) of normal human anagen hair follicles is likely to show relative immune privilege (IP), and at examining the usefulness of selected antigens as markers for the human

bulge region, its stem cells and/or its niche characteristics *in situ*.

MHC class Ia and class II antigen expression was relatively downregulated in the human bulge, compared to the more distally located ORS. Instead, immunreactivity for CD200 receptors and locally generated potent immunsuppressants like TGFb1 and aMSH were upregulated in the bulge.

Immunoreactivity for keratin15, keratin19, tenascinC, fibronectin, fibrillin2 and the transcription factor Lhx2 was found to be upregulated in the human bulge. In contrast, b1integrin, a6integrin, nidogen and LTBP1, showed no increased immunreactivity here. For connexin43 and CD34 no bulge immunreactivity was seen, while connexin43 was prominently expressed in the stratum spinosum of the epidermis and the ORS of the distal part of the HF and CD34 in the outermost layer of the ORS beyond the bulge. Consistent with previous reports, these two antigens therefore, may be exploited as useful negative human bulge markers *in situ*.

In summary, the bulge may indeed represent an additional area of relative IP in human skin (though to a lesser extent than the anagen hair bulb). The therapeutic restoration and protection of this bulge IP may be a sensible strategy in cicatricial alopecia management. These IP markers are welcome additions to a defined panel of useful positive and negative markers that help to demarcate the human bulge region and its niche characteristics in situ.

P-223

Inner Root Sheath Morphology in the Histology of Trichotillomania

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Trichotillomania is a condition typified by self-manipulation of hair, usually of the scalp. This results in localized or diffuse alopecia producing a clinical picture characterized by broken hairs of varying lengths or absent hairs. Histologic clues to trichotillomania that may be present to varying degrees include completely or partially avulsed or torn-away hairs, perifollicular hemorrhage, twisted follicles, pigment casts, trichomalacia, overlying lichen simplex chronicus, and increased catagen and telogen follicles. Herein we describe another histologic clue to the diagnosis of trichotillomania. Normally the inner root sheath (IRS) is a round or oval shape, but in the context of torn-away hairs (shafts that are ripped from the follicle, leaving the inner and outer root sheaths behind), the inner root sheath collapses inward, assuming geometric configurations that include in decreasing frequency: [1] linear (flattened), [2] triangular, [3] round, and less likely a [5] square shape. The force of the dermis and outer root sheath pressing on the IRS produce these shapes, since the IRS lacks support internally after the hair shaft is removed by the patient. The probability of finding a particular shape is determined by the stability of the configuration, with linear (flattened) being the most stable (and therefore the most prevalent), followed by triangular, then round, and finally a square morphology. Observation of these geometric IRS configurations is highly suggestive of trichotillomania and is a useful histologic clue to the diagnosis.

P-224

Aging of Hair I: Hair Properties and Structure

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The effects of aging on hair thinning and on hair graying are well known, but the change of other hair properties and microstructure with age has, so far, not been clarified. Therefore, we have systematically investigated the change in hair properties and hair microstructure as a function of age.

230 panelists of Japanese women aged from 10 to 70 years old were randomly selected. Hair luster and hair bounce were evaluated by both hair stylists and hair researchers. Around 100 hair fibers were sampled from each panelist to analyze the shape, physical properties and microstructure of hair.

We have found that lustrous hair is frequent in young women but not in older women. The shape of lustrous hairs was relatively straight and fibers were well aligned, while the shape of lusterless hairs was often curved and fiber alignment was disordered. The mean curl radius of hair also decreased with age. These results suggest that the increase in curved hair with age causes the decrease in hair luster. Furthermore, the microstructure of hair was investigated by synchrotron microbeam X-ray. Higher structural inhomogeneity was found in the curved hair.

In addition, it was confirmed that hair bounce (bending stress of the hair fiber) decreases after 40 years of age. Although the bending stress depends on both hair thickness and elasticity, it was found that only hair thickness decreases with age while the hair elasticity does not decrease.

P-225

The Quality of Life Implications of Androgenetic Alopecia and the Importance of Helping Patients Deal with its Psychological Effects

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Androgenetic alopecia often affects an individual's, physical attractiveness, body image, and general psychological state. In particular, it can cause anxiety, depression, psychosocial problems, personality disorders, and an inability to cope.

To help quantify how specific quality of life (QoL) issues impact patients experiencing hair loss, a questionnaire, called the Kingsley Alopecia Profile (KAP) was produced. The KAP, a valid and reliable measure, was developed following interviews with participants suffering from androgenetic alopecia and after evaluating the literature and seeking expert views.

This study showed that hair loss sufferers had increased anxiety and depression, and reduced self-esteem and social interaction. Younger and/or single patients were more impacted. The clinical picture of the condition did not correlate with QoL effects. Furthermore, the results of groups with hair loss who were not concerned (called "hair loss contented") compared favorably with groups with no hair loss ("normals"). The results of groups without hair loss who believed they had the condition ("hair dysmorphic") were similar to patients with hair loss who were concerned about their condition ("motivated").

It is important to help patients deal with psychological issues as part of an overall treatment strategy for hair loss. If time is a limiting factor, it is advisable to either have trained staff to counsel and advise a patient, or to use a practitioner that specializes in this field. It is also important to help the patient be pro-active with relevant treatment, lifestyle, and cosmetic advice.

P-226

Control of Oxidative Hair Fiber Damage from Permanent Colorant Products

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Background: Use of permanent hair colorants is widespread and allows the consumer to either change their natural hair color and/or cover gray. However, one of the main trade-offs of coloring is the fiber damage that is sometimes seen over multiple uses.

We have discovered that the uncontrolled production of free radicals during the coloring process can be a significant contributor to fiber damage. We will share two key strategies that we have utilised to control the reactivity of the radical species.

Controlling Radical Reactivity during Hair Coloring

Two key reactive species in the colouring process have been shown to be responsible for the majority of the fiber damage. These two species are the perhydroxyl anion (HOO-) and the hydroxyl radical (HO*). The hydroxyl radical is formed from the activation of hydrogen peroxide by a transition metal capable of readily undergoing 1-electron oxidation such as copper.

(1) Chelation

We have demonstrated that the addition of a chelant to the hair colourant such as N,N'-ethylenediamine disuccinic acid (EDDS) can significantly reduce the formation of the hydroxyl radical. We have also shown that the choice of chelant is crucial. In particular, the chelant must have a high selectivity for complexing to copper, especially in relation to other metals such as calcium that are commonly found in hair.

(2) Radical Scavengers

The purpose of a radical scavenger is to trap a highly reactive radical rapidly converting it into a less reactive species. We have demonstrated the effectiveness of adding a range of radical scavengers to hair colorants. We have shown that when formulated to provide equivalent levels of bleaching (dL), the addition of a radical scavenger such as glycine, glutamine, glucosamine, arginine or proline can reduce the fiber damage significantly.

P-227

Childhood Trichotill Versus Trichotillomania

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The diagnosis of trichotillomania (TTM) is reserved for persons who recurrently pull out their hair, experience increased tension before and gratification after the act, and have significant occupational or social impairment as a result. We propose the term trichotill (TT) to describe children with a hair-pulling habit not associated with psychological impairment and which resolves with time. We report our observations of 13 children with hair-pulling behavior. Eight children had TT whereby hair-pulling resolved in seven cases without psychiatric intervention. Precipitating factors were noted in 4 of the 8 cases. TT is a habit disorder which does not fulfill diagnostic criteria for TTM.

P-228

Aging of Hair III: The Anti-Aging Efficacy of Eucalyptus Extract

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Older women have the complaint of hair bounce reduction because of hair thinning with age. For the complaint, there are many types of hair growth enhancer, which increases hair density and/or hair thickness. On the other hand, older women also have the complaint of decrease in hair luster with age. We have found that curved hair increases with age and the curved hair causes the hair luster decrease. Furthermore, we have found that Eucalyptus extract can improve not only hair bounce but also hair luster of older women. In this study, we studied the mechanism of Eucalyptus extract on hair properties.

A scalp lotion containing 3% of Eucalyptus extract was prepared. The lotion was applied to the scalp of female panelists (aged 40-60), who had the complaint of hair bounce and hair luster. The lotion was applied twice per day for three to twelve months. Hair fibers were sampled before and after the application and used for the analyses of hair properties. Hair luster and bounce were evaluated by hair stylists. Hair curvature and hair elasticity were measured.

We have confirmed that the hair luster and bounce of older women are improved by the application of Eucalyptus extract. It was found that hair curvature is reduced and hair elasticity is raised by the application. These results suggest that Eucalyptus extract has an anti-aging efficacy in terms of hair shape and bounce.

P-229

The Role of Laminin-332 and -511 in the Regulation of Hair Cycling and Chemotherapy-Induced Alopecia Models

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Objectives: In order to assess the role of laminins on the hair cycle and on the induction of chemotherapy-induced alopecia.

Approach: The expressions of laminin-332 and -511 and their binding partners, a6b4 and a3b1 integrins, were assessed by real time RT-PCR, immunoblot, in situ hybridization and immunohistochemistry using murine hair cycling model and cyclophosphamide-induced alopecia model. Moreover, functional aspects were assessed using recombinant laminin-332 and -511 on human hair culture.

Results: (1) In the anagen, laminin-332 and a6b4 integrin were once upregulated in anagen I-III, then became downregulated and diminished after anagen VI in the BM around hair bulbs. In contrast, laminin-511 and a3b1 integrin became constantly upregulated throughout each anagen stages. The functional study suggested that laminin-511 had a positive effect on the hair growth and laminin-322 suppressed such an effect.

(2) In the catagen, the expressions of laminin-332 and a6b4 integrin were gradually recovered in the BM around hair bulbs. Intriguingly, strong expressions were observed in the epithelial strand (ES) and connective tissue sheath (CTS).

(3) In the dystrophic catagen caused by cyclophosphamide, the expressions of laminin-332 and a6b4 integrin were strikingly upregulated in the BM around hair bulbs. They were more marked in the ES and CTS. In contrast, the expressions of laminin-511 and a3b1 integrin in the BM around hair follicles were gradually depressed.

Conclusion: The laminin-511 and a3b1 integrin positively regulate hair cycle. The laminin-332-a6b4 integrin suppressed it. Rapid disruption of such interactions possibly induces dystrophic catagen caused by the chemotherapy.

P-230

North American Hair Research Society Mentorship Program

Hickman, Janet G.;[1] Duvic, Madeleine;[2] McMichael, Amy;[3] Elston, Dirk;[4] Roberts, Janet L.;[5] Sundberg, John P.;[6]

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Grants for up to $3000 each are available annually to scientists in training, dermatology or dermatopathology residents, fellows, or junior faculty to enable study with an expert in hair research or clinical hair disorders. Either the mentor or the applicant must be a member of the North American Hair Research Society. The goal of this program is to foster the careers of young physicians, veterinarians, and basic scientists interested in hair biology or hair disorders by acquiring additional research or clinical skills, thereby furthering their careers as leaders in the field of hair research. The focus of the program is on establishing mentoring relationships. In the 5 years of the program, we have funded over 30 individual mentorship grants for

recipients to work on projects ranging from learning specific clinical procedures to mapping mutated genes responsible for a variety of hair diseases. The short applications are due 31 December each year with funding beginning in mid-February.

P-231

Aging of Hair II: Gene Expression Pattern of Vascular Endothelial Growth Factor in Hair Root and Relation to Hair Properties

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Loss of hair elasticity by aging is one of the serious troubles in men and women. It is assumed that this physical change of the hair shaft is caused by metabolic changes in hair root cells. Then, we investigated into the factors which closely related to the hair elasticity.

Sixty-six healthy female volunteers aged between 11 and 70 years participated in this study. Approximately fifty anagen hairs were plucked from each participant's scalp. Transcriptional profiles in hair root cells of the plucked hair were examined by DNA microarray and quantitative RT-PCR. Hair properties such as diameter, elasticity and luster were also measured from the plucked hair shaft. Next, female volunteers with elastic hair (n=15) and with no or less elastic hair (n=15) were recruited, and the transcriptional profiles in hair root cells and the hair properties were examined similarly.

From among the multiple gene expressions found in hair root cells, we focused on vascular endothelial growth factor (VEGF). The VEGF gene expression level in hair root cells was the highest in teens, and thereafter declined with age. In addition, the VEGF gene expression level in participants with elastic hair was significantly higher than that in participants with no or less elastic hair. A positive correlation was determined between the amount of VEGF mRNA and the bending elasticity value of the hair shaft.

These results suggest that the VEGF in hair root cells might be a factor contributing to the maintenance of the hair elasticity.

P-232

Comparison of Hair Follicle Forming Properties Between Dermal Papilla and Dermal Sheath

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Objectives: Epithelium-mesenchymal interaction is essential component in the formation of hair follicles. The mesenchymal components, both dermal papilla(DP) and dermal sheath(DS), showed hair follicle forming, in other word, trichogenic properties but their optimal features were not revealed yet. So we investigate the differences of the trichogenic property of the DP and DS.

Approach: DP, upper and lower DS cells were dissected by surgically or enzymatically from the wild type vibrissae. Cells from the culture with low passage or fresh dissected were implanted to mouse ear or foot pad. The implantation depth was controlled by upper, mid or lower dermis. Reconstituted hair follicles were compared and histologic observation was performed.

Result: Cells from the DP and lower DS, when implanted in the upper dermis, showed similar trichogenic properties but upper DS did not induce hair follicles in any depth. Surgically dissected DP or DS cells were more apt to hair formation than enzymatically digested one but the results were not consistent. Fresh dissected DP or lower DS also showed hair follicle formation but yield was low.

Conclusion: Trichogenic property of mesenchymal cells, DP and lower DS, is well maintained when these cells were surgically dissected, cultured with low passage, and implanted in upper dermis.

P-233

Differential Expressions of Biomarkers in Human Interfollicular Keratinocytes In Situ and In Vitro

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Introduction: Mammalian interfollicular keratinocytes (IFKC) have differentiation capacity into hair follicles and a unique expression profile of cell surface markers and cytokeratins, which are distinct from epidermal keratinocytes (EKC). To characterize human IFKC, we investigated and compared expression patterns of biomarkers between IFKC and EKC, both in situ and in vitro.

Materials and Methods: Immunohistochemistry (IHC) of human scalp skin and hair follicles for biomarkers previously reported as specific for IFKC was performed. Expressions of the biomarkers in freshly-isolated and cultured IFKC and EKC were also investigated by FACS analysis and immunocytochemistry (ICC).

Results: Keratin 15 (K15) was expressed in the bulge area in IHC. CD34 was expressed in the lower area, which includes the sub-bulge area and outer root sheath (ORS). CD271 (p75 neurotrophin receptor) was expressed in the lower ORS that was negative for K15. All of them were expressed only in the outermost layer adhering to

the basement membrane. ICC of cultured IFKC revealed transitory expression of K15 in passage 1, but not of CD34 and CD271. ICC of cultured EKC showed similar expression pattern to cultured IFKC. However, FACS analysis showed prolonged expressions of K15 and CD34 up to passage 3 in cultured IFKC, contrary to cultured EKC.

Discussion and Conclusion: The expression profile of biomarkers was distinct between IFKC and EKC in situ, but less distinct when both populations were cultured in vitro. In addition, expression pattern of CD200 will be presented.

P-234

Comparative Analysis of Hair Conditions By Phototrichogram in Scalp Hair Shedding Subjects

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Objectives: Although many patients complain about their hair shedding, It is very difficult to evaluate the hair loss state objectively. The aim of the current study was to investigate the findings of phototrichogram (PT) of affected areas in hair loss with various kinds of hair shedding and to compare them with those of healthy subjects.

Approach: On a subjective global and clinical basis, 212 hair shedding subjects were classified in 88 male pattern androgenic alopecia (MPAA), 75 female pattern hair loss (FPHL), 49 chronic telogen effluvium (CTE). To compare the state of normal conditions, twenty controls not having hair loss and any other systemic disease were included. Eleven scalp sites such as right, center, left of frontal, vertical, occipital areas and right, left temporal areas were evaluated with phototrichogram.

Results: Base phototrichogram profiles of hair shedding subjects showed significantly decreased hair density and thickness than controls, respectively. Among hair shedding groups, CTE showed most low hair density. In MPAA group, hair thickness had a significant decreased in frontal and vertical areas compared to other groups and occipital areas. Also FPHL showed similar changes of hair density and thickness but the quantity of that was not great as MPAA.

Conclusion: We concluded that phototrichogram is very useful instrument to clarify the hair shedding state. Especially when subjects complain of non specific shedding without obvious hair loss, basic phototrichogram data is very informative to differentiate the exact hair loss state.

P-235

Trichogram and Immuno-Histological Analysis of the Scalp in Psoriasis

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Objectives: Is there alopecia in psoriasis? How is the inflammatory infiltrate of the scalp composed comparing uninvolved and lesional skin?

Approach: 10 patients with psoriasis were examined. Trichograms were evaluated with regard to telogen and anagen hair and compared with 20 healthy individuals. Biopsies from uninvolved and lesional scalp psoriasis were examined. Epidermal thickness was determined microscopically. In cryostat sections immunocompetent cells in epidermis and dermis were stained with monoclonal antibodies (mAb) against CD3, CD4, CD8, CD45RO, 4KB5, HLA-DR, CD1a, CD11a, CD54, CD25.

Results: With regard to trichograms, no difference in the number of anagen and telogen hairs could be found between healthy subjects, uninvolved and lesional psoriatic skin lesional hair shafts tended to be thinner and more brittle. Alopecia could not be established. Comparing epidermal thickness, lesional epidermis was about 3 times thicker than that from uninvolved sites. In the epidermal infiltrate, CD4/CD8 Ratio in Lesional Psoriatic Scalp was 0.4

Conclusion: Hair growth is largely unaffected in psoriasis. The infiltrate of the psoriatic scalp lesions is more intense in the dermis. The findings suggest an immunological stimulation utilizing predominantly CD8+ cells in psoriatic scalp.

P-236

Comparing Phototrichoscopy – an Imaging Device – to Scalp Histopathology for the Diagnosis of Female Pattern Hair Loss

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Objectives: Evaluation of the effectiveness of phototrichoscopy for the diagnosis of female pattern hair loss (FPHL) compared to scalp histopathology.

Approach: It's difficult to determinate if lack of hair volume and density is consequent to an initial FPHL or connected to other problems, such as chronic or acute telogen effluvium causes. In many cases scalp biopsy is a necessary step in establishing diagnosis. Since an invasive exam

is not always tolerated for patients, we studied the use of phototrichoscopy – which is faster, cheaper and non traumatic – as a substitute to scalp histopathology since 2000 with an excellent accuracy.

Before taking the scalp biopsy, we performed a phototrichoscopy – using an adapted dermatoscope attached to the frontal lens of a digital camera at the same place that would be further compared to the biopsy.

Results: For patients with initial FPHL, phototrichoscopy and scalp histopathology were both able to show hair miniaturization.

In general, a pure CTE shows the same pattern in the frontal and occipital areas, presenting a normal biopsy and phototrichoscopy, while FPHL presents progressive miniaturization, usually severe in the frontal area and decreasing in severity towards the occipital area. Both methods presented good accuracy and correlation for presence of miniaturized follicles.

The diagnosis criteria adopted for FPHL histopathology has a problem: the "empty" follicles are not counted and so the anagen/telogen rate is affected, limiting the diagnosis criteria; with phototrichoscopy it is possible to virtually scan the entire scalp, avoiding this deficiency.

Conclusion: Compared to scalp histopathology, phototrichoscopy as a method of evaluation of FPHL is useful for diagnosis in initial stages and allows the differentiation between FPHL and CTE. As an advantage to scalp histopathology, the phototrichoscopy avoids "false negative" results and is useful for advanced FPHL with "empty" follicles.

P-237

Hair Loss Diagnosis Tool or ALGORITHM

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While there are number of reasons of hair loss, the proposed idea is that etiology depends on range of symptoms that can give clear understanding about the way what patient is suffering from and how s/he has to be investigated and treated accordingly.

Primary purpose of this job was to collect knowledge accumulated in the 10 years of trichological practice and made them useful broadly and easily in use of patient themselves and in dermatology or general practitioners practices as well.

Approach was to develop easily usable PPT file with more as 300 slides that include (1) general information about hair loss, (2) methods that can be used for diagnostic purposes, (3) questionnaire that allows getting to diagnosis of hair loss type or problem of skin, (4) short explanations that are given for every type of hair loss in conformity with current understanding of the problem. There are a lot of pictures included in the tool. For easy traveling through the tool a huge amount of hyperlinks are inserted, that gives possibility to find necessary information fast.

There is separate section for hair loss for children and teens, and additional section with drawings for hair shaft problems.

Constant research to find new ways to increase understanding about hair diseases and help trichological patients is a challenge. This algorithm is developed to make exact hair loss diagnosis, so physicians and patients are offered reliable product that performs as claimed. Further management of specific trichological disease after diagnostic is in hand of physician.

P-238

Examination of the in Vitro Follicle Closing Technique Using Caffeine, an OECD Test Substance For Skin Absorption Tests

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Objectives: Recent investigations presented during the workshop "Follicular Penetration and Targeting" at the 4th International Meeting of Hair Research Societies in Berlin, 2004 confirmed preliminary indications that the hair follicles also play an important role in skin penetration.

This study presents the first in vitro data on the follicular closing technique using static Franz diffusion cells.

The feasibility of implementing a technique developed in vivo after modification for in vitro experiments is shown.

Approach: The in vitro experiments were conducted in compliance with the OECD Testguideline 428 with static Franz diffusion cells. Two formulations using caffeine, the reference substance recommended in this guideline, were applied for comparison. The follicle closing technique was implemented on different areas of human full-thickness skin (female breast and abdomen).

Results: Results were obtained from control samples with open follicles as well as from test samples with closed follicles. A separation into the different skin layers provided information about the variant amount of caffeine after the 24 hour skin absorption test. All samples were analyzed with HPLC. The samples with open follicles demonstrated a more efficient penetration route for caffeine in full-thickness skin.

Conclusion: The results in this study suggest that the follicle closing technique can be implemented for in vitro skin absorption tests. In addition, the follicular as well as the intercellular penetration pathways were used by caffeine to overcome the skin barrier. New in vitro information regarding caffeine, as one of the OECD reference substances, was found.

P-239

Effects of Cyanacrylate Skin Surface Stripping on the Percutaneous Penetration of 200 nm Polystyrol Particles in Human Skin Explants

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We recently demonstrated, that the penetration depth of topically applied particles in human skin explants depends on the size of the particles. Pre-treatment with cyanacrylate skin surface stripping (CSSS) improves the penetration of microparticles >750nm into human scalp terminal hair follicles. Skin cell targeting with functional nanoparticles below this size range, however, is a newly emerging concept in hair and skin therapy, and detailed knowledge on their penetration profile is crucial for future developments in this field. The aim of this study was to investigate the effects of CSSS on the penetration profile of solid 200nm particles in human vellus hair-bearing skin. 1471 skin sections including 698 hair follicles were analyzed microscopically in skin explants from three different donors. We found a 47% increase of nanoparticle-positive hair follicles in skin samples pretreated with 2 CSSS (65% positive hair follicles in treated with 2 CSSS vs. 33.35% hair follicles in untreated skin). The overall penetration depth along the follicular duct was also increased with 18% vs. 7% of hair follicles showing penetration deep into the hair follicle infundibulum and 16% vs. 5% showing penetration further down to deeper compartments. Consistent with previous studies, we found that the penetration depth into intermediate hair follicles was deeper than in vellus hair follicles.

In summary, CSSS increased the follicular penetration of topically applied 200nm nanoparticles in human skin explants. Its relevance for clinical applications will be a key question to be addressed in future pilot studies on human volunteers.

P-240

A New Three-dimensional Hair Follicle Model To Investigate Epidermal-Mesenchymal Interactions In-Vitro

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The human hair follicle is a highly specialized skin appendage continuously renewing itself to produce the visible hair shaft. However, the complex biological mechanisms controlling hair growth, fibre formation and pigmentation as well as the reasons for biological alterations such as hair loss or loss of pigmentation are still poorly understood. In order to evaluate principles of epidermal-mesenchymal interactions it is essential to provide a test system as close to nature as possible. The cell-cell communication of various, highly specialized cell types in this complex microcosm as well as the spatial cellular orientation determines the system's response to endocrinal and environmental stimuli. Therefore we established a novel three-dimensional in vitro model, which allows different cell types to interact concordantly to the in-vivo situation. In this hair follicle model we integrated reconstructed dermal papillae into a pseudo dermis with dermal fibroblasts, covered by a layer of ORS keratinocytes. To show the high similarity between the reconstructed model and native human hair follicles we demonstrate the expression of characteristic follicular markers such as versican and the effect of a well-recognized potent stimulator of human hair growth in vivo, Cyclosporin A.

With this test system we set up a powerful tool to study hair follicle metabolism and epidermal-mesenchymal interactions. In combination with advanced molecular techniques it enables a deeper insight into the molecular events within the hair follicle and discloses new possibilities to elucidate the mechanisms controlling the "living" part of the hair.

P-241

Robotic Expansion of Cells for Use in Tissue Engineering of Hair

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In order for hair multiplication by follicular cell implantation to be a practical proposition, the number of cells returned to the patient must be significantly greater than the number harvested. Moreover, for this process to be commercially successful and cover the high costs of cell culture, a manufacturing facility must have the capacity to expand

the cells of many patients simultaneously. For safety reasons, each culture must be maintained in total isolation from the others to ensure that no cross-contamination can occur between the various patients' cells. This has been a long standing issue with organisations involved in tissue engineering, especially those involved in autologous therapies. Three basic approaches have been employed to deal with the issues, and all three will be presented and their advantages and disadvantages discussed. Intercytex is following a strategy based on a robotic cell culture system that was previously developed and proven in the area of high throughput screening. This system uses standard tissue culture vessels and dispensers to feed and passage mammalian cells although they are net yet approved by regulators for use in tissue engineering. The adoption of a robotic system will impact research decisions made early in the development of a cell culture process so that the process will be made "robot friendly". The system will be presented and the route to regulatory approval discussed.

P-242

Large Scale Manufacturing of Cell Therapy For Hair Regeneration

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The implantation of follicular cells, expanded in culture, to induce potentially unlimited amounts of hair has been suggested ever since the work of Oliver and Jahoda. Companies are currently in Phase I and II studies to test preparations of cells for hair induction. It seems from the long history of research in this area that processes will soon be developed to successfully achieve this long sought after treatment. But how will these processes be translated into an industry whereby thousands or hundreds of thousands of people could be treated annually? Tissue Engineering is an industry now in its third decade and over a quarter of a million people have been treated by a variety of cultured cell constructs. The early pioneers developed processes often by trial and error, and only now is "best practise" beginning to emerge. The lessons learned in the past are crucial to the current development of tissue engineered hair and are the subject of this presentation. All tissue engineering processes can be broken down into six stages: "Tissue Procurement; "Cell Isolation"; "Cell Expansion"; "Assembly"; "Shipping"; and "Application". Regulations, industry standards, and developments in other fields are rapidly evolving and influencing each of these stages. The talk will cover these six stages and describe how an industrial process could be developed to meet the commercial needs of large scale follicular cell implantation.

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Proto-Hair Development In Vitro

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Objectives: To develop an in vitro system in which to grow partially formed hair follicles that, when implanted, will continue to develop into fully formed hairs.

Approach: Hair follicle cells were prepared by enzymatic digestion followed by two sequential sievings. Cell aggregates were made and cultured to allow proto-hair development in vitro. Both freshly made and cultured aggregates were implanted onto an immune deficient mouse ear skin to test for mature hair development.

Results: Aggregates made with freshly isolated cells consistently developed hairs after implantation. Aggregates cultured in vitro consistently developed proto-hairs, which are partially formed hair follicles with distinctive morphology. Such in vitro-produced proto-hairs further developed into mature hairs after implantation. Most implants developed hairs that grew out of the skin, while some developed underneath the skin surface but failed to emerge. Histological studies confirmed immature hair structures formed from cell aggregates during cultivation in vitro.

Conclusion:

- We demonstrated that proto-hairs can be produced in vitro from cultured cells.
- We proposed a concept of the immature 'proto-hair' as an option for clinical transplantation.

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A Comparison of Cutaneous Fibroblast Subtypes Reveals That Human Dermal Sheath Fibroblasts Exhibit Preferential Wound-Healing Characteristics, and These Are Modulated By POMC Peptides and CRH

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Although human skin contains several distinct fibroblast subpopulations, clinical evidence indicates improved wound healing in haired body sites – reflecting, possibly, the proportionately greater numbers of dermal sheath (DS) and follicular papilla (DP) fibroblasts in such skin. This in vitro study investigated fully-matched DS, DP and dermal fibroblasts (DF) isolated from five healthy individuals for proliferative, migratory, collagen-producing and contractile

capacity. Proopiomelanocortin (POMC) peptides and corticotropin-releasing hormone (CRH) effects on these parameters were also assessed.

While DF exhibited the greatest baseline proliferation rates and DS exhibited the greatest baseline migration ability, ACTH, a-MSH and CRH all significantly increased both parameters for all cutaneous fibroblasts subtypes. DS cells contracted collagen gels to a significantly greater extent than DF or DP cells, reflecting a higher incidence/expression of a-SMA in DS cells. Under wounded conditions DS cells secreted significantly more collagen than DF cells, though this level was significantly increased for both in the presence of TGF-b1. Importantly, this TGF-b1 effect was antagonised by ACTH, a-MSH and CRH. Similarly, ACTH, a-MSH and CRH raised cAMP levels. b-Endorphin had no effect on any of the above parameters.

Follicular and interfollicular fibroblasts exhibit very different behaviors in vitro, with the greatest wound-healing features exhibited by DS cells. As POMC peptides antagonized TGFb1-induced collagen production in these cells, these peptides may have a role in the treatment of hypertrophic and keloid scars. In conclusion, our data indicates that DS cells are likely to be more effective wound-healing cells than other cutaneous fibroblast subtypes.

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Long-Term Hair Repigmentation Following a Hair Transplant For Frontal Scarring Alopecia

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Hair greying invariably manifests as part of ageing and is considered irreversible. Pigment loss in canities is due to a reduction or absence of actively melanogenic hair follicle melanocytes in grey and white hairs respectively. There is also dysfunctional pigment transfer to cortical keratinocytes as a result of melanocyte degeneration. Amelanotic melanocytes of the mid-to-lower outer root sheath (including the bulge region) are still present in white hairs but incomplete melanocyte stem cell maintenance leads to greying. Repigmentation of grey or white hairs can occur with certain medical conditions, usually as a post inflammatory phenomenon, and as a side effect of some medications. However, most cases of repigmentation are unsustained.

We describe pronounced and long-term repigmentation of white donor hairs in a 57 year old woman who underwent hair transplant surgery for an area of frontal scarring alopecia secondary to a burn from childhood. The repigmented hairs have remained stable at more than two years post transplant. Although repigmentation of hairs is thought to be a post-inflammatory phenomenon or secondary to altered signally in the hair bulb pigmentary apparatus after surgery, the mechanisms behind the long-term upkeep of the repigmentation remain elusive. Further studies focussing on the pathophysiology of the repigmentation mechanisms will advance the understanding of the greying process. Such studies may also provide insights into strategies to reverse hair greying in the future.

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P-246

Donor Site Dominance in Action: Transplanted Hairs Retain Their Original Hair Pigmentation Long-Term

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The concept of 'donor dominance' in hair transplantation refers to autografts which continue to maintain their integrity and characteristics after transplantation to a new site. Such hairs may retain their original texture and rate of growth. Hair transplantation for patients with androgenetic alopecia rely on this concept of donor dominance for a successful and long-lasting result. Recently, the concept of 'recipient dominance' in hair transplantation has been debated. In a study of patterns after hair transplantation to the scalp and eyebrows in patients affected by madarosis, Lee et al found that the greying rate of hairs approximated the recipient site rather than the donor site.

We report on the long-term maintenance of follicular pigmentation in transplanted hairs. We describe two patients affected by both androgenetic alopecia and hair greying in the transplant recipient area. They were given autografts of normally pigmented hair follicles harvested from the occipital area. More than one year post-transplantation, their donor hairs have remained pigmented long-term, despite being implanted in scalp affected by greying. In one patient the pigmented hairs have remained stable for 10 years. As the process of greying usually affects the temporal scalp first, then progresses onto the vertex and occiput later, the maintenance of long-term follicular pigmentation in our patients may be attributable to donor dominance.

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P-247

Staged Hair Transplantation in Cicatricial Alopecia After CO2 Laser-Assisted Scar Tissue Remodeling

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Objective: To evaluate whether the laser-assisted dermal remodeling before follicular unit transplantation in cicatricial alopecia (CA) could improve the vascularity of the recipient bed and to enhance the hair growth of transplanted follicles.

Approach: A high-energy ultrapulse CO2 laser with a 400-mJ pulse set at 100 Hz was used to create round serial 1.0 mm-sized holes about 3-5 mm deep into the skin with a pattern density spacing of 5 mm hole-to-hole distance. Clinical relevance was assessed over 1-month intervals. Retreatment was performed if the sclerotic tissue still remained firm and inelastic and if additional treatment was indicated by clinical examination.

Results: All patients demonstrated fibrotic scar tissue improvement and the production of a pinkish appearance after laser-treatment of 1 or 2 sessions. None of the CO2 laser-treated sites had visible new scarring or showed hypo- or hyper-pigmentation, persistent edema, or infection. In all patients, we achieved acceptable cosmetic results after only one to two FU transplant sessions at a density of 50 to 70 hair follicles/cm^2. Moreover, the grafted hair follicles grew hairs fast comparable to those transplanted in normal recipient areas and well covered the formerly alopecic areas.

Conclusion: Staged hair transplantation after CO2 laser-assisted scar tissue remodeling could be a useful means of achieving cosmetic improvement in cases of CA, and was found to be suitable for Asians who would be more vulnerable to stretch-back scar formation after reduction surgery.

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Hair Restoration Surgery in a Patient with Stabilized Cicatricial Alopecia

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Objectives: We report a case of successful treatment of burnt out cicatricial alopecia with hair restoration surgery.

A 51 year old female patient was referred to our clinic for the evaluation of hair loss in 2001. She first noticed patches of hair loss in 1995. Histopathology confirmed our clinical diagnosis of cicatricial alopecia and was consistent with Pseudopelade of Brocq. We treated the patient with topical Clobetasol twice daily for 2 years. We stopped the topical treatment in 2004. The lesions remained stable.

Approach: Hair restoration surgery was performed in 2005. A total of 1200 follicular units were transplanted into the scarred areas.

Results: The patient showed good hair density and scalp coverage 6 months after the surgery. She discovered a great improvement in her quality of life.

Conclusion: Hair restoration surgery is a treatment option for burnt out cicatricial alopecia. The lesions should be stable without treatment for at least 1 year. The potential of reactivation of the cicatricial hair loss post surgery has to be discussed with the patient in detail.

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Cyclic Dislocation of Hair Follicular Stem Cells and Its Importance in Hair Transplantation

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Background and *Objectives:* Apoptosis is a major biological process in the hair follicle cycling and is controlled by pro- and anti-apoptotic proteins. Because stem cells in general need to be protected from apoptosis, the presence of the apopotosis-suppressing Bcl-2 protein may be used as an indicator of the stem cells population in the hair follicle. Localization of stem cells at the bulge region of the hair follicle has been proven by some recent research. Stem cells have been detected in the area of attachment of arrector pili muscle to the follicle. However, until now there is scanty information about dislocation of stem cells during cyclic development of hair follicles.

Methods: Hair follicles were derived from the occipital area of the patients who underwent the hair transplantation procedure. For immuno-histochemical studies Bcl-2 antibodies(clone124) were used.

Results: The data obtained clearly indicated that stem cells are not only positioned in the are of attachment of arrector pili muscle, but can surround the hair follicles and spread towards distal and proximal parts of the follicle. This phenomenon is especially obvious during the initial stage of anagen, when migration of the stem cells has been noticed along with the downward development of the follicle. Mono-positional localization of stem cells in the bulge area was more characteristic for the telogen phase. To prevent the possibility of the removal of mono-positional stem cells, a special method of hair follicular dissection has been developed. The essence of this method is to avoid inter-follicular dissections at the areas of attachment of arrector pili muscle.

Conclusion: Thus, new information has been obtained about cyclic dislocation of follicular stem cells that allows maximum preservation of those cells during follicular dissection and improves the results of hair transplantation.

P-250

Use of Phototrichoscopy in Female Pattern Hair Loss to Evaluate Donor and Recipient Areas for a Hair Restoration Surgery

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Objectives: Evaluate the use of phototrichoscopy for donor and recipient areas in female pattern hair loss.

Approach: Clinical treatment for FPHL can't reverse severe miniaturization and hair restoration surgery (HRS) is a valuable option. The success of this procedure is related to a correct donor area evaluation. We perform phototrichoscopy since 2000: the best candidates for HRS has localized frontal miniaturization and preserved donor area, while those with diffuse thinning and compromised donor area are not.

Results: The phototrichoscope is a device similar to a dermatoscope attached to a digital camera (Sony W1). After parting the hair a clear alcoholic gel is applied over the contact glass and pressed over the scalp. We document four areas: central frontal area, usually the most compromised (1) fronto-parietal area, moderately affected (2), the lateral occipital area, could be mildly compromised (3) and the central occipital area, usually the fuller area (4). In all areas we evaluate the density and miniaturization.

- **Good candidate:**
  Miniaturization – intense in the central-frontal area, moderate in the fronto-parietal area and absent in the occipital area.
  Density – severe reduction in the central-frontal area, mild reduction in the fronto-parietal area and preserved in the occipital area.
- **Not indicated:**
  Miniaturization – severe in the central-frontal area, intense in the fronto-parietal area and also moderate to intense in the occipital area.
  Density – moderate reduction in the central-frontal area and fronto-parietal area. Moderate reduction in the occipital area.

Conclusion: Good candidates have a great contrast between donor and recipient areas to justify a hair restoration procedure. Phototrichoscopy allows the dermatologists to correct evaluate the entire donor area in reference to miniaturization and density besides helps the surgeon finding a "safe donor area".

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Case Report: Lipedematous Alopecia – a Surgical Outcome

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We report the first case of surgical correction of lipedematous alopecia. Lipedematous scalp is characterized by asymptomatic boggy swelling of the scalp.(1) It has been reported mainly in African-American women. When hair loss is present, this condition is termed lipedematous alopecia. The etiology and natural course are unknown. No effective treatment has been described. Our patient is a 67-year-old woman who presented with a 10-year history of a gradually enlarging boggy swelling with overlying alopecia over the vertex of her scalp that measured 61mm x 35mm. Ultrasound showed thickening of the underlying subcutaneous tissue in this region. Biopsy revealed hyperplasia of subcutaneous tissue and loss of hair follicles. Surgical excision of the alopecia and surrounding swelling was performed and primary closure was achieved with minimal skin tension. There is no evidence of relapse at three months post-operation.

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P-252

A Relationship Between Early Greying and Extent of Male Pattern Baldness?

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Both androgenetic alopecia and loss of hair pigmentation advance gradually with increased age. However, androgenetic alopecia is a predominantly male, androgen-dependent condition, while androgen-independent canites occurs in both sexes. Observations suggest that men with early pigment loss retain scalp hair, but this may be an inaccurate impression due to the greater visibility of white hair.

To determine whether there is any relationship between these processes, the extent of balding and pigment loss was compared between men over 18 who were, or were not, greying before 30. A single observer scored balding extent using the Hamilton scale and pigmentation loss on a scale of 1 to 5 in 364 Thais. A further 216 Europeans completed the same questionnaire assessing their own hair status. Data was analysed in each group separately and combined.

Mean ages at assessment did not differ between men grey before, or after, 30: 26 early Thais 38.7 years, others 39.4; 50 early Europeans 49.4, others 52.8. The extent of both male pattern balding and pigment loss was positively correlated with increasing age whenever canites started. Aging was more strongly correlated with pigment loss. Mean pigment scores were higher with pigment loss before 30; contrastingly, mean Hamilton scores were lower.

These results concur with the age-related nature of both conditions and indicate that early pigment loss remains advanced with age. However, the lower Hamilton scores in early canites opposes predictions if both were solely aging related. Early pigment loss appears inversely related to male pattern alopecia extent.

P-253

Expression of Human Cultured Epidermal Melanocytes in the Reconstructed Mice Hair

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To elucidate the behavior of melanocytes (MCs) in the hair follicles, we have constructed reconstructed mice hair follicles that included xenografted human MCs. These MCs could functionate in the graftings of epidermal and dermal cells derived from albino mice and turned the color of white hairs into gray color. Melanin pigments were observed in the reconstructed epidermis and hair follicles and human MCs were observed around dermal papilla. The increased amounts and tyrosinase activities of MCs increased the darkness of reconstructed hair colors. By ACK2 treatment of pregnant ICR mice, the color of reconstructed hairs increased significantly. For the further studies, we used Wsh/sh mice as donor mice, which lacks both follicular or epidermal melanocytes in their skin. The color of reconstructed hairs also becomes dark significantly. These results strongly suggested that human MCs can functionate effectively in the vacant niches in the ACK2 treated mice and Wsh/sh mice that lacked their endogenous melanocytes. After plucking out all reconstructed hairs, secondary hairs were re-grown in the same area and their colors became lighter compared with the color of the first reconstructed hairs. This result suggested that xenografted melanocytes could not maintained well but partially functionate in the next hair cycles.

P-254

The Reflectance Confocal Microscopy in the Study of Hair Follicle Pigmentary Unit

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The biology of hair bulb shows how close is the hair growth cycle and follicle melanogenesis, and how many different factors contribute to hair aging and canities. Comparing the response of normal hair follicle pigmentary unit during catagen and telogen phase, and the effects of some immunological diseases on the hair bulb and melanogenesis, it is possible to have evidence about the role of apoptosis in premature aging of hair follicle melanocytes. The evidence that aging and pathological stress produce the alteration of the "unit" anagen phase-melanogenesis and therefore the reduction of follicle melanocyte function and decrease in hair production, also provides the evidence that only acting on both the follicle compartments it could be possible to reduce hair graying.

The Reflectance Confocal Microscopy (RCM)is a useful method to study the changes of hair follicle pigmentary unit in vivo in normal, aging and pathological hair, and to evaluate the effects of some active principles on anagen prolongation and melanocyte function. We tested the main expressions of apoptosis in catagen grayng hair,to compare the findings from RCM, and to show if some treatment had any effect to slow grayng hair.

We used RCM in a clinical evaluation on 60 subjects with grayng hair trying to clarify the different pathways of graying, and the effects of topical liposome containing specific active principles on follicle pigmentary unit. At the end of the clinical trial we can conclude that RCM is

an useful device to evaluate the hair follicle pigmentary unit in vivo, and that it is possible to evaluate the efficacy of active principles (5 different actives, used in liposome preparation),showing that 3 of these gave a reduction of grayng hair ($p < 0.01$)in 65 % of subjects treated with active principles, respect no difference in placebo group.

P-255

Breakthroughs in the Characterisation, Location and Tracking of Modifications in Fibrous Proteins – Unravelling the Mystery of Wool Photodegradation

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UV-induced photomodification of proteins has been implicated in a diverse range of deleterious processes including hair damage and skin ageing. In the case of wool, exposure to direct sunlight results in gradual photoyellowing of the fibres, while exposure to sunlight filtered through glass results in photobleaching. The underlying chromophoric species and processes responsible for this degradation have remained a mystery through over forty years of research.

For the first time, yellow chromophore-containing photo-oxidation products have been directly characterised within the proteins of photoyellowed wool fabric utilising ESI-MS/MS. To date, fifteen chromophores have been identified and located within known wool peptide sequences. Eleven tryptophan-derived photo-modifications were characterised, including hydroxytryptophan, kynurenine derivatives, tryptophan diones, carboline derivatives and nitrotryptophan. Four tyrosine-derived modifications have been characterised, namely dopa, topa, dityrosine, and a previously unreported modification consistent with a hydroxylated dityrosine residue. These modified residues were located within a range of wool peptides, but particularly in peptides derived from wool intermediate filament proteins. The range of photo-oxidation products characterised provides direct insight into photochemical pathways leading to protein photodegradation, while supplying experimental evidence in support of current theories as to ROS-derived photomodification mechanisms. These breakthroughs have been extended to the direct tracking of specific marker photomodifications through a range of irradiation and treatment protocols.

P-256

Age-Associated Down-Regulation of Catalase in Human Scalp Hair Follicle Melanocytes

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Although epidermal melanocyte numbers gradually decrease with age, hair graying (canities) is often dramatic, suggesting a different "melanogenetic clock" for these two cutaneous melanocyte subtypes. Currently, canities is thought to result from a combination of reactive oxygen species-associated damage in hair follicle melanocytes (HFM), impaired anti-oxidant status and failure of melanocyte stem cell renewal.

To explore the role of oxidative stress in canities we examined catalase expression in situ and its activity in cultured HFM derived from young and aged donors. Cell survival, catalase expression / activity, and p38 stress kinase expression were examined after exposure to exogenous H2O2.

Results showed that catalase expression in situ was reduced in HFM with advancing age and contrasted with the high expression of this anti-oxidant enzyme in hair follicles from young donors. Catalase expression and activity in vitro was also higher in young donor HFM compared to aged donor cells. By contrast, no age-related change in catalase was observed in matched dermal fibroblasts. Catalase expression / activity were up-regulated after exposure to H2O2 in young, but not, aged donor HFM. This correlated with high cell survival after exposure to this oxidant in young donors. HFM from aged donors expressed higher baseline levels of p38 stress kinase compared with younger donors, and this was further increased after exposure to H2O2.

In summary, an age-dependant decrease in catalase expression / activity in HFM support the view that a reduction in anti-oxidant defence capability may contribute to loss of hair pigmentation with age.

P-257

Photo Damage of Human Hair: Color Changes as a Function of Hair Pigmentation

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It is well known that keratins are damaged by exposure to solar radiation, predominantly by ultraviolet wavelengths. In a previous work (Journal of Photochemistry and Photobiology B: Biology, 74/2-3, 109-117, 2004) we showed that UVA is the main radiation responsible for color changes and that UVB radiation is responsible for the higher protein loss in human hair. In this work we show that the effect of long-term exposure to UV and visible radiations depends on hair pigmentation. Blended virgin blond, red and dark-brown Caucasian hairs were irradiated with a 125 W mercury vapor (full or UVB filtered radiation), in controlled temperature, humidity and radiation dosage conditions. Color data was obtained by reflectance spectrophotometry, using CIEE L (lightness coordinate), a (green-red coordinate) and b (blue-yellow coordinate) measuring system. The following trend is observed for the irradiated hair samples: all hair types become clearer after lamp exposure, quantitatively measured as an increase in L values. On the other hand, changes in the true color parameters (a and b) depend on the hair type and wavelength range. Blond hair turns yellower after full radiation exposure, but not when UVB radiation is filtered. Dark-brown and red hairs turn yellower after both full radiation exposure or UVB filtered radiation exposure. Regarding changes in redness, blond hair turns less red and dark brown turns redder after both full radiation exposure or UVB filtered radiation exposure. Red hair turns redder after full radiation exposure, but not after UVB filtered radiation exposure. Our results show that hair color damages caused by UV and visible light exposure are different for each hair type. Since we have other photo-sensitive components on hair, adding to the melanin chromophores, this behavior is probably related also to the overall hair chemical composition.

P-258

Expression of BMP2, FGF5 and Follistatin mRNA Throughout the Rat Hair Cycle

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A number of candidate molecules have been implicated as key regulators of the hair cycle including Follistatin (FST) and several members of the bone morphogenetic protein (BMP) and fibroblast growth factor (FGF) families. Evidence from FGF-5 mouse knockouts has shown that it may play an important role in the switch from anagen to catagen. TGF-â superfamily members are also involved in follicle initiation and cycling in vitro, as well as interacting with growth factors such as the BMPs.

Objectives: The aim of this investigation was to determine the role, if any, of BMP-2, FGF-5 and FST in the control of the rat hair cycle.

Approach: The expression of BMP-2, FGF-5 and FST mRNA in 40 rat skin samples, taken throughout the hair cycle was quantified using real time PCR employing pre-validated TaqMan(r) assays. All data were normalised against ribosomal 18S RNA. Skin samples were histologically classified into four stages of the hair cycle; early and late anagen and early and late catagen.

Results: Analysis of the data revealed a 6-fold increase in FGF-5 mRNA levels from early to late anagen ($p<0.0001$). BMP-2 mRNA levels were significantly higher in late compared to early catagen ($p=0.006$) and FST showed a gradual increase in expression from early through to late anagen and early catagen, peaking at 1.6-fold increase during late catagen ($p=0.005$).

Conclusion: These results suggest an important role for FGF-5 in the transition from anagen to catagen, and perhaps indicate a concentration dependent effect of BMP-2 and FST for transition into follicle shutdown.

P-259

Requirement of Hair-Follicular Dermal Sheath for Growth of Hair Shaft

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Objectives: The rat dermal papilla (DP) cells in multiple subcultures retain the capacity to induce epidermal cells to differentiate into hair follicles when transplanted to the back skin. However, these hair follicles were not encapsulated with the dermal sheath (DS) and did not develop the hair shaft. We observed that these DP cells induced hairs (the hair follicle with the shaft), when transplanted with DS cells. In the present study, we examined the role of DS cells in the induction of hairs by DP cells.

Approach: Primary EGFP-labeled DS cells were obtained by culturing peribulbar dermal sheath cups of vibrissa follicles of EGFP-transgenic Wistar rats. DP cells from syngeneic wild-type rats were subcultured and labeled with DiI. Hair-inducing ability of each of DP and DS cells,

and of the mixture of both types of cells were examined by transplanting the test cells to the back of immunodeficient nude mice.

Results: DS cells (passage 1, p = 1) and DP cells (p = 60) each alone induced a few hairs and no hairs, respectively. However, the DP and DS cells (mixed cells) frequently induced longer hairs. Histological examinations demonstrated that the DPs of the induced hairs contained DiI-labeled cells. EGFP-positive cells were located at the peribulbar dermal sheath cup of follicles.

Conclusion: These results suggested that the DS formation in hair follicles is important for the growth of hair shafts and that DP cells cooperates with DS cells in hair induction

P-260

Alopecia Mucinosis: Premature Hair Follicle Regression As Evidenced By Increased Catagen Phase Follicles On Horizontally Sectioned Scalp Biopsies

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Two cases of primary, idiopathic alopecia mucinosis were characterized by rapidly progressive hair shedding which resulted in patchy, reversible alopecia. Besides the typical accumulation of mucin in the outer root sheath of hair follicles, the most characteristic finding on transversely sectioned scalp biopsies from our two patients was a greatly elevated catagen-telogen count, composed primarily of follicles in catagen(avg 68% of resting-phase follicles), with the remainder being telogen germinal units. The infundibular portion of follicles in catagen did not show hair shafts in the follicular canal, suggesting loss of the hair shaft prior to telogen. The fact that hairs obtained on gentle hair pull appeared to be dystrophic anagen hairs lends support for an anagen effluvium in primary, idiopathic alopecia mucinosis.

P-261

Hox-Lacz Reporter Gene Mice as Tools For Dissecting Hair Follicle-Specific Transcriptional Control Elements Regulating the Dynamic Patterns of Hox Gene Expression During Hair Follicle Morphogenesis and Cycling

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Objectives: Members of the Hox family of transcriptional regulators are known to play pivotal roles in cutaneous and follicular patterning and cycling. Understanding these functions requires to define the dynamically changing Hox expression patterns during follicle morphogenesis and cycling, and information about transcriptional control mechanisms regulating these complex patterns.

Methods: Starting with Hoxc13, located at the 5' end of the Hoxc cluster, we proceeded in the 3' direction to prepare various Hoxc-lacZ fusion constructs that contained the corresponding Hox promoters and surrounding regulatory sequences. Transgenic mice carrying these constructs were analyzed by X-gal staining of skin at different stages of the hair cycle. Authenticity of specific Hox-lacZ expression patterns with regard to corresponding endogenous gene expression patterns was validated by in situ hybridization analysis. Hair follicle-specific control elements were mapped by deletion analysis in vivo.

Results: This approach revealed novel patterns for several Hoxc genes that were difficult to discern by conventional expression analysis. For example, unlike Hoxc13-lacZ, which was globally expressed in all hair follicles, expression of both Hoxc11- and Hoxc10-lacZ was restricted to follicles in posterior regions and exhibited complex patterns, predominantly in the dermal papilla, the matrix and the cortex. The cortical patterns suggested cyclical activity in anagen follicles as we observed two separate zones of lacZ activity along the proximal-distal axis of differentiation in that compartment. Our deletion analysis indicated that these patterns are regulated by separate and autonomously acting control elements.

Conclusions: Hox-lacZ reporter gene mice are useful tools for (i) defining dynamic changes of Hox expression patterns during the hair cycle at high resolution and with great sensitivity, (ii) monitoring responses of Hox-expressing cells to specific stimuli, (iii) isolation of hair-specific cis-regulatory elements, and (iv) isolation of distinct Hox-expressing cell populations.

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Atrophy of Sebaceous Glands in Two Cases of Pityriasis Amiantacea

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Pityriasis amiantacea is a well-recognized, inflammatory condition manifested by thick, asbestos-like shiny scales on the scalp.

We herein present two cases of pityriasis amiantacea along with newly reported histological findings. Both patients presented with asbestos-like scale of acute onset involving the scalp diffusely. Four millimeter scalp biopsies sent for horizontal sectioning revealed significant atrophy of sebaceous glands. After successful treatment with

fluocinolone acetonide oil, repeat biopsies for horizontal sectioning revealed normal sebaceous gland morphology.

We will focus our discussion on the relationship of the gross findings of thickened scalp scale and the microscopic findings of sebaceous gland pathology.

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Hair Cycle-Dependent Changes of Alkaline Phosphatase Activity in the Mesenchyme and Epithelium in the Hair Bulb of Mouse Vibrissal Follicles

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Alkaline phosphatase (ALP) activity was detected in the bulbar mesenchyme and epithelium in mouse vibrissal follicles. Its localization and strength dramatically changed during the hair cycle. The activity in the dermal papilla (DP) was moderate in very early anagen, reached a maximal level in early anagen, decreased at the proximal region of DP after mid anagen, and was kept at a low level during catagen. The bulbar dermal sheath showed a strong ALP activity only in early anagen. Although most bulbar epithelium did not show ALP activity, germinative epidermal cells that were adjacent to the ALP-negative DP cells became ALP-positive in mid anagen and rearranged in the area surrounding the DP in mid catagen. During catagen, the outermost layer of bulbar epithelium became ALP-positive, which should be follicular epithelial precursors migrating from the bulge. Before the initiation of hair formation, ALP activity in the bulbar epithelium rapidly decreased and that in DP increased instead. These dynamic changes of ALP expression might be related to DP's functions in hair induction, and also to reconstruction of the hair matrix during the hair cycle.

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Role of Insulin-like Growth Factor Binding Protein 5 on Human Hair Shape

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The curliness of the hair shaft is determined by the distributions of ortho- and para-cortical cells, the quality and the quantity of keratin associated proteins, the amount of disulfide bonds between the hair proteins, the activity of transglutaminase and/or other keratinization-related enzymes in hair root, and the shape of the hair follicle itself. Recently, it has been reported that forced transgenic expression of insulin-like growth factor binding protein 5 (IGFBP5) in the hair follicle of Foxn1::dnFgfr2-IIIb transgenic mice caused the reduction in the size of hair medullae and resulted in the bending hair shaft, suggesting that FGF signals specifically regulate the structure of hair shaft medulla via IGFBP5. However little is known about the involvement of IGFBP5 on human hair shape. In this study, we examined the role of IGFBP5 with isolated human kinky and straight hair follicles. Real time quantitative RT-PCR analysis suggested that expression of IGFBP5 was higher in kinky hair follicles than that in straight fair follicles. When immunohistochemical analysis was performed, IGFBP5 was asymmetrically expressed in the inner layer of outer root sheath, not in medulla, in kinky hair follicles while the localization of IGFBP5 was found to be evenly dispersed in straight hair follicles. finally, supplemented human recombinant IGFBP5 in kinky hair follicles organ culture was shown to inhibit hair growth and to significantly augment the degree of hair shaft bending compared to control. Taken together, these findings suggest for the first time that asymmetrical IGFBP5 expression contributes to human hair shape.

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