BIODERMA
CONGRESS REPORTS

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PLENARY LECTURES A

Speakers: Dr. M. Peter Marinkovich, Prof. Anne Dompmartin-Blanchere, and Dr. Sonja Ständer

Report written by Prof. Anna Zalewska-Janowska

Topical gene therapy for RDEB

Dr. M. Peter Marinkovich (Redwood City, United States)

The first plenary lecture was delivered by Dr. M. Peter Marinkovich, representing Redwood City in the USA. The speaker presented the issue of topical gene therapy for recessive dystrophic epidermolysis bullosa (RDEB) in which collagen VII anchoring fibril protein is deficient in the skin. Dr. Marinkovich acquainted the audience with the procedure of collagen VII (C7) engineered epidermal gene therapy (in detail Siprashvili Z et al JAMA 2016;316(17):1808-17). In brief, RDEB skin biopsy is taken for production and expansion of the cells in culture. In general 6 grafts per patient are performed. Patient spends a week in hospital for graft take and subsequent biopsies are taken at intervals and assessments of safety healing follow. Then the speaker presented phase III trial of C7 fibroblast gene therapy. Namely, dermal fibroblasts are harvested from a patient using one set of three 3-4 mm biopsies and cultured in the laboratory. Vector is created using a self-inactivated lentivirus modified to encode COL7A1 gene under the control of a CMV promotor and then the vector is introduced to the fibroblast cell culture and delivers the therapeutic gene to the patient' cells ex vivo and allows for the expression of collagen 7. Subsequently the genetically-corrected fibroblasts are intradermally administered to the patient. In this trial intradermal wound injections of the patient delivered C7 overexpressing autologous fibroblasts. This procedure is based both on ex vivo skin correction when skin is harvested and manufactured in the lab together with viral gene integration and graft production and in vivo graft placement, called beremagene geperpavec (B-VEC), performed under general anaesthesia in operating room within 1 week of hospitalization. Phase 1 and 2 of in vivo topical gene therapy for RDEB is described in detail in Nat Med 2022;28:780-8. The speaker presented beautiful and convincing photographs of the patients skin engrafted with B-VEC at baseline and at 3-months demonstrated effectively healed wounds. This procedure presented in N Engl J Med 2022;387:2211-9 by Guide SV at al. describing phase 3 double-blind, intra-patient randomized placebo-controlled trial evaluating B-VEC efficacy and safety in RDEB. Once weekly treatment was performed until would closure and treatment resumed, when wound closure reopened. No adverse events (AE) lead to therapy discontinuation and the most common AE were pruritus, chills and squamous cell carcinoma (SCC) on the skin - each of which appeared in 3 patients (10%). All 3 SCC appeared at wound sites that did not receive B-VEC or placebo. B-VEC therapy proved long-term efficacy and durability, still after 17 months off therapy the

patients did not require further grafting. Also topical B-VEC therapy of the eye was successfully introduced leading to further breakthrough of RDEB treatment and considerable improvement in visual acuity. The speaker modesty concluded his lecture that still longer follow-up and future, larger studies are required for further and consistent evidence.

Theragnostic approach in vascular malformations

Prof. Anne Dompmartin-Blanchere (Caen, France)

The second plenary lecture was delivered by Prof. Anne Dompmartin-Blanchere from Caen in France on theragnostic approach in vascular malformations. Beautiful clinical pictures of vast diversity of vascular abnormalities were presented to the audience followed by a new classification dividing them into vascular tumor and vascular malformations (https://www.issva.org/classification). The presenter focused on vascular malformations pointing out at clinical variability in the same family and necessity of identification of etiopathogenesis and molecular pathways. Accurate diagnosis is a must and only a few complementary examinations are required such as echo doppler, MRI, arteriography and coagulation tests (D-dimer and fibrinogen). Then, always in an interdisciplinary team (oncologist, translational surgeon, plastic dermatologist, pediatrician, radiologist, hematologist, orthopedist pediatric, surgeon maxillofacial ENT, stomatologist, neurosurgeon, neurologist, vascular surgeon, anesthesiologist, anatomopathologist, pediatric cardiologist, ophthalmologist, physiotherapist all coordinated by physician and nurse team) individualized treatment is elaborated for the patient. Elucidation of the underlying genetic mechanisms has led to better pathophysiological understanding of these lesions and paved the way for the use of targeted therapies such as rapamycine, alpelisib – PIK3CA inhibitor, trametinib – MEK inhibitor, thalidomide – anti VEGF). However, despite the hope of these treatments have generated professionals should be cautious as regards long-safety issues. It is of importance to point out that gene mutations found in endothelial cells with a stable genome are often implicated in cancer but mutations in cancer occur in other cell types with many other somatic mutations whereas vascular abnormalities are benign lesions. We should bare this information in mind.

Brain-skin axis: itch and beyond

Dr. Sonja Ständer (Münster, Germany)

The final lecture of the first plenary session was delivered by Dr. Sonja Stander from Munster in Germany entitled “Brain-skin axis: Itch and beyond”. Currently brain-skin connections are regarded as the hottest topics in dermatology. Brain and skin share ectodermal origin with common molecular factors thus there is a clear ante-natal link between skin and neurodevelopment. As for post-natal link neuroanatomical connection is present and keratinocytes express many receptors found in the brain in many dermatoses (Jameson C et al Mol Psychiatry 2023;28: 108-17). The brain skin-axis is a bidirectional relationship in itchy dermatoses where keratinocytes, endocrine and immune system, nerve fibers, stress hormones, emotion processing are involved. The speaker underlined that itch can be induced in the whole peripheral and central nervous system and that scratching reduces intraepidermal nerve fiber numbers in chronic pruritic diseases but also induces stronger branching pattern in them thus observations that under scratching more or less nerve fibers are observed are both true. Final conclusion of such studies depends on the method used. The speaker also pointed out that scratching in chronic pruritus group was regarded as pleasure and suggested addictive scratching that possibly inducing or contributing to neural hypersensitization. Thus it could be stated that itch leading to scratching alters cutaneous neuroanatomy, induces neuronal hypersensitivity, increases spinal pruritogen receptor expression and activates the reward system. Such situation definitely form addictive scratching. The speaker also beautifully pointed out that brain is very receptive to verbal instructions (VI) and VI may strongly influence outcome expectations. Placebo and nocebo effects may modulate itch (more details in Meeuvis SH at al Neurosci Biobehav Rev 2020;113:325-37). There is also a strong evidence that immune functions can be modulated through behavioral conditioning. A good example of such a situation is when cyclosporine is administered together with a taste stimulus (conditioning). Re-exposure to taste stimulus only significantly

reduces IL-2 levels in PBMCs even after 5 to 11 days after conditioning. Stress activated HPA axis and keratinocytes produce stress hormones e.g. CRH, ACTH (in more details Papa V et al Cells 2023 Jul12;12(14):1828). In conclusion, itch involves many mechanisms in brain-skin axis, brain modulation is an important factor in scratching behavior and itch worsening. Long term duration of itch involves more mechanisms (e.g. activation of HPA axis, immune system, neurogenic skin inflammation). Both pharmacologic and non-pharmacologic (VI) are important in patient management and we should focus on patient psychoeducation and investigate the role of expectations in health and disease. It was underlined that antidepressants improve epidermal barrier function and the theory behind is that stress and endogenous glucocorticoids activate the peripheral HA axis in the skin and thus worsen carrier function. (Choe SJ et al Sci Rep 2028;8:6334). Currently available therapies (antidepressants, opioid modulators, gabapentinoids, biologics, small molecules) demonstrate promising approaches of breaking itch-scratch cycle and inflammation.

MICROBIOME AND SKIN DISEASES

Speakers: Dr. Chris Callewaert, Prof. Brigitte Dréno, Prof. Gregor Borut Jemec, and Prof. Dr. Tilo Biedermann

Report written by Prof. Anna Zalewska-Janowska

Microbiota and skin barrier function

Dr. Chris Callewaert (Gent, Belgium)

The first lecture on **microbiota and skin barrier function** was delivered by Dr. Chris Callewaert from Ghent in Belgium. The presenter is also nicely called in social media Dr. Armpit (https://drarmpit.com/). Congratulations on this nickname!

Human skin is home to around 1 trillion bacteria. Skin microbiome is very important for skin barrier function and has the following roles: microbial, chemical, physical and immunological. Microbial barrier is composed of different microbes and in healthy conditions is diverse and different in different anatomical locations. Skin microbiome produces bacteriocidins, antimicrobial peptides, lantibiotics and virulence factors that either kill or inhibit activity of other bacteria. As regards chemical barrier, skin microbes produce lipases and cleaves sebaceous lipids into free fatty acids. Thus, acid mantle of the skin of around 5.5 pH is formed and human beta defensins are produced. As for physical barrier skin microbiome promotes keratinocytes and produce antioxidants, furthermore skin microbiome enzymes produce ceramides and lower TEWL. As for immune barrier skin microbiome is working hard to preserve homeostasis and not allow for dysbiosis development and exerting anti-inflammatory effect. Now, different microbiota species are used in different diseases or symptoms such as atopic dermatitis, wound healing, rosacea, psoriasis, acne ageing or dandruff. Underarm microbiome is the main reason for body odor (Callewaert *et al.*, Plos One 2013). Higher underarm diversity is more malodorous. Armpit bacterial transplantation is – by definition – the act of transferring the underarm microbiome of a person without body odor (the donor) to the washed armpit of a person suffering from body odor (the recipient) (Callewaert *et al.* Exp Derato 2016; Callewaert *et al.* Comput Struct Biotechnol J 2021). This procedure shifts the microbiome and together with bacteriotherapy shifts the microbiome and improves the underarm odor. Of note, *Staphylococci* in the bacterial spray can replace malodor-associated bacteria and using such a spray can improve underarm odor. During the discussion, Dr. Callewaert also stated that people who eat more fast foods smell worse and due to large bacteria load in the anal region this area renews very well. Of note, we have even more bacteria in the gut tan on the skin.

Microbiome and acne

Prof. Brigitte Dréno (Nantes, France)

The second lecture, on **microbiome and acne**, was presented by **Prof. Brigitte Dreno** entitled. Acne is a barrier deficiency disorder with increased TEWL. Normal skin microbiome controls activation on innate immunity and invasion of any antigen. Alteration of skin barrier induces dysbiosis with activation of innate immunity and penetration of antigens and pathogen bacteria.

In acne dysbiosis is linked with loss of diversity of *C. acnes* phylotypes with a predominance phylotype IA1. Adult acne in women is not associated with a specific type of *C. acnes*. Predominant phylotype of *C. acnes* is the same in adult acne and severe acne than in teenagers. *C. acnes* is not the only bacteria implicated in acne. *C. acnes* inhibits proliferation of *S. epidermidis* and *S. pyogenes* – induces secretion of AMPs by keratinocytes, hydrolyses sebum triglycerides with production of propionic acid. *S. epidermidis* inhibits proliferation of *C. acnes* – favors the fermentation of glycerol, naturally produced in the skin and induces production of succinic acid. Bacteria interact between each other by producing AMPs. The question was put forward whether *S. epidermidis* is another player in acne?

In severe acne no difference between *C. acnes* and *S. epidermidis* was observed however abundance of some less reported Gram-negative bacteria and fungi was noted. Metabolomic studies revealed changes in functions of skin microbiome namely modifications in the metabolism of key substances such as lipids, vitamins and amino-acids which can significantly disturb host skin status.

Bacterial microbiome in comedo exhibited stronger metabolic activity including production of enzymes related to acne than skin surface microbiome.

Full DNA sequences of *C. acnes* strains find that acne-related *C. acnes* carry virulence genes compared with healthy strains for the same phylotype. Acne generated strains produce more porphyrin and more inflammatory factors in keratinocytes – ROS, cytokines) IL-8, 17, 1 beta, CAMPs, lipase, MMPs.

C. acnes obtained from normal skin or acne skin activates differently the Th1/Th17 pathway. Use of Th-17 inhibitors may have an interest in the control of Th17 response.

It was also revealed that patients with acne vulgaris have a distinct gut microbiota to healthy controls.

Of importance, isotretinoin alters cutaneous microbiome. It is crucial to add a cleanser of about pH 5 and moisturizing cream to restore skin barrier and the microbiome. Influence of drug applied to acne patients on skin microbiota was presented:

- benzyl peroxide – decrease number and diversity of bacterial species,
- systemic antibiotic minocycline – reduce *C. acnes* abundance and exerts variable changes on other species, together with increase of AMP in the skin,
- systemic antibiotic – doxycycline – reduce C. acnes abundance and increase alpha diversity, photodynamic therapy (PDT) – reduce *C. acnes* abundance, increase alpha diversity and increase abundance of other taxa,
- medium peeling 30% salicylic acid – decrease richness and evenness of cutaneous microbiome.

Skin microbiome opens the door to bacteriotherapy as regards vaccination, bacteriophage, probiotics/prebiotics and postbiotics areas. As for vaccination based on ex vivo findings of modulation of inflammation with monoclonal antibodies to the CAMP factor 2, injection of the CAMP factor-targeted acne vaccine directly into acne lesions was proposed for potential use in the future. Acnes bacteriophages exist in the pilosebaceous unit, and a potential phage therapy targeting only *C. acnes* phylotype implicated in acne (mainly IA1) has also been proposed for future research. The rationale for a potential role of probiotics (live microorganisms) or prebiotics is based on their potential to correct dysbiosis. Postbiotics namely antimicrobial peptides produced by commensal bacteria of microbiome could also be of usefulness.

Crucial role of microbiome in maintenance of skin barrier function was underlined heavily. It is the first barrier against the environment, and it contributes to the differentiation and epithelialization of the skin barrier through the transfer factor signaling acryl hydrocarbon receptor (AHR), further it boost the chemical barrier of the skin – producing lipases that digest sebum triglycerides to free fatty acids which amplify the acidity of the skin and restrict colonization by pathogenic bacteria. Moreover, microbiome modulates innate and adaptive immunities – release antimicrobial peptides (AMPs) directly or by activating their secretion by skin cells. Skin microbiome in media was even called "the second skin". Of note, the protective effect of microbiota on *S. aureus* skin colonization depends on the integrity of the epithelia barrier.

Skin microbiome plays a central role in inflammation in acne. Dysbiosis in acne is characterized by the loss of diversity of *C. acnes* phylotypes. *C. acnes* IA1 is the predominant phylotype. Another commensal bacteria play a role – mainly *S. epidermidis* and perhaps others in severe acne. Sebaceous gland is a key actor interacting with *C. acnes* inducing a virulent profile. Dysbiosis of bacteria is associated with modification of their metabolism. Skin and gut microbes interact together. Acne drugs can induce dysbiosis and thus have to be associated with skin care products.

Hidradenitis suppurativa: an illness of the follicular microbiome

Prof. Gregor Borut Jemec (Roskilde, Denmark)

The third lecture of the session was missed due to absence of Professor Gregor Jemec.

How do microbiome and skin barrier interact in atopic dermatitis?

Prof. Dr. Tilo Biedermann (Munich, Germany)

The last lecture of the session on **microbiome and skin barrier in atopic dermatitis** (AD) was delivered by **Prof. Tilo Biedermann** from Munich in Germany. The presenter focused on 3 points

1. pathogenesis of AD composed of 3 pillars,
2. interaction and interdependence of microbiome and skin barrier function in AD
3. the way we can intervene now and in the future in the above findings and observations.

AD pathogenesis is based on 3 pillars namely barrier function is deteriorated (dry skin, barrier defect), type 2 immunity is upregulated (allergy, Th2 disease) and microbial dysbiosis (and outgrowth of *S. aureus*). Of note, barrier dysfunction and type 2 inflammation are promoting each other. Fillagrin mutation and barrier dysfunction allow for *S. aureus* spreading – increased inflammation and transition from acute to chronic AD. By blocking type 2 inflammation we reduce *S. aureus* and restore barrier function.

Once again during this session cutaneous barrier was divided into 4 entities i.e. microbiome barrier, chemical barrier, physical one and finally immunological barrier (Eyerich S *et al.*, Trends Immunol 2018). Of importance, *S. aureus* in AD is associated with both skin barrier function and immune activation. Actually all 3 pillars described in AD pathogenesis are interconnected.

Professor Biederman reminded the audience about the historical works aiming at using emollients as a cure for AD. Definitely, antibiotics produced by skin commensals are effective against *S. aureus* as for example lantibiotics produced by S. hominis strains. However, good microbes need reduced type 2 inflammation to control *S. aureus*. So, beneficial microbes could serve rather as prevention than treatment of AD.

PLENARY LECTURES B

Speakers: Prof. Thomas Tüting, Assoc. Prof. Georg Stary, and Dr. Victoria P. Werth

Report written by Prof. Anna Zalewska-Janowska

Immunotherapy of melanoma: mission accomplished?

Prof. Thomas Tüting (Magdeburg, Germany)

First lecture on **immunotherapy of melanoma** was delivered by Professor Thomas Tüting from Magdeburg in Germany.

The presenter went trough historical pathway how in 1960s "the vision became reality" and that time experimental discovery of anti-tumoral T cell immunity took place. In 1980s another milestone was presented - discovery of molecular mechanisms how T cells recognize tumor cells. And then 1990s brought identification of melanoma antigens recognized by T cell Also this decade witnessed molecular control of T cells by dendritic antigen-presenting cells phenomena. Thus, enhancement of antitumor immunity by CTLA-4 blockade was discovered for which Nobel Prize was awarded in 2018. Definitely, research in basic immunology and advances in biotechnology brought immunotherapy to our melanoma patients – it is the first important mission that has been accomplished.

A fundamentally new concept for cancer treatment developed namely T cells can specifically recognize and control genetically damaged cancer cells. "Proof of concept" for T cell immunotherapy using adoptive cell transfer (ACT) is a real breakthrough in cancer research. In brief, tumor is excised, and fragments placed on the plates, then cultured in the lab and specific anti-tumor T cells generated ACT procedure. Subsequently, these cells are reinfused into the patients post-lymphodepletion and finally do the thing in the organism.

Professor Tüting also underlined that adjuvant and neoadjuvant approaches increase treatment efficacy but melanoma cells can still evade immune recognition during their evolution. Of note, Early adjuvant treatment with e.g. pembrolizumab leads to improved patients survival.

Of importance, IFN-g-producing CD4+ effector T cells can contribute to tumor immunity! CD4+ T cells cluster with antigen presenting cells at tumor invasive margins where they cooperate with IFN-activated antitumoral myeloid immune cells to eradicate MHC-deficient melanomas that evade CD8 T cell recognition.

Refinement of the available techniques, mastering them further together with bringing new technologies (e.g. gene-engineered T cells, mRNA vaccines) that can overcome therapy resistance to checkpoint blockade immunotherapies is an important next mission to be accomplished in the future and seems to be quite realistic for the current decade and a goal of transforming cancer into chronic disease.

Vaccination in STIs: what is the current state?

Assoc. Prof. Georg Stary (Vienna, Austria)

The second plenary lecture of the day on **current status of vaccination in STIs** was delivered by Assoc. Prof. Georg Stary from Vienna in Austria.

The presented pointed at the following STI prevention strategies: behavioral interventions (outreach activities, increase knowledge), structural interventions (political, economic and education) and biomedical interventions (PrEP/PEP, treatment as prevention, prophylactic vaccination) and decided to focus on vaccines. In general, we want vaccines to induce immunological memory. There are more than 30 pathogens causing STI. The presenter demonstrated a concise overview in agraph format of vaccines for STI. Professor Stary pointed that in basic research there are vaccines for *trichomonas vaginalis, mycoplasma genitalium* and *treponema pallidum*, in preclinical development – Neisseria gonorrhoeae, in clinical evaluation herpes simplex virus, *chlamydia*

trachomatis and HIV, in clinical practice HPV, Hepatitis B virus and MPX. The underlined species were further elaborated by the presenter.

Of importance vaccines delivered through the skin induce memory T cells in skin-draining lymph nodes and unfortunately present poor migration to mucosal surfaces. We really need mucosal protection but there are few mucosal vaccines approved attenuated live pathogens – potential safety risks.

The presenter pointed also at prophylactic versus therapeutic vaccines. Of note in prophylactic viral vaccines often virus neutralizing antibodies are used and this approach leads to limitation in vaccine efficacy for some pathogens. Therapeutic viral vaccines have primarily cell-mediated immune effects and CTL and T-cell-derived cytokines are used.

Professor Stary presented current status of HPV vaccines that are comprised of virus-like particles (VLP) HPV 16,18, 31,33, 45, 52 and 58 (1 vaccine) and the other of HPV6 and 11. VLP is an empty shell (virus capsids) self-assembled from L1 major capsid protein (L1 subunit vaccines). They are highly immunogenic and safe – no replication and no viral DNA is present. Vaccine efficacy is up to 100% against infection and disease caused by vaccine types. Protection is type-restricted and mediated by neutralizing antibodies to L1 major capsid protein.

Four years after introduction of HPV vaccine in Australia (girls of 12-17 years old vaccinated) the incidence of genital warts diminished by 90%. Of importance, the presenter demonstrated a very informative graph showing predicted reduction of a properly vaccinated, gender neutral, HPV-negative cohort over their lifetime: decrease in 77% of all HPV-related cancers (both women and men), 90% of reduction in cervical cancer, 80% reduction of high-grade cervical precancers and 90% decrease in genital warts (both/all sexes).

Next generation prophylactic HPV vaccine should be based on L2 N-terminal linear epitopes. Such vaccines induce low titer of neutralizing antibodies and cross -neutralization of HPV types *in vitro* and could confer cross-protection *in vivo*. L2 vaccines would have increased immunogenicity. The presenter in detail pointed at sophisticated lab methods of immunogenicity improvement. He hen focused on genetic insertion of L2 peptide RG1 into L1 (chimeric VLP, in detail Schellenbcher 2009). Such vaccine namely RG1-VLP HPV vaccine would give protection against more high-risk and low-risk mucosal types and also skin types. Such vaccine would have single antigen formulation thus leading to lower production costs. Its safety profile would be similar to current vaccines. Currently prevent program in a form of phase I human trial is planned.

Therapeutic HPV vaccines are now in development for treatment of existing HPV infections. There are several HPV vaccines in clinical trials aiming at assessing their safety and efficacy among them HPV16 E6/E7-based mRNA, protein-based vaccines, peptide-based, DNA-based, recombinant virus and dendritic cell-based vaccines.

Next part of the lecture focused on current status of knowledge on vaccination against *N. gonorrhoea*. There is an increasing threat of gonococcal antimicrobial resistance and this observation led to renewed interest for vaccines. WHO set a goal to reduce gonorrhoea incidence by 90% by 2030. In preclinical studies in mouse models for gonococcal infections the following vaccines were used: gonococcal outer membrane vesicles (OMV) vaccines, lipopolysaccharide epitope ones, purified protein subunit vaccines and DNA/RNA ones. Also, novel vaccine delivery systems were and are investigated.

A retrospective case-control study on effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhoea in New Zealand was published in Lancet in 2017. It comprised 1,430 individuals and estimated vaccine effectiveness was 31%. Currently phase 3, double-blind randomized placebo-controlled multi-center trials are already ongoing in Australia on 730 participants, whereas in USA 2,200 participants are planned to be enrolled. So lets wait for the results.

The last part of the lecture was focused on *Chlamydia trachomatis* against which no vaccine is currently available. Historically speaking in 1960s and 70s attenuated or inactivated *C. trachomatis* in humans and

nonhuman primates were tried. However, those vaccines induced incomplete or short-lived protection and worse inflammation post-vaccination. Current ideas of recombinant protein and DNA vaccines that are in preclinical development, demonstrated poor induction of cell-immunity and thus a partial protection. Currently nanoparticle-based mucosal chlamydia vaccines are investigated. They seem to present convincing model for immunization against *C. trachomatis*. They also explain post-vaccine hyperinflammation (tolerance) in clinical trials. Those vaccines provide distant mucosal protection. Of importance, tissue-resident memory T cells are highly protective against genital *C. trachomatis* infection.

Recent publications by prof. Frank Follmann group demonstrated that simultaneous subcutaneous and intranasal administration of CAF01-adjuvanted Chlamydia vaccine elicit elevated IgA and protective Th1/Th17 responses in the genital tract. The first in-human, randomized double-blind, placebo-controlled, phase 1 trial, published in Lancet Infect Dis in 2019, revealed safety and immunogenicity of the chlamydia vaccine candidate CTH522 adjuvanted with CAF01 liposomes or aluminium hydroxide. So, we are on a good truck.

New insights and therapeutic approaches in lupus erythematosus

Dr. Victoria P. Werth (Philadelphia, United States)

The third lecture on new insights and therapeutic approaches in lupus erythematosus was presented by Dr. Victoria P. Werth from Philadelphia in the USA. The presenter gave an overview of the lecture pointing on factors affecting trials in cutaneous lupus erythematosus (CLE), new insights about its pathogenesis and therapeutic approaches.

Dr. Werth pointed at clinical difficulties in proper diagnostic process of CLE. Early clinical presentation can be difficult to tell which subtype is present, can be difficult to differentiate scarring from dyspigmentation, 20% of patents has more than one subtype of CLE. Amyopathic dermatomyosits (DM) is often misdiagnosed as systemic LE (SLE). Skin biopsy is often indistinguishable between CLE and DM. Of importance Bohan and Peter criteria require presence of muscle disease to make a diagnosis of DM. The presenter demonstrated clinical usefulness of Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) – (in detail Albrecht and Werth JID 2005, 125: 889). This index has a good reliability, responsiveness and correlates wit skin specific quality of life (Skindex).

As for new insights into CLE pathogenesis there is a big role of type I interferons, efficacy of drugs targeting pDCs and type I interferon production. Different cell subsets and cytokine signatures in CLE are associated with heterogeneity of response to therapy – pDCs play a critical role in disease in many patients. Increased myeloid DCs correlate with response to quinacrine.

Finally, treatment algorithm of CLE was presented: start with topical glucocorticosteroids (GKS), then consider topical tacrolimus or pimecrolimus as long-term alternative to GKS or in thin-skinned areas.

If severe or widespread add hydroxychloroquine (< 5 mg/kg body weight QD) – if partial or no response add quinacrine (100 mg QD PO) if no response with quinacrine – switch hydroxychloroquine to chloroquine (< 2.3 mg/kg body weight QD PO) 9250 mg tablets dosed 4-7 days per week (Borucki R and Werth VP, Arthritis Rheumatol 2020:72: 1777-1785).

If no response considers adding dapsone (25-125 mg QD PO) 0, if still no response add methotrexate (15-25 mg QW PO or IM) or add mycophenolate mofetil (1,440-3,00 mg QD PO), if still no response lenalidomide – thalidomide analogue (5-10 mg QD PO) should be delivered. Methotrexate (MTX) and mycophenolate mofetil (MMF) are interchangeable or based on patient comorbidities.

Rituximab is a good option for bullous LE refractory to dapson and oral steroids/immunosuppressive drugs. It should be noted however that rituximab can induce DLE and SCLE when SLE patients treated.

In general CLE treatment should comprise sun avoidance, sunscreens use – broad spectrum, sun clothing, stopping exacerbating medications, if possible and definitely stopping smoking.

As for systemic drugs Iberdomide is a novel high-affinity ligand of cereblon (CRBN) and screened to be more potent than thalidomide or lenalidomide. Belimumab anti-BlyS monoclonal antibody – another option in clinical trials. New medications targeting IFN pathway: anifrolumab, litifilimab daxdilimab, deucravacitinib (Tyk2 inhibitor).

In conclusion, there is a clear need for clinical trials in CLE in order to provide patients with the adequate armamentarium of efficient drugs.

CHRONIC URTICARIA

Speakers: MD, PhD Mojca Bizjak, Dr. Pavel Kolkhir, Prof. Dr. Emek Kocatürk Göncü, and Dr. Clive Grattan

Report written by Prof. Anna Zalewska-Janowska

News in chronic inducible urticaria

MD, PhD Mojca Bizjak (Golnik, Slovenia)

The first lecture on news in chronic inducible urticaria (CindU) was delivered by Dr. Mojca Bizjak from Golnik in Slovenia.

Objectives of the lecture were very the following subtypes of CIndu, practical approach, novelties, unmet needs wrapped up with personal experience. Subtype of CIndU should always be defined, mainly 1 trigger is revealed, very rarely 2 or more triggers could be found. The most common CIndU are (all % in relation to the whole group of CIndU):

- symptomatic dermographism (urticaria factica) – 50-78% of adults and 38% of children with CINdU are affected,
- cold urticaria (cold contact urticaria) - 8-37% of adults and 9-14% of children,
- delayed pressure urticaria 3-20% of adults and 3-9% of children and
- cholinergic urticaria 6-13% adults and 19% of children, all % in relation to the whole group of CIndU.

Detailed history taking is crucial and CIndU should only be diagnosed when provocation test is positive. Beware that external stimuli can exacerbate the course of chronic spontaneous urticaria (CSU). Patient for provocation tests should not take antihistamines for more than 3 days, glikokorticosteroids for more than 7 days and on provocation sites wheals/angioedema should not be present for more than 1 day (Maurer *et al.* Allergy 2019;74:2550-3). Use standardized tool for provocation tests where available. There is no biomarker for disease activity in any of subtypes of CIndU. Urticaria control test (UCT) should be used in all subtypes.

As for unmet needs there is limited data on the natural course of CIndUs, current provocation protocols often fail to confirm CIndU, routine laboratory workup is poorly defined and finally new treatment options are needed. So, there is still a lot of areas to be investigated.

Relevant biomarkers in chronic urticaria

Dr. Pavel Kolkhir (Berlin, Germany)

The second lecture on **relevant biomarkers in chronic urticaria** was delivered by Dr. Pavel Kolkhir from Berlin in Germany.

Definition of a biomarker – the shortest one presented by the speaker is "objective, quantifiable characteristics of biological processes". Currently there are above 300 publications on biomarkers in CSU. As for biomarkers for prediction of loner disease duration – there are no reliable one but there is some evidence for antithyroid antibodies. Features associated with longer chronic urticaria (CU) duration – CSU severity, concomitant chronic inducible urticaria (CindU), systemic hypertension and need for multiple antihistamine drug doses per day or second-line treatments. There is no reliable biomarker as regards prediction of disease activity but some evidence exists for increased levels in D-dimer, F1+2, CRP, IL-6, MPV. There is also no reliable biomarker as regards prediction of CU recurrence but some evidence exists for increased total IgE and anti-thyroid peroxidase antibodies. Features associated with CU recurrence are: unknown etiology of urticaria, existing bronchial asthma and alternative agent use and antihistamine refractoriness. Furthermore, there is no reliable biomarker as regards differential diagnosis and identifying CSU endotypes.

Positive basophil tests are likely best single test for autoimmune CSU (aiCSU) diagnosis. Low total IgE and high IgG-anti-TPO are linked to aiCSU. IgG-anti-TPO is a marker of autoimmune thyroiditis and all CSU patients should be asked for signs and symptoms of Hashimoto's thyroiditis.

CRP and D-dimer correlate and are linked to worse response to single dose of antihistamines. Baseline low total IgE is linked to nonresponse to omalizumab (OMA), whereas high total IgE is inked to good and early response to OMA. Baseline low total IgE and positive basophil test are linked to good response to cyclosporine. Dr. Kolkhir concluded that in all CSU patients the following biomarkers should be checked: CRP+/-ESR, basophils and eosinophils absolute counts, IgG anti TPO and total IgE. Whereas in selected patients basophil tests should be performed in order to check for aiCSU.

Incoming treatments for chronic urticaria

Prof. Dr. Emek Kocatürk Göncü (Istanbul, Türkiye)

The third lecture on **incoming treatments for chronic urticaria** was delivered by Prof. Emek Kocatürk Göncü from Istanbul in Turkey. The presenter demonstrated numerous factors leading to mast cell (MC) degranulation and releasing vast number of different mediators involved in allergy, autoallergy, autoimmunity, complement cascade, inflammation, coagulation cascade, infections and neurogenic inflammation. Of clinical importance, treatment algorithm according to the current guidelines was presented when we start from second generation H1 blockers 1 tablet daily and, if not effective, we go up to 4 tablet daily before adding adding omalizumab (OMA). If still there is no effect we increase OMA up to 600mg and/or shorten intervals before switching to cyclosporine and still continue with second generation H1blockers. However, available treatment still leave 15-30% of patients with uncontrolled disease. The speaker presented vast options of possibilities for CSU treatment including:

- meprolizumab,
- dupilumab vastly used in atopic dermatitis treatment,
- Bruton Tyrosine kinase (BTK) inhibitors - fenebrutinib, remibrutinib, rilzabrutinib,
- Tezepelumab - anti-TSLP human monoclonal antibody,
- C-kit inhibitor – barzolvolimab,
- Siglec-8 monoclonal antibody – lirentelimab,
- Benralizumab – anti IL-5Ralfa,
- Povorcitinib - anti JAK,
- Vixarelimab – anti IL-31.

There are also further treatment possibilities in development and ongoing clinical trials in order to "fil all" patients and help that combat their disease in an individualized approach.

Managing angioedema without urticaria

Dr. Clive Grattan (London, United Kingdom)

And the final lecture of the session on **managing angioedema (AE) without urticaria** was delivered by Dr. Clive Grattan from London in the UK. He pointed out at the published guidelines (Zuberbier *et al.*, Allergy 2022;77:734-66, Maurer *et al.*, WAO Journal 2022;15:1006-27). He gave tips how to distinguish bradykininergic from histaminergic angioedema. Bradykininergic angioedema has slower onset (hours), is painful, not itchy, wheals are NEVER present, in HEA bowel, face and larynx could be affected, in ACEi-induced AE face and oropharynx are effected, suspicion should be executed in children with family history of HAE and does not respond to antihistamines, steroids or adrenaline. Histaminergic angioedema presents rapid onset (minutes), may itch, wheals may be present, initially – often asymmetrical, no bowel involvement except in anaphylaxis, choking very rare except in anaphylaxis, responds to antihistamines, steroids or adrenaline. The above features could help in distinguishing between these two entities and implement effective treatment.

TOP ADVANCES IN 2023 PRESENTED BY ESDR

Speakers: Prof. Dr. Sara Brown, Prof. Dr. Knut Schäkel, Dr. PhD Clarisse Ganier, and Dr. PhD Fernando Larcher

Report written by Prof. Anna Zalewska-Janowska

European Society for Dermatological Research (ESDR) this year session was focused on atopic dermatitis, non-classical monocytes in skin inflammation, basal cell carcinoma and genodermatoses.

From GWAS to patient care – how genetic studies can help in clinical practice

Prof. Dr. Sara Brown (Edinburgh, United Kingdom)

First lecture of the session on **implementation of genome-wide association study (GWAS) to patient care** was delivered by Professor Sara Brown from Edinburgh in the UK. The presenter acquainted the audience with the difficult issue how genetic studies help in clinical practice and focused on atopic dermatitis. Multi ancestry meta-analysis based on 1,086,394 individuals revealed that skin barrier (epidermal differentiation complex including fillagrin) and immunity (cytokine cluster IL-4, IL-13) are equally important in AD pathogenesis and both should be treated in the clinic. Moreover, skin is extremely important as regards AD genes expression but blood may be even more important due to the very strong signal coming from the blood and observed in the studies. We should remember about that in the clinic and act accordingly. Prof. Brown also pointed out that observational epidemiology shows association between obesity and inflammatory skin diseases. However, we do not know whether it is association and/or causation. This knowledge is important for treatment. In order to investigate the process of causation/association professor Brown briefly presented Mendelian randomization technique (MRT) which is analogous to randomized controlled trial (RCT). MRT thanks to using genetic definition of exposure is less susceptible to confounding and reverse causation. This technique investigates the effect of outcome, however it requires knowledge of genetic factors that can be drawn from GWAS studies. The studies revealed that higher BMI increases risk of eczema – 2% increase risk of eczema for each 1kg/m2 increase in BMI. When checking the revers relation no causal effect of eczema on BMI was discovered. How this information can help our patients? Eczema is an added incentive to lose weight if possible but there is no rationale for aggressive treatment of eczema to reduce BMI.

Non-classical monocytes in skin inflammation

Prof. Dr. Knut Schäkel (Heidelberg, Germany)

Professor Knut Schäkel from Heidelberg in Germany presented the lecture on **non-classical monocytes in skin inflammation**. First the speaker demonstrated vast functional repertoire of monocytes in numerous processes like antigen-presentation, tissue-repair, trained immunity, emergency monopoiesis, inflammation, patrolling and tissue reservoir. There are 3 types of human monocytes classical (cM) CD14+CD16-, intermediate (iM) CD14+CD16+ and nonclassical (ncM) CD14dimCD16+, out of which 6-sulfo LacNAc (slan)+ monocytes (slanMo) can be differentiated. Why this knowledge is important? This ncM have high pro-inflammatory capacity, they are found in different inflammatory skin diseases, they also possess unique capacity to handle complexed immunoglobulins and finally immobilized immune complexes induce directional migration of non-classical monocytes. Of importance, ncM form IL23+ TNF-alfa+ inflammatory dermal monocyte subset in psoriasis, they are highly responsive to TLR7/8 ligands and possess strong capacity to induce Th17/Th1 T-cell responses. The speaker presented a very promising slide with numerous diseases, including psoriasis, atopic dermatitis, lupus nephritis, lupus erythematosus, multiple sclerosis, Crohn's disease, HIV, carcinomas, renal cell carcinoma and diffuse large B-cell lymphoma, demonstrating location and potential role of slanMo in their course.

Fine mapping of cell states in healthy human skin across anatomical sites and basal cell carcinoma

Dr. PhD Clarisse Ganier (London, United Kingdom)

Dr. Clarisse Ganier from London in the UK delivered a lecture on **fine mapping of cell states in healthy human skin across anatomical sites and basal cell carcinoma** (BCC). First the speaker acquainted the audience with the huge project of Human Cell Atlas (https://www.humancellatlas.org). of note another link to investigate is http://spatial-skin-atlas/cellegeni.sanger.ac.uk. The mission of this project is to create comprehensive reference maps of all human cells as a basis for understanding human health and diagnosing, monitoring and treating diseases. The speaker presented numerous impressive images of single cells in different anatomical locations in cancer tissue. Dr. Ganier concluded her talk that due to combination of single cell transcriptional profiling, global special transcriptomics (ST) and targeted *in situ* sequencing (ISS) the group described cellular-resolution atlas of cell populations across multiple anatomical sites in healthy human skin and in BCC. Of note, epithelial and mesenchymal cell populations are spatially restricted within the skin. Furthermore, cell populations are conserved between anatomical sites and BCC. POSTN+ fibroblasts *i.e.* located near the hair follicle bulb, are expanded in BCC. Finally, special profiling and *in silico* lineage tracing analyses support follicular origin of BCC. So, as for perspectives search for cancer associated fibroblasts in tumor progression and invasion of nonmelanoma skin cancer will be further investigated.

Therapeutic approaches for genodermatoses based on CRISPR/Cas genome editing

Dr. PhD Fernando Larcher (Madrid, Spain)

The last lecture of the session on therapeutic approaches for genodermatoses based on CRISPR/Cas genome editing (GE) was presented by Dr. Fernand Larcher from Madrid in Spain. In the group of about 6,000-7,000 rare diseases more than 300 genodermatoses could be found including keratinization/cornification disorders (*e.g.* ichytyoses), skin fragility disorders (*e.g.* Epidermolysis Bullosa), DNA repair disorders (*e.g.* Xeroderma Pigmentosum), pigmentation (*e.g.* Albinism), ectodermal dysplasias and collagen disorders.

GE is a method of gene therapy elaborated for genodermatoses. It is based on the issue that a mutant gene in the cell is repaired or exchanged by a normal one, using editing tools. Thus protein expression is restored and

normal phenotype follows. Of importance, gene expression is not dependent on vector copy number and there is no risk of insertional mutagenesis.

Several genodermatoses are amenable for Clustered Regularly Interspaced Short Palindromic Repeat CRISPR/associated protein Cas-based GE therapeutic approaches. There is a growing variety of GE tools enabling very precise and diverse gene manipulations. GE strategies including nonhomologous end joining (NHEJ), homology directed repair (HDR) and Base editing applied to keratinocytes showed high therapeutic efficacies comparable to those achieved with conventional *i.e.* gene addition strategies. Non-viral GE methods will facilitate their transition into clinical practice. Of importance, CRISPR-associated protein systems (cas) generate a highly specific double-strand break at the target site that can be repaired by NHEJ.

Gene editing clinical trial for recessive dystrophic epidermolysis bullosa (RDEB) using autologous bioengineered skin containing patient keratinocytes and fibroblasts edited through a non-viral CRISPR/Cas9-mediated precise excision of mutant COL7A1 exon 80" was launched. Grafting is planned on a limited skin surface namely on chronic wounds of the patient. This trial is planned in 2024.

As for future directions efficient delivery systems are required to achieve clinically relevant *in vivo* skin G and are most promising in genodermatoses treatment> Currently RDEB and pachyonychia congenita are most closer ones.

TRANSLATIONAL IMMUNOLOGY FOR DERMATOLOGIST

Speakers: Prof. Dr. Sophia Karagiannis, Prof. Dr. Rolland Gyulai, Dr. Karoline Krause, and Prof. Dr. Christoph Schlapbach

Report written by Prof. Anna Zalewska-Janowska

Cancer immunology and basis of immunotherapy

Prof. Dr. Sophia Karagiannis (London, United Kingdom)

Professor Sophia Karagiannis from London in the UK delivered a lecture on cancer immunology and basis of immunotherapy. The speaker gave the objectives of the talk namely antibodies and their anti-tumor activities (antibody isotypes, antibody mechanisms of action against cancer), the influence of melanoma on tumor-infiltrating B cells and their expressed antibodies and finally example of antibody therapeutic development to activate immune responses.

As for mechanisms of antibody action against cancer the following could be differentiated – direct attack by Fab-mediated functions thus blocking growth factor receptors, arresting proliferation of tumor cells, inducing apoptosis. Such monoclonal antibody could be equipped with toxins, cytokines or radioisotope to strengthen their anti-tumoral action. Further mechanisms include antibody dependent cellular cytotoxicity (ADCC) where recruitment of NK cells, monocytes, eosinophils, macrophages is performed in order to kill cancer cells. Antibody-dependent cell mediated phagocytosis (ADCP) by monocytes and macrophages and complement dependent cytotoxicity (CDC) initiating complement cascade with membrane attack complex and finally cell lysis are also active in anti-tumor activity. Another mechanism is checkpoint inhibition i.e. PD-L1 on tumor cells with PD-1 on T cells, as in the case of nivolumab action.

It was underlined by the speaker that the tumor microenvironment may influence the antibody response in melanoma and maybe B cells around melanoma form part of cutaneous immune surveillance. B cells display IgG isotype-biased expression in melanoma in favor of modulatory isotypes - IgG4. IgG4 is ineffective in activating effector cells and may interfere with anti-tumor function of cytotoxic IgG1 antibodies in vivo.

There is a vast armamentarium of monoclonal antibodies for cancer in the clinic – a very exhausted table was presented. The vast majority of monoclonal antibodies are of class IgG1, single of IgG2 or IgG4 (Nivolumab and pembrolizumab, both against PD-1 and for melanoma approved in 2014)

Humoral immunity forms part of immune surveillance in melanoma. Tumor-associated B cells have altered phenotypes. Tumor associated inflammation promotes class-switching to modulatory isotypes e.g. IgG4 (impaired activation of immune cells and their effector functions, interfere with IgG1 functions, correlate with risk of melanoma progression). Novel therapies development based on designing antibodies with Fc regions less prone to tumor modulatory mechanisms. Anti-tumor IgE has demonstrated promise as anti-cancer therapy in disparate model systems of cancer. B cell immune responses may inform the design of antibody therapies.

At the end of the lecture 3 very important questions were asked to the audience presenting crucial information. I was once again stressed that IgE antibodies may offer a potential therapeutic option for solid tumors such as melanoma. Checkpoint inhibitor antibodies are monoclonal antibodies approved for clinical use in melanoma treatment and the last issue anti-PD-1 antibody function is to blockage of T cell exhaustion.

Antibody-mediated skin diseases

Prof. Dr. Rolland Gyulai (Pécs, Hungary)

The second lecture of the session was presented on antibody-mediated skin diseases by Professor Rolland Gyulai from Pecs in Hungry. In the almost first slide the speaker promised that after his lecture the audience will be able to understand the type and physiological functions of antibodies and potential mechanisms how antibodies can cause skin diseases, furthermore how to recognize major groups of antibody-mediated skin diseases and finally to rationalize potential diagnostic and therapeutic approaches to antibody mediated skin disease.

The very compact lecture with numerous schemes presenting immunological phenomena was nicely enriched with two clinical questions demonstrating patients with Henoch-Schönlein purpura and dermatitis herpetiformis.

Taking home messages from this informative lecture were the following: 1 antibody formation is driven by both physiological an pathological processes and can be directed against ether foreign or self-antigen and may result in one or more immunoglobulin class formation. The second point was that antibodies frequently lead to type I (immediate) and III (immune complex) reactions. Next it was underlined that diagnosis of antibody-mediated skin diseases is complex and involves detection of immunoglobulins in skin and blood (clinical picture, immunohistology, serology and in vivo tests. Finally therapy came forward indicating that therapeutic approach to antibody mediated diseases should include B cell depletion (corticosteroids, CD20 monoclonal antibodies – rituximab, ofatumumab, BAFFR inhibitor – ianalumab, CAAR T cells), antibody depletion (corticosteroids, omalizumab - anti IgE, efgartigimod – neonatal Fc receptor antagonists, IVIG, plasmapheresis) and reduction of tissue inflammation (corticosteroids- topical and systemic, azathioprine, mycophenolic acid, Cyclophosphamide, cytokine depletion – anti-IL-17, anti-IL-23, anti-IL-6, anti TNF mAbS and antihistamines.

Autoinflammation and neutrophilic skin diseases

Dr. Karoline Krause (Berlin, Germany)

Dr. Karoline Krause from Berlin in Germany delivered a lecture on autoinflammation and neutrophilic skin diseases. The learning objectives were spectrum and concept of autoinflammatory diseases, phenotype of selected autoinflammatory and neutrophilic diseases and mechanisms underlying skin inflammation. The speaker stressed and autoinflammation and autoimmunity are distant spectra on the immunologic diseases continuum of the skin, whereas neutrophilic dermatoses are chronic inflammatory skin diseases with neutrophil-dominated skin infiltrates and associated with systemic disease. Classification of selected systemic

autoinflammatory diseases (sAIDs) and their division into monogenic (e.g. FMF, TRAPS, CAPS, DIRA), multifactorial acquired (e.g. AOSD, PFAPA, Schnitzler syndrome, Behcet disease) common diseases with autoinflammatory aspects (e.g. gout, diabetes, Alzheimer disease, cardiac injury) and overlapping immune-mediated diseases (e.g. PRAAS, PLACID) was presented (in detail Bolukbasi and Krause, Clinical Dermatol 2015).

Take home messages from the lecture are the following, first - neutrophilic dermatosis is a hallmark sign of monogenic and polygenic autoinflammatory diseases, second diagnostic tests such as inflammatory markers, skin biopsy, genetic tests are key to establish the proper diagnosis and last but not least neutrophil extracellular traps (NETs) contribute to cutaneous and systemic inflammation in neutrophilic dermatoses. Two interesting questions were prepared for the audience namely neutrophilic urticarial dermatosis (NUD) should be suspected in a patient with the following symptoms: non-pruritic wheals, evening chills and subfebrile temperatures, arthralgia and fatigue. And the second one was to the spectrum of neutrophilic dermatoses belong Schnitzler syndrome, pyoderma gangrenosum and Sweet syndrome but not systemic sclerosis.

Chronic inflammatory T-cell mediated skin diseases

Prof. Dr. Christoph Schlapbach (Bern, Switzerland)

Final lecture of the session was presented by Professor Christoph Schlapbach from Bern in Switzerland on chronic inflammatory T-cell mediated skin diseases and cutaneous T cell lymphoma. To warm up the audience, the speaker presented a clinical picture of the armpit with erythematous lesion asking for diagnosis among which there were the following allergic contact dermatitis, atopic dermatitis (AD), inverse psoriasis, intertrigo and mycosis fungoides. Bearing in mind the title of the lecture, the speaker wanted to demonstrate not very classical location of mycosis fungoides. The second question was which cell type is the main driver of cutaneous T cell lymphoma and the audience had the choice of keratinocyte, dendritic cell, T cell, fibroblast and "hard to say" answers. The majority i.e. 78% of the audience has chosen T cell. As for AD the T cell was chosen by 47% of the audience.

The speaker focused on comparisons between inflammatory skin diseases (ISD) and cutaneous T cell lymphoma both clinically and histopathologicaly. And common genetic background and chronic skin inflammation in both groups of diseases. Namely in psoriasis (pso) and atopic dermatitis (AD) as regards cytokine signaling gene variants in STAT3 and STAT5 are encountered whereas in CTCL cytokine signaling mutations in STAT3 and STAT5 are observed. Moreover, as for T cell receptor signaling/ NF-kB pathway, in AD and Pso gene variants on CARD11 and TNFAIP3 are found whereas in CTCL mutation in CARD11 and TNFAIP3 are observed. Of importance, the risk of CTCL increases with severity of AD which should be beard in mind in the clinics.

At the end of the talk, the speaker asked the audience once again about the main cell driver in AD giving a choice between keratinocyte, dendritic cell, T cell, fibroblast and "hard to say". The result of pointing at T cell by 69 % od the audience satisfied the speaker.

HOT TOPICS IN DERMATOLOGY SELECTED BY THE EADV PRESIDENT

Speakers: Prof. Eli Sprecher, Dr. Lucinda Claire Fuller, and Prof. Axel Hauschild

Report written by Prof. Anna Zalewska-Janowska

From genetics to clinical care in dermatology: time to bring down the walls

Prof. Eli Sprecher (Tel Aviv, Israel)

The first speaker professor Eli Sprecher from Israel did not turn up due to the sudden war outbreak in his country.

Leveraging the impact and influence of dermatology in the International Health Arena?

Dr. Lucinda Claire Fuller (London, United Kingdom)

The second speaker of the session Dr. Claire Fuller from London in the UK delivered a lecture on **leveraging the impact and influence of dermatology in the international health area**. Dr. Fuller is a chair of International Foundation of Dermatology. Aims of the presentation were the following global health challenges and priorities, universal health coverage, dermatology in international health, opportunities for promoting the influence of our specialty worldwide, achieving skin health for everyone everywhere, skin health as a global health. The aim of this presentation was to make audience aware where our specialty is situated as regards global heath and how we could improve it to be more visible and where "we can make most noise". It was underlined that we should do more lobbing as for skin health. As regards WHO agencies dermatology is somewhat situated within tropical neglected diseases (TND). Of note, TND should have an important position in dermatology training. Dr. Fuller presented numerous projects undertaken within TND group to make dermatology more visible, most accessible to the patients and thus more important worldwide. Dr. Fuller asked dermatologists and EADV to support the projects of TND, got involved with energy and commitment. The speaker invited everybody to join GLODERM international Alliance for Global Health Dermatology www.gloderm.org.

Immune checkpoint inhibition in skin cancer: a Nobel price-winning innovation!

Prof. Axel Hauschild (Kiel, Germany)

The final lecture on **immune checkpoint inhibition in skin cancer**, that was granted a Nobel prize was delivered by professor Axel Hauschild from Kiel in Germany. The speaker presented developments and mile stones of melanoma treatment. Of note, BRAF inhibitors induce rapid induction of positive responses, confirmed on PET, however development of drug resistance to BRAF develops in a few months. In conclusion, overall survival of melanoma patients was improved but not as we wanted it to be. A discovery of immune checkpoint inhibition targeting PD-1L on tumor cells was a real breakthrough. So, anti PD-1 antibodies were introduced with a very good results. Currently 20 different diseases are already improved for anti PD-1 antibodies.

The speaker underlined the very good effects of neoadjuvant therapy. This therapy is based on the fact that tumor is not excised straight away but first immunotherapy is administered, just a few cycles. Such situation activates many different T cells, subsequently tumor is removed by the surgeon, immunotherapy is continued and many more diverse T cells search for tumor cells in the organism are present. Such therapy with neoadjuvant is much more effective than when adjuvant is only used *i.e.* excision of the tumor is performed before immunotherapy both number and diversity of T cells in not that reach and results of the treatment much worse than in case of neoadjuvant therapy.

(Neo)-adjuvant immunotherapy if you give pembrolizumab before surgery gives much better survival to melanoma patients namely up to 80%, not 50% as in the case of implementing adjuvant therapy *i.e.* introduction of immunotherapy after surgery. It is enormous progress when bearing in mind that 8 years ago survival of melanoma patients was mean 8 months.

Short and long term immune related adverse-events associated with immunotherapies are observed in 2-4% of the patients. The speaker underlined that autoimmunity events in patients once they are on immunotherapy are linked with the treatment success. This situation ought to be explained to the patients. And success has its costs. But the older the patient is the better the drug is tolerated.

Prof. Hauschild pointed also to so called "financial toxicity", namely the drugs are not available because of the high cost, unfortunately.

The whole lecture was beautifully illustrated by impressive clinical pictures showing marvelous results of neoadjuvant therapy like for example avelumab (PD-1 antibody) for metastases of Merkel cell carcinoma - great results without the knife were presented.

Of importance anti PD-1 antibodies are used as the backbone treatment, always in combo preparations. Fecal microbial transplants and individualized neoantigen-based mRNA Vaccine for melanoma were also mentioned. Of note, this year Nobel Prize was awarded for mRNA vaccine technology.

In the questions and answer section Prof. Hauschild underlined that targeted therapies are excellent as a second line treatment if checkpoints inhibitors fail, they present 25% worse survival. Targeted therapies work only if the patient has BRAF mutation (40% of MM patients) if does not – the treatment is ineffective due to lack of target.

ESDR PLENARY LECTURES

Speakers: Dr. Muzlifah Haniffa, Prof. Dr. Christine Bodemer, and Dr. Andrew F. Alexis

Report written by Prof. Anna Zalewska-Janowska

Decoding healthy and inflammatory skin disease at single cell resolution

Dr. Muzlifah Haniffa (Cambridge, United Kingdom)

The first plenary lecture of the last day of EADV Congress was named **ESDR plenary lecture** and delivered by Dr. Muzilifah Haniffa from Cambridge in the UK. The lecture was focused on decoding healthy and inflammatory skin diseases at single cell resolution. The speaker concisely presented human cell atlas project and compared it with human genome project completed in 2003. The latter is called the book of life (http://www.genome.gov/genetics-glossary). One genome encodes all cells in the human body *i.e.* around 37 trillion cells.

Dr. Haniffa acquainted the audience with single cell genomics, multi-omic profiling and spatial transcriptomics and human cell atlas which is an ongoing project and called book of cells. Nowadays it is a rapidly growing global initiative (https://www.humancellatlas.org/join-hca/). The atlas is to be used as a guidebook for mapping skin disorders and a blueprint. A roadmap for a consensus human skin cell atlas and single-cell data standardization was published by Almet AA *et al.* in JID in 2023.

Of importance, this atlas contains also prenatal skin cell atlas for mapping pediatric skin diseases, understand hair formation, phenomenon of scarless healing in first trimester (regeneration), developmental programs co-opted in skin disease. The aim is to use atlas as a blueprint-benchmark *in vitro* models. The aim of this project is to have equitable access and translation of the data – the cycle of data generation, bioinformatics – computation and using research software engineering. Multimodal webportal was created (Horsfal *et al.* Nat Med 2023. Of importance the Atlas presents 3 modalities single cell RNA-sequencing, *in situ* sequencing and visium spatial which gives most advanced picture of the studied issue.

René Touraine plenary lecture: paediatric mastocytosis

Prof. Dr. Christine Bodemer (Paris, France)

The second presentation, named Rene Touraine plenary lecture was on **mastocytosis and mast cell disorders in children** and presented by Professor Christine Bodemer from Paris in France. By definition mastocytosis is characterized by clonal proliferation of mast cells in the skin and potentially in various tissues with prevalence 1/20.000. Spontaneous remission usually is observed in children whereas in adults non-regressive lesions are present and systemic forms predominate. According to Prof. Bodemer mastocytosis in children and in adults is not the same disease. Adult mastocytosis is associated with c-KIT mutations leading to abnormal mast cell accumulation and activation. KIT D816V mutation is present in 90% of adult mastocytosis patients whereas only in 42.4% of children. Evolution and prognostic factors of regression were reviewed by Prof. Bodemer's research group and based on the history of 272 children with mastocytosis (JACI in 2021). Spontaneous regression occurs in more than 80% of cases, evolution to aggressive form or sarcoma is very rare, age of 6 years is an average beginning of regression time. Ags of onset below first year of age and no KIT mutation are prognostic factors of regression. As for management of pediatric mastocytosis, the speaker underlined that there is no systemic treatment. Medical health provider should keep reassuring the parents about the benign nature of the disease (more than 99% of children) and avoiding mast cell degranulation triggering factors such as physical stimuli, drugs (aspirine, codeine, morphine, NSAIDs). Emergency card and self-injecting pen with adrenaline should be delivered if there is a history of anaphylaxis or diffuse cutaneous mastocytosis is present. If absence of severe anaphylaxis – normal vaccinations should be administered. Clinical follow-up should be performed at first every 6 months than yearly. If symptoms such as growth problems, pain, diarrhea, flushing, pruritus, malaise etc. develop specific investigations should be performed without further delay and handled accordingly. The following symptomatic treatment is recommended: topical steroids (anti-pruritic effect), antiH1 blockers (anti-pruritic effect), anti H2-blockers (against heartburn, diarrhoea and food reactions) combination of H1 and H2 blockers, anti-leukotriens (montelukast) and finally omalizumab. In severe forms such as diffuse blistering or systemic involvement – steroids in a dose of 0.5-1.0 mg/kg/day for short periods, imatinib (if pediatric mutations present), if c-KIT D816 mutation present – sirolimus or midostaurin could be implemented.

The speaker also acquainted the audience with mast cell activation syndrome (MCAS) characterized only by qualitative abnormality of mast cells which diagnostic criteria were proposed by prof. Valent in 2020. MCAS is further divided into:

- primary MCAS in which a KIT D816V mutation is present without mastocytosis,
- secondary MCAS where activation of mast cells is triggered by IgE-related allergy, inflammatory diseases, infections and neoplasms
- idiopathic MCAS where no identifiable case could be determined.

Prof. Bodemer concluded her talk with invitation to the 2nd World Congress on Rare Skin Diseases scheduled between 12 and 14th June 2024 in Paris (https://www.wcrsd.com/en/).

Diagnostic and therapeutic pitfalls in skin of colour

Dr. Andrew F. Alexis (New York, United States)

The final lecture of the session was on **diagnostic and therapeutic pitfalls in skin of color** delivered by Dr. Andrew A. Alexis from New York in the USA. The speaker acquainted the audience with dermatologic diseases that are more prevalent in populations with skin of color namely pigmentary disorders, keloids, scalp/hair disorders and multisystem disorders beautifully illustrated by clinical pictures. Of importance laser/light based procedures, corticosteroid injections and liquid nitrogen cryotherapy arise safety concerns when performing on patients with skin of color. It was also underlined that Black, Asian and Hispanic/Latino patients reported greater impact of psoriasis on their health related quality of life, as measured by DLQI, than White patients.

There is a considerable educational gap because dermatology is still taught from the perspective of how dermatologic disorders present in individuals of European origin. Research demonstrated that 47% of

dermatologist felt that their training was inadequate to diagnose skin diseases in skin of color. Of note, unfamiliarity with darker skin may lead to considerably delayed diagnosis and finally treatment.

Development of an eczema area and severity index atlas for divers skin types was presented (Silverberg JI, Horeczko J, Alexis A, Dermatitis 2023).

Dr. Alexis demonstrated the following skin classification challenges: understanding a patient "skin type an ancestral/ethnic background is more complex than perceived skin color. Assumptions based on visual assessment of facial skin color can lead to inaccurate conclusions. And finally dichotomous classification of divers populations into white *versus* non-white of skin of color *versus* non-skin of color is important.

Finally, dr. Alexis presented his face image enriched by race, Fitzpatrick skin phototype, pigmentation phototype, geographic ancestry, genetic ancestry, cultural/geographic background. After all these steps true presenter face appeared on the screen. The presenter pointed at the importance of performing clinical trials also on patients with skin of color and shared with the audience the idea of health equity (Davies CM *et al.* JACI 2021). Dr. Alexis invited everybody to join Skin of Color Society (https://skinofcolorsociety.org/membership-2/).

SKIN AGEING AND REJUVENATION

Speakers: Prof. Dr. Rolf-Markus Szeimies, Dr. Lidiya Todorova, Dr. Peter Velthuis, and MD, PhD Emanuel Carvalheiro Marques

Report written by Dr. Ricardo Limongi Fernandes

Facial rejuvenation with daylight PDT

Prof. Dr. Rolf-Markus Szeimies (Recklinghausen, Germany)

The session was opened by Prof. Dr. Rolf-Markus Szeimies talking about **facial rejuvenation with daylight PDT** (photodynamic therapy). According to him, PDT brings direct epidermal effects, like less roughness and sallowness, balanced epidermal architecture, improvement of pigmentary changes. It also brings indirect dermal effects via cytokine induction (IL-1, TNFα, etc.), leading to skin tightening, less fine wrinkles, less erythema. Photo rejuvenation with PDT is the only non-oncologic indication with highest levels of recommendation and quality of evidence (A1) besides treatment Tx of AK, Bowen´s disease and BCC (basal cell carcinomas). So far, it is still an off-label use, especially in the US.

Results can be optimized by pre-treatments strategies:

- Intensified PDT – drug delivery assisted – chemical or mechanical peeling pre-PDT (microdermabrasion), micro needling 250-500µm after the photosensitizer. Great importance of penetration of the drug in stratum corneum.
- Synergistic PDT – additional procedure-induced collagen stimulation – laser-assisted drug delivery prior to the photosensitizer (CO2, Er:YAG – if possible with no anesthesia, due to the pH conflict), micro needling 1,000-2,000µm after the photosensitizer. Thulium-laser and NASHA skin boosters are also options to treat AK lesions and improve skin quality.

It takes weeks to months to reach the expected results with daylight PDT (improvement on skin texture, roughness, fine lines, telangiectasias, dyspigmentation, remission and prevention of Aks). Adverse effects are tolerable and reversible, with almost no pain. On the other hands, expectations should be realistic – mild

improvement. Other recommended treatment protocols when Aks/NMSC in the target area should be maintained.

Safety and effectiveness of PRP

Dr. Lidiya Todorova (Plovdiv, Bulgaria)

Dr. Lidiya Todorova talked about **the safety and effectiveness of PRP** (platelet-rich plasma). She defined PRP as a volume of autologous plasma with platelet concentration above basal line (x3-7). Main limitations are related to little consensus on the large variety of methodologies available, lack of standardization in the use of PRP, concentrations and quality of platelets in the PRP can vary, effectiveness of PRP varies from patient to patient, improvements achieved require multiple treatment sessions over time to maintain results. PRP effectiveness is related to the growth factors (GFs) released by α-granules of platelets, primary cytokines (IL1, IL6, TNF-α), bioactive substances in platelets dense granules (serotonin, histamine, dopamine, calcium and adenosine), anti-inflammatory and analgesic effect, antimicrobial peptides.

GFs stimulate cellular proliferation and differentiation, activation of fibroblasts, collagen synthesis, tissue granulation and regeneration, neo angiogenesis, extracellular matrix (ECM) synthesis, de novo protein synthesis, cell growth, antimicrobial action, inflammatory modulation. They promote healing, wound and tissue repair, hair follicle proliferation, skin rejuvenation, improves periorbital hyperpigmentation, melasma, mild and moderate forms of alopecia areata.

PRP is related to low side effect profile (autologous product), no systemic effects, no reports of immune reactions of allergies, no oncogenic effect. Injection pain is moderate. Reported adverse events are related to reactivation of HSV (herpes simplex virus), like all traumatic procedures. Prophylaxis may be considered. It is contraindicated in patients with active autoimmune disease. One case of serum sickness disease was reported after PRP. One case report of permanent blindness was reported after PRP treatment in a "Spa facility".

According to her, PRP is promising and safe method, needs standardized PRP preparation protocol and well-designed studies to become a routine treatment with well-defined indications in Dermatology.

Ultrasound to improve the safety of hyaluronic acid filler treatment

Dr. Peter Velthuis (Rotterdam, Netherlands)

The third speaker was Dr. Peter Velthius, presenting **ultrasound (US) to improve safety of hyaluronic acid filler treatments**. According to him, a 12MHz capacity is the basic prerequisite for cosmetics. Ultra-high frequency (>50MHz) is indicated for epidermal evaluation.

With the US, anyone can search any artery over the muscle and avoid it (lips), sometimes find deep artery in Ristow space (3% of the patients). According to him, many malar edemas occur due to compression of veins, detectable by US. Arthur Swift´s gunshot technique – sometimes is not safe, but arteries can be found by the US. He also uses the US to evaluate noninflammatory nodules, related to injections inside the superficial musculoaponeurotic system (SMAS). It can also be a good tool in case of complications, for the guided injections of hyaluronidase.

In his Opinion, high-frequency ultrasound imaging offers a new and great opportunity to gain a better understanding of skin and subcutis. US findings already improve daily practice of cosmetic dermatology. Further research will help making cosmetic dermatology a real science.

Myomodulators: latest update

MD, PhD Emanuel Carvalheiro Marques (Prague, Czech Republic)

Last, but not least, Dr. Emanuel Carvalheiro Marques presented **the latest update on myomodulators**, suggesting new promising indications based on recent publications:

- Nose reshaping – only 1 study (injections at dilator naris anterior, dilator naris vestibularis, elevator labii superioris alaeque nasi and dilator naris). BoNTA (botulinum toxin type A) can effectively restrain alar mobility without any significant adverse events and improve alar dynamic esthetic, which can serve as a minimally invasive method or supplemental treatment for rhinoplasty. It makes the nose look smaller at rest, better results smiling.
- Infraorbital hollows – based in 4 points of injections of 12,5U of AbobotulinumtoxinA linearly disposed 1cm above the lower border of the mandible. It alleviated platysma tension, and skin moves cranially, improving infraorbital hollows.

Talking about BoNT longevity, recent studies bring up again the controversy about efficacy of zinc supplementations. One of them, showing increase in longevity of about 30%. Considering the 12% of Americans are zinc deficient, and the proteolytic activity of the BoNTA is zinc dependent, perhaps its supplementation (beginning 4 days before the injection) can make sense for some groups of patients. Zinc Gluconate 50mg or Zinc Citrate 50mg + Phytase 3,000PU.

Concerning immunoresistance, recent study suggests maximum risk for BoNT resistance is around 0.4% (in patients with maximum 6 years of exposure to BoNTA), with the following classification ABO>ONA>INCO. Mixing brands can rise the risk up to 13%. Higher doses, shorter intervals, higher overall lifetime exposure and purity of formulation may be associated to the immunoresistance. Intradermal injections>intramuscular injections (higher concentration of dendritic cells).

Highlights of novel therapeutics:

- RelabotulinumtoxinA (Alluzience®) – "liquid toxin" approved for glabellar lines in Europe (June 2021). Same dosage as AbobotulinumtoxinA, lactose free, albumin (or any other animal excipient) and lower risk of error in preparation.
- LetibotulinumtoxinA (Letybo®) - approved for glabellar lines in Europe (February 2022). Same dosage as OnabotulinumtoxinA.
- PrabotulinumtoxinA (Nuceiva®, Jeauveau® - US) - approved for glabellar lines in Europe. Same dosage as OnabotulinumtoxinA.
- DaxibotulinumtoxinA (Daxxify®) – considered a real "game changer", FDA approved in September 2022 (recommended dosage is double the OnabotulinumtoxinA dosage). Formulated with a stabilizing peptide (RTP004) that enhances internalization of the toxin. No accessories proteins, albumin free. Median duration of effect is 6 months (50% of the patients).
- Botulinum toxin E – still phase I study. Very fast onset (24h), but short duration 1-7 weeks.
- Choosing the right toxin involves approval, availability, safety, resistance issues, price, preference of the patient and durability of treatment effect.

HAIR DISORDERS

Speakers: Prof. Jerry Shapiro, Prof. Dr. Ulrike Blume-Peytavi, Prof. Ramon Grimalt, and MD, PhD Sergio Vaño-Galván

Report written by Dr. Ricardo Limongi Fernandes

Evaluation and diagnosis of scarring alopecia

Prof. Jerry Shapiro (New York, United States)

Regarding the theme "**Evaluation and diagnosis of scarring alopecia**", Prof. Jerry Shapiro's approach consists in:

1. Obtain a thorough clinical history.
2. Observe the scalp with the naked eye.
3. Maneuvers: hair pull and card test
4. Take a closer look at the scalp with a dermatoscope: check for the presence/absence of follicular ostia, note erythema, hypo/hyperpigmentation, atrophy, hyperkeratosis, telangiectasias.

Evaluation and diagnosis of scarring alopecia
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	Frontal fibrosing alopecia (FFA)	Lichen planopilaris (LPP)	Chronic cutaneous lupus erythematosus (CCLE)	Central centrifugal cicatricial alopecia (CCCA)	Foliculitis decalvans	Dissecting cellulitis
Demographics	Older adults, more women	Adults	Young/middle aged adults, more women	Young adults, more females Afro-Caribbean descent, onset, hair cosmetics history	Young/middle aged adults, more men	young adults, more men African descent
Onset	gradual	gradual	gradual or abrupt	gradually progressive	gradually progressive	gradual onset
Symptoms	rarely associated with itch, burn, pain	+itching (early sign), burn, pain	+itching, burning, pain	+itching, burning, pain	+itching, burning, pain	+pain
Hair shedding	variable	variable	variable	variable	variable	variable
Pull test	pull test + on edges (active phases)	+	+ anagen hairs	+ anagen hairs	+ anagen hairs	+ anagen hairs
Card test	no regrowth	no regrowth	no regrowth	no regrowth	no regrowth	no regrowth
Key features	alopecia of the eyebrows frequently associated, band-like cicatricial alopecia involving frontal hairline	bare patches or diffuse thinning, often starts at vertex, perifollicular erythema and scaling	well-circumscribed round/oval plaques, scaly erythematous plaques, changes within the alopecic patch rather than the periphery, follicular plugging, telangiectasias, atrophy, dyspigmentation	Symmetric, centrifugal scarring without overt inflammation, scalp may be soft on palpation	predominantly vertex and occipital scalp, crusting and pustule formation, tufted folliculitis	most commonly vertex of back of scalp, formation of firm or fluctuant nodules, pustules and crusting, +/- sinuses with purulent drainage
Trichoscopy	loss of follicular ostia, perifollicular hyperkeratosis, perifollicular erythema and inflammation, pili torti	loss of follicular ostia, perifollicular scaling, pigment incontinence (blue-grey dots) in patients with dark skin	peripilar erythema, thick arborizing vessels, keratotic plugs, large yellow dots, follicular red dots	peripilar white/grey halo around emerging hair, white patches of follicular scarring that interrupt regular honeycomb pigmented network, lack of follicular ostia	significant polytrichia, peripilar white-yellow scale, peripilar hyperplasia, white and milky-red areas, lack of follicular ostia	marked erythema, follicular pustules, cutaneous cleft with multiple emerging hairs

Except FFA, for all diagnosis, biopsy is usually necessary. Early diagnosis and treatment is mandatory, to have a chance to save the follicles

Management of frontal fibrosing alopecia

Prof. Dr. Ulrike Blume-Peytavi (Berlin, Germany)

Prof. Dr. Ulrike Blume-Peytavi talked about **the management of frontal fibrosing alopecia** (FFA). She began highlighting the 5 pillars for the therapeutic approach:

1. Inflammation
2. Inflammation – immune signaling.
3. Genetic susceptibility
4. Hormonal link
5. Cosmetic products and UV-screens

Current therapeutic recommendations:

1. First line treatment: topical corticosteroids (as solution, emulsion or foam), Triamcinolon-injections in the active rim, topical calcineurine inhibitor. 3-6 months.
2. Second line treatment (offlabel): Doxycicline 100mg OD or minocycline 50mg BD, Hydroxyxhloroquin (5mg/kg/day) 6-9 months up to 24 months, oral corticosteroids pulse therapy alone or in combination, Finasteride 2,5mg/s alone or combined with topical minoxidil solution or dutasteride 0,5mg/d.
3. Third line treatment: Mycophenolatmofetil 2X1g/day, Cyclosporine A.
4. Monitoring: Severity Index (FFASI), serial management of the frontal hairline, serial photography, trichoscopy and video-trichoscopy.
5. Supporting measures: surgery (only in long-standing inactive disease). It may reactivate disease! cosmetic camouflage and psychologic counselling.

Low dose oral minoxidil for androgenetic alopecia

Prof. Ramon Grimalt (Terrassa, Spain)

Prof. Ramon Grimalt talked about **low dose minoxidil for androgenetic alopecia** (AGA). He made an evidence-based approach, showing recent robust literature concerning the use of low dose minoxidil, and showing difficulty in finding good quality literature concerning Post Finasteride Syndrome. He highlighted that only concerned patients attends dermatologists for AGA treatment, and they tend to be more observant. For this kind of patient, any health problem, sexual or not, that might appear during the treatment might erroneously be attributed to the drug. Obsessed men tend to "notice" with more detail, and web pages and journalists not always act adequately. In this way, he does not prescribe Finasteride to high concerned patients and uses instead oral minoxidil, with visible results in 3 months. He starts with 1,5mg/day at night for women and 5mg/day at night for men. Control in 3 months and ajust the dosage according to hypertrichosis.

Emerging therapies for androgenetic alopecia

MD, PhD Sergio Vaño-Galván (Madrid, Spain)

The following speaker was Dr. Sergio Vaño-Galván, presenting "Emerging therapies for androgenetic alopecia." The highlights were:

Emerging therapies for androgenetic alopecia
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Oral minoxidil	He showed new data on safety (no severe adverse events), even in patients with hypertension and arrythmia and reinforced that for him, it is one of the most useful new therapies for AGA in daily practice. Concomitant use of spironolactone or bicalutamide can decrease the risk of hypertrichosis. Spironolactone can also reduce water retention. Some conditions require a visit to cardiologist prior to prescribing minoxidil: coronary disease, heart failure, severe valvar disease, recent pericardial disorders, advanced renal disease.
Bicalutamide 10-50mg daily	Effective for female AGA, especially interesting in pre-menopausal women with associated seborrhea. It requires liver enzymes monitoring (pre, 1month, 3-6 months) – low hepatotoxicity risk, usually during first months. It must be discontinued 2 months before seeking pregnancy.
Mesotherapy with antiandrogens (Dutasteride 0,01-0,025%, Bicalutamide 0,5%)	For patients who don´t want to take oral antiandrogens, require more intensive treatment, or to optimize outcome in patients taking low doses of oral antiandrogens.
Botulinum toxin A	Two theories: - One is the toxin relaxes the muscles, increases blood flow in scalp and increases the wash out of DHT. - The other is the decrease of TGFβ. Protocol suggested: 60U intradermal (4mm needle) and 40U intramuscular (13mm needle), dilution 100U/5ml. 0,1ml (2U) per point. 30 points intradermal, 16 points in temporal and 4 points in occipital muscle.
Others, for the future…	GT20029, pyrilutamide (topical antiandrogens), SAMiRNA (self-assembled micelle inhibitory RNA – decrease androgen receptors in dermal papilla cells. Topically applicated 1-2X a month), exosomes (still with FDA warnings!), HMI-115 (monoclonal antibody that inhibits prolactin receptor).

For male AGA, he recommends dutasteride 0.5mg 3-7 times a week, +/- Oral Minoxidil 2.5-5mg daily +/- topical minoxidil 5% at night.

For female AGA, his recommendation is Oral Minoxidil 0.5-1mg daily +/- topical minoxidil 5% at night +/- oral antiandrogenic drugs (spironolactone or bicalutamide premenopausal and dutasteride postmenopausal).

Other therapies may be considered for exceptions.

HAIR DISORDERS

Speakers: Dr. Anna Waskiel-Burnat, Prof. Dr. Lidia Rudnicka, Prof. Antonella Tosti, and Prof. Bianca Maria Piraccini

Report written by Dr. Ricardo Limongi Fernandes

Telogen effluvium: evaluation and treatment

Dr. Anna Waskiel-Burnat (Warsaw, Poland)

Dr. Anna Waskiel-Burnat presented **the evaluation and treatment of Telogen Effluvium**. Effluvium is considered chronic with durations more than 6 months. Sometimes history is enough for the diagnosis, but it is good to perform the pull test to confirm it. To perform it, we need to pull up gently 40-60 hairs, and it is considered positive when 10% are extracted (patient with no hair washing for 5 days). Trichoscopy is good to exclude AGA (androgenetic alopecia) and AA (alopecia aerata). It may show solitary folliculum, yellow dots. Trichogram can be performed with 20-60 hairs finding >20-25% telogen hairs. Established the diagnosis, we look for an underlying cause (most important), that can be found in history or laboratory tests (more relevant in chronic cases). It should always include complete blood count, thyroid function tests, iron profile and vitamin D level. When indicated, liver and kidney function tests, vitamin B12, B2, zinc, HIV (immunodeficiency virus), VDRL (Venereal Disease Research Laboratory), ANA (AntiNuclear Antibodies), prolactin, biotin tests can be performed. Most times, treatment is just to explain cause and course of the disease. Other possible treatments:

- Iron supplementation (ferritin below 30) maintaining ferritin levels between 40-70.
- Minoxidil and topical corticosteroids may be also considered.
- Controversial indications involve PRP (platelet-rich plasma), BoNT (botulinum neurotoxin), multivitamin supplements, dietary supplements, herbal solutions, shampoos.

Managing alopecia areata through trichoscopie

Prof. Dr. Lidia Rudnicka (Warsaw, Poland)

Prof. Dr. Lidia Rudnicka presented **the management of alopecia areata (AA) through trichoscopy**. Predicting the hair regrowth is not possible in the first visit trichoscopy, but some signs after the regrowth may warn for upcoming hair loss, suggesting it is not a good moment to reduce doses or discontinue treatment.

Markers of disease activity or reactivation are: exclamation mark hairs, tapered hairs, black dots and Pohl-Pinkus constrictions, broken hairs. In this case, increase the dose or considering a second medication may be encouraged.

Upright regrowing hairs and pigtail hairs, on the other hands, are positive markers.

Considering the negative and positive markers, it is possible to create a predictive score, that indicates the chance of regrowth with the current therapy.

Attention to AA (alopecia aerata) trichoscopy: lack of yellow dots does not exclude alopecia areata. It depends on the age of the patient and concentration of sebaceous glands.

Attention to tinea capitis: usually trichoscopy signs disappear before negativation of culture!

Late onset alopecia areata

Prof. Antonella Tosti (Miami, United States)

Prof. Antonella Tosti talked about **the late onset alopecia areata** (AA). This refers to the first onset of the disease occurring after the age of 50, and represents 7-18.7% of the cases. More common in females, usually mild disease, family history is not common and association with atopic dermatitis is not common. It can be triggered by medications, Covid-19, vaccines, anti-TNF, ribavirin, interferon. Response to treatment is usually good. Better prognosis compared to early onset cases. Alopecia totalis (AT) and alopecia universalis (AU) might not follow this general rule. It preferentially affects pigmented hair, sparing graying/white hair. Sometimes may be difficult to distinguish from scarring alopecia, sometimes requiring biopsy.

JAK inhibitors in alopecia areata

Prof. Bianca Maria Piraccini (Bologna, Italy)

Prof. Bianca Maria Piraccini talked about **the use of JAK inhibitors in alopecia areata** (AA). There are 11 molecules, only 2 of them FDA approved for the treatment of AA (Baricitnib – only adults, and Ritlecitnib ->12 years old). There are different trajectories of the hair regrowth: early (12 weeks), gradual (24 weeks) or late response (>24 weeks). Side effects are equivalent for all JAK inhibitors. Effectiveness and safety seem similar. Choice depends on the age of the patient and availability of the drug. Right indication is extension between 50-95%, longstanding cases respond less. Patients should be followed each 3-4 months. Effective evaluated after 9-12 months.

NAILS DISORDERS

Speakers: MD Francesca Pampaloni, Dr. Matilde Lorizzo, Prof. Asja Prohic, and Prof. Bertrand Richert

Report written by Dr. Ricardo Limongi Fernandes

Managing nail disorders through onychoscopy

MD Francesca Pampaloni (Bologna, Italy)

Dr. Francesca Pampaloni presented the **management of nail disorders through onychoscopy**. According to her, onychoscopy should be used routinely in the evaluation of nail diseases. It can be performed with a handheld dermoscope, which allows visualization of the entire nail at once, or with a videodermoscope, which allows different magnifications. It permits better visualization of nail signs. For some diseases, it adds a lot to clinical and reveals suggestive features. In inflammatory nail diseases, onycholysis is the crucial dermoscopic sign to observe in differential diagnosis *versus* onychomicosis. It is important to look at the distal margin, look at the periungual tissues. Put this information together with clinical examination and history.

Management of nail disorders through onychoscopy
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Subungual hematoma	Mainly first and fifth toenail, round, banded, whole nail plate, purple red, fading at the margins, peripheral blood spots. Foreign bodies differ for their sharp edges and protruding tip.
Pseudomonas	Color black + green + yellow, peripheral convexity
Psoriasis	Bright yellow orange discoloration, patchy and surrounding distal detachment, splinter hemorrhages, diffuse yellowish pigmentation. Periungual capillaries irregularly distributed, dilated and tortuous.
Dermatophytoma	Subungual accumulation of hyphae and scales – irregular subungual accumulation with a round shape, yellow orange, connected by a thin narrow channel to the distal edge of the nail plate
Hansen´s disease	Branching of the proximal nail fold, honeycomb pigmentation with interspersed orange globules, white, shiny desquamation.

Paediatric nail disorders

Dr. Matilde Lorizzo (Lugano, Switzerland)

Dr. Matilde Lorizzo introduced **pediatric nail disorders**, that can be hereditary (at birth or later), congenital (some potentially prevented) and acquired.

- Congenital total/subtotal leukonychia – limited to nails or syndromic (auditory abnormalities/generalized peeling syndrome
- Congenital anonychia/micronychia – related to drugs during pregnancy
- Congenital Onychodysplasia of the index finger (radial part of the nail). X-Ray helps diagnosis.
- Nail Patella Syndrome- sometimes mild alterations, kidneys involvement, no patella
- Pachyonychia congenita- palmo plantar painful hyperkeratosis
- Dyskeratosis congenita- attention to lichenoid nail changes in children
- Hypertrophy of the lateral/distal nail folds- very common – lack of pressure on the thin nail plate. Make the differential with pseudo hypertrophy – triangular nail.
- Toenail malalignment
- Parakeratosis pustulosa- exclusively in children
- Psoriasis- parakeratosis with clusters of polynuclear cells make the diagnosis in a clipped (3mm) nail.
- Lichen striatus- usually one nail + skin
- Nevi- wait and see is the best approach. Follow up 3-6 months, excise when worrisome features are present.
- Exostosis
- Nail dystrophy due to toe malposition in children

Update on onychomycosis treatment

Prof. Asja Prohic (Sarajevo, Bosnia and Herzegovina)

Prof. Asja Prohic brought an **update on onychomycosis treatment**. Pathogenic organisms are Dermatophytes (60-90%), No dermatophyte moulds (10%), and Yeasts (20%). Complete clinical cure comprehends mycological + clinical cure. Laboratory confirmation of onychomycosis before beginning a treatment regimen is cost effective and avoids misdiagnosis. Oral treatments are indicated when >50% of the nail is affected, multiple nails (>3), nail matrix involved, dermatophytoma. Terbinafine, Itraconazole and Fluconazole are classically indicated. Novel oral therapies include Posaconazole, Fosravuconazole, Oteseconazole, Voriconazole and Albaconazole. Amorolfine is related to the best cure rates among the topical options. Recurrence can be prevented with some lifestyle modifications, like keeping feet cool and dry, avoiding occlusive shoes, use flipflops in public and wet spaces, discard or wash socks with hot water, trim nails to avoid trauma, prophylaxis on feet and webs, treat family members with onychomycosis or tinea pedis, appropriate treatment and counselling on adherence, treat shoes with antifungals, ozone, UV.

Trachyonychia: evaluation and treatment plan

Prof. Bertrand Richert (Brussels, Belgium)

Prof. Bertrand Richert talked about the **evaluation and treatment plan of trachyonychia**. Trachyonychia is related to surface alterations due to proximal matrix inflammation. There are two forms: opaque (subtle longitudinal striation, thin scales) and shiny (superficial ridging and small geometric pits). He remembers the term “Twenty-nail syndrome” is incorrect, as there are plenty nail disorders that affect the 20 nails. In

trachyonychia, the whole surface of the nail is affected. Mainly present in children, fingers>toes. It can be associated to alopecia areata (AA), lichen planus, psoriasis, or isolated (Idiopathic trachyonychia). Histology is the only way to know the etiology. Recent publications shows that it is more common in males (2/3) average age 19, idiopathic in 55%, opaque type in 78%, number of nais affected: 8 finger and 4 toe. Involvement of 20 nails: 33% (AA in 70%). It heals by itself (usually > 4 years). Biopsy not recommended in children. 40% Urea cream and/or Hydroxypropylchitosan lacquer may be indicated. Association of calciprotriol/betamethasone dipropionate, intralesional corticosteroid in adults, systemic corticosteroids, systemic retinoids can also be indicated.

SCALP DISORDERS

Speakers: Dr. Natalia Caballero Uribe, Prof. Krisztian Gaspar, Dr. Petra Dikrama, and Prof. Adriana Rakowska

Report written by Dr. Ricardo Limongi Fernandes

Diagnostic and therapeutic algorithm in folliculitis decalvans

Dr. med. Natalia Caballero Uribe (wallisellen, Switzerland)

Dr. Natalia Caballero Uribe showed the **diagnostic and therapeutic algorithm in folliculitis decalvans**:

- Clinical examination: chronic, recurrent, pustulofollicular, scalp inflammation, crown area, exudative crusted areas, grouped follicular, pustules, centrifugal progression, central scarring.
- Dermoscopy: Tufted hairs (5 or more), perifollicular hyperplasia, starburst pattern, follicular pustules, yellowish tubular scaling, white and milky red areas, loss of follicular openings, elongated looped vessels.
- Histopathology: neutrophilic primary scarring alopecia, scarring alopecia, important hair tufting, diffuse pattern of effaced dermal elastic fibers, important number of plasma cells
- Microbiology: *S. aureus*, Gram negative bactéria
- Predisposing factors: trauma, immune deficiency, ectodermal dysplasia with clefting, cutis verticis gyrate and folliculitis keloidialis nuchae, hair transplantation
- Clinical variants: Classical folliculitis decalvans (Quinquaud), cicatrizing seborrheic eczema, tufted hair folliculitis, ulcerative folliculitis decalvans, folliculitis decalvans with linear arrangement, folliculitis decalvans presenting frontal fibrosing alopecia-like
- End-stage folliculitis decalvans: chronic lichenoid phase or folliculitis decalvans pseudopeladic state (Degos)

Treatments include clorhexidingluconate 0.2-2% shampoo, ketoconazole in associated seborrheic dermatitis, topical corticosteroids + topical antibiotics. Orally, Fusidic Acid + Zinc Gluconate, Rifampicin + Flucloxacillin, Rifampicin + Clindamycin, dapsone, Isotretinoin. In chronic lichenoid phase, intralesional corticosteroids + Doxycycline, punch excision or hair tufts, total indication excision with scalp expander in extreme cases.

Scalp psoriasis

Assoc. Prof. Krisztian Gaspar (Debrecen, Hungary)

Prof. Kristián Gáspár talked about **scalp psoriasis**, defining as a common condition (up to 80% of psoriasis patients have scalp involvement) difficult-to-treat area, pruritus with non-histaminergic mediators involved. Recent results:

- Topical: calcipotriol/betamethasone dipropionate foam. roflumilast foam (Ph II study), new formulation trial.
- Systemic: Apremilast, Anti-IL-17, Anti-IL-23

Tips and tricks for scalp itch

Dr. Petra Dikrama (Utrecht, Netherlands)

Dr. Petra Dikrama brought some **tips and tricks for scalp itch**:

Most frequent causes: "SCALLP": Seborrheic dermatitis, Contact dermatitis, Anxiety, Lichen planopilaris, Lice, Psoriasis

Local therapy involves use of glucocorticoids, calcineurin inhibitors, others (menthol, capsaicin, LCD), combinations (5-10% ketamine, 5% amitriptyline, 5% lidocaine, Tacrolimus, Gabapentin), shampoos (zinc, ketoconazole, selenium, coal tar), phototherapy.

Medications like antihistamines, anticonvulsants, opioids, antidepressants, and others can also be uses for itchy scalp.

Acne, hair loss and hirsutism

Assoc. Prof. Adriana Rakowska (Warsaw, Poland)

Prof. Adriana Rakowska discussed about **acne, hirsutism, and hair loss**, all androgen-mediated disorders. Idiopathic cases are related to androgens within the pilosebaceous unit. Ovarian cases are the most common (2-7% women in reproductive age), related to PCOS (polycystic ovarian syndrome), anovulation or oligoanovulation, clinical or biochemical hyperandrogenemia, polycystic ovarian morphology.

Biochemical hyperandrogenism (3rd-7th day of the cycle): serum total testosterone, free testosterone, free androgen index, androstenedione, dihydrotestosterone (DHT), dehydroepiandrosterone (DHEA), DHEA-sulfate (DHEA-S)

Important:

- DHEA-S > 8000 – suggestive adrenal tumour
- 4000 < DHEA-S < 8000 – suggestive of congenital adrenal hyperplasia
- Total testosterone >150-200 – suggestive of ovarian tumour
- Total testosterone mildly elevated – suggestive PCOS
- LH/FSH rates 2,5-3 – suggestive PCOS

Glucose abnormality is more prevalent in patients with SAHA syndrome (seborrhoea, acne, hirsutism, and alopecia): 21.4% *vs.* 7% in patients with no clinical features.

PCOS account for 70-80% cases or hirsutism.

In younger patients with PCOS, we find more acne (15-80%) and hirsutism (38-80%) than female pattern hair loss (FPHL , 2-24%). After the age of 30, FPHL is the most important feature.

Oral contraceptive pill lead to suppression of ovarian androgen production Drospirenone has 30% of Cyproterone acetate antiandrogenic potency.

Dexamethasone in low doses are treatment for non-classical congenital adrenal hyperplasia.

Hirsutism treatment can be done with Flutamide + Finasteride (70% reduction), Spironolactone + Finasteride (53% reduction), or Spironolactone (30% reduction).

FPHL is generally not associated with elevated androgens, there is an increased sensitivity to normal androgen levels, hyperandrogenism by itself does not cause necessarely FPHL.

She ends the presentation proposing the term SAH syndrome instead of SAHA, as FPHL is not a hyperandrogenism sign.

FILLERS II, ADVANCED

Speakers: Dr. Hugues Cartier, Dr. Luigi Leonardo Polla, Dr. Pierre Andre, and Dr. Peter Velthuis

Report written by Dr. Ricardo Limongi Fernandes

Anatomy of the most dangerous areas for face injections

Dr. Hugues Cartier (Arras, France)

Dr. Hugues Cartier, talking about the **anatomy of the most dangerous areas for face injections**, considers ultrasound (US) a real game changer to the safety of injections, due to its real time vessel mapping and visualization of the layers under the skin. According to him, it locates and evaluates fillers and remove them under guidance if necessary. Permits monitoring side effects (migration, compartment formation, abscesses, adenitis, and granulomatous pathologies). With the use of US, injectors avoid the classic "deep" or "superficial" blind technique to secure the injections. Talking about BoNT (botulinum neurotoxin) injections, in his opinion, US-based evaluation provides information about the dynamic movement of the facial muscles and the clinical application of BoNT. It also allows clinicians to understand muscle movement and achieve optimal results by considering the relationship with the surrounding muscles. Furthermore, detailed anatomical information about the facial muscles is crucial for optimizing the effectiveness of BoNT treatment.

Medical rhinoplasty: how to get the best result without complication

Dr. Luigi Leonardo Polla (Geneva, Switzerland)

Dr. Luigi Leonardo Polla, talking about **how to get the best result without complication in medical rhinoplasty**, highlighted it is a very popular procedure due to patient appreciation and effectiveness. On the other hand, it is the second most frequent cause of skin necrosis and blindness. Risks should not be omitted. In his opinion, to increase safety, first of all, clinicians must know the anatomy, perform procedures together with a senior and start with primary rhinoplasty. Plan and draw the procedure, proceed with a rigorous technique, inject slowly with stable hand, have a control over the area and never inject too much are other safety tips. He suggests, if necessary, do complete rhinoplasty in two or more sessions, stay alert to any clinical sign of embolism, keep patients in the clinic for at least 30 minutes after injection and give a mobile number, explaining late onset side events. In case of embolization, arterial events occur fast (sharp pain, whitening, livedo, slow capillary refill), while venous event occur slowly (blue-purple color and blunt pain). In terms of degree of severity, mild cases show skin color changes, moderate show pustules and ulcerations and severe, skin blackening and necrosis. In the management of embolism, with history <5 hours, he suggests, massages, hot compresses, aspirin, venous access, hyaluronidase skin test (5 min), solucortef i.v. injection, EpiPen available,

hyaluronidase deep and superficial, one point every 0,5cm, 10U/point/hour. In cases with duration <3 days, hyaluronidase injections, slow i.v. injections of alprostadil 10µg diluted in 10ml saline 1X/day 3 days, Dexamethasone 10mg in 100ml saline daily – 3 days, oral antibiotics, aspirin 100mg daily, hyperbaric oxygen, if possible, gentle wound care. In cases with duration >3 days, promote wound healing and lasers to reduce scars. Other possible side effects/respective orientation are: lateral diffusion of the product to the under-eye area/hyaluronidase, nose oedema/oral cortisone, bruising/PDL, erythema in the tip of the nose/oral cortisone, asymmetry, irregularities/hyaluronidase, granulomas/oral cortisone, hyaluronidase. Medical analysis involves inspection, palpation, ultrasound. Special concern in post-surgical rhinoplasty. To perform injection with needle, he suggests transferring the HA to a 0.3cc syringe 8mm/32G needle. With the cannula, the aim is to reshape the tip of the nose. In his opinion, there is no need to correct nasolabial angle nor to inject the base of the columella.

How to manage the complications of non-permanent fillers

Dr. Pierre Andre (Paris, France)

Dr. Pierre Andre discussed **how to manage the complications of non-permanent fillers**, dividing them in three phases:

1. Immediate
2. Delayed – in case of nodules, simple drainage. For delayed inflammatory reaction (often after vaccines, viral, bacterial infections), corticosteroids PO or injections and hyaluronidase.
3. Late- granulomas – sometimes require biopsy. In case of non-inflammatory, hyaluronidase. In case of inflammatory, hyaluronidase and corticosteroid. In case of foreign body reaction, hyaluronidase, antibiotics and corticosteroid (or 5-FU). Resistant cases can respond to methotrexate. Drainage in case of abscess (consider biological analysis)

When using animal derived hyaluronidase (over-correction, misplacement, nodules, granulomas, vascular emergencies), he suggests performing a prick test before, although allergic reactions are rare. Human recombinant Hase is 100 times purer, though safer.

Vascular compromise: how manage it with duplex ultrasonography

Dr. Peter Velthuis (Rotterdam, Netherlands)

Dr. Peter Velthius talked about "**Vascular compromise: how manage it with duplex ultrasonography**". According to him, the incidence of vascular obstruction is calculated: 1:6600. Most of the events seem to be due to spasm (pattern resembles livedo reticularis).

BOTULINUM TOXIN II, ADVANCED

Speakers: Prof. Berthold Rzany, MD, PhD Emanuel Carvalheiro Marques, Prof. Christopher Rowland Payne, and Dr. Hugues Cartier

Report written by Dr. Ricardo Limongi Fernandes

Botulinum toxin indications in dermatology

Prof. Berthold Rzany (Wien, Austria)

Prof. Bertold Rzany talked about **botulinum toxin indications in dermatology**, focusing on hyperhidrosis and bruxism. For axillary hyperhidrosis, he uses AbobotulinumtoxinA 200-250U per side (subdermal) in 10-15 points. For palmar, he uses 250U, superficially in 40-50 points per hand, preferent with no nerve block. Efficacy and duration depend on the dosage injected. For bruxism, regarding masseter injection, he suggests 3-4 points, total 40-50U per side. Paradoxal bulging occurs due to incomplete treatment of the masseter and is easy to correct.

Botulinum toxin indications in basic research and outside dermatology

MD, PhD Emanuel Carvalheiro Marques (Prague, Czech Republic)

Dr. Emanuel Carvalheiro Lopes showed **botulinum toxin (BoNT) indications in basic research and outside dermatology**. In Ophthalmology, strabismus, blepharospasm, alternative to surgical tarsorrhaphy and keratoconjunctivitis sicca. In Otorhinolaryngology, allergic rhinitis, cricopharyngeal spasm, laryngeal granulomas, laryngeal dystonia/spasmodic dysphonia. In Neurology/Psychiatry, migraine, trigeminal neuralgia, chronic low back pain/myofascial pain, nothalgia paresthetica, peripheral neuropathy, Bell´s palsy, Depression, Tic disorder/Tourette, Tardive dyskinesia, essential tremor, cervical dystonia, Spasticity. In Dentistry, bruxism, temporomandibular joint disorders, mandibular spasm. In Gastroenterology, chronis sialorrhea, achalasia, gastroparesis, anal fissures, contractile stoma. In Urology/Gynecology, detrusor instability, erectile dysfunction, benign prostatic hyperplasia, vulvar pain disorders, vaginism, chronic pelvic pain. In cardiovascular surgery, prevention of atrial fibrillation after surgery, blood pressure control (Celiac plexus). There are also applications of BoNT in Veterinary medicine.

How to improve your botulinum toxin injection technique for the lower face

Prof. Christopher Rowland Payne

Prof. Christopher Rowland Payne talked about **how to improve your botulinum toxin (BoNT) technique for the lower face**. He defends mosty intradermal injections, exactly in the dimples, insertions of the muscles to the skin. In case of Rosacea, he suggests 2U of AbobotulinumtoxinA/point intradermal, For lower face, 20U of AbobotulinumtoxinA/total. For masseter, 20-40U of AbobotulinumtoxinA/side, in average 10 points (3 along the masseter border). He recommends 4 points linearly under the mandibular border for Nefertiti lift. If injection was too much, he recommends toilet training (exercises each time the patient goes to the toilet)

Can botulinum toxin be used to improve wound healing?

Dr. Hugues Cartier (Arras, France)

Dr. Hugues Cartier answered the question "**Can botulinum toxin be used to improve wound healing?**". BoNT can reduce muscular tension to the skin, reduce fibroblast activity. The most difficult thing is to define when to inject. Late injections and excessive dosage are related to increasing the scar size. In prevention, it works. In many studies, injections from the first day to the nineth after surgery show promising results. To prevent hypertrophic scars, few study in humans, potentially good results in animal studies. Reduces itch and pain, with no atrophy – compared to corticosteroids injections.

NAIL AND HAIR DERMOSCOPY

Speakers: Prof. Adriana Rakowska, Dr. Anna Waskiel-Burnat, Prof. Luc Thomas, and Prof. Dr. Iris Zalaudek

Report written by Dr. Ricardo Limongi Fernandes

Trichoscopy findings in alopecia

Assoc. Prof. Adriana Rakowska (Warsaw, Poland)

Prof. Adriana Rakowska showed **trichoscopy findings in alopecia**. She suggests trychoscopy in every case. The main findings according to the diagnosis are:

- Alopecia Areata- Exclamation mak hairs, indicates high disease activity. Tapered hairs Pohl-Pinkus's constrictions, triangular hairs, broken hairs at the same level, yellow dots, velus hairs unpigmented (not good prognosis), upright regrowing hairs (good prognosis), circle hais/pigtail hairs (good prognosis). Markers of disease activity or reactivation are: exclamation mark hairs, tapered hairs, black dots and broken hairs, broken hairs. Upright regrowing hairs and pigtail hairs, on the other hands, are positive markers. Considering the negative and positive markers, it is possible to create a predictive score, that indicates the chance of regrowth with the current therapy. Think about possibility of malignancy (Mycosis Fungoid) if pili torti, thick interfollicular bands and perifollicular arrangement of blood vessels are found.
- Trichotillomania- Irregularly broken hairs, trycoptilosis, flame hairs, coiled hairs, V-sign, Hook hairs, tulip hairs.
- Tricotheiromania- Trichorrexis nodosa at the same level, broom hairs
- Tinea capitis- Comma hairs, morse code-like hairs, zigzag hairs
- Temporal triangular alopecia- short vellus hairs, no signs of alopecia areata
- Aplasia cutis congenita- follicular starburst pattern
- Lichen planopilaris- white dots, perifollicular erythema, perifollicular scaling, acquired pili torti
- Frontal Fibrosing Alopecia- perifollicular erythema, perifollicular scaling, lonely hairs, acquired pili torti
- Discoid Lupus erythematosus- red dots, thick/serpentine arborising vessels, red spider on a yellow dot, diffuse brownish pigmentation.
- Patchy alopecia in SLE- thick arborising vessels, grey hairs
- Monilethrix- multiple constrictions

Trichoscopy-guided biopsy of the scalp

Dr. Anna Waskiel-Burnat (Warsaw, Poland)

Dr. Anna Waskiel-Burnat discussed **trichoscopy-guided biopsy of the scalp**. Main indications for scalp biopsy are inflammatory disorders, scarring alopecia, tumors and, in some cases, non-scarring alopecia. Trichoscopy shows the most representative area to take a biopsy. In inflammatory diseases, the preferred area is the one that shows most features of the disease. For scarring alopecia, never in white areas (just fibrosis). For lupus erythematosus, areas rich in red dots and vessels are the best. Use, at least, a 4mm tool. It is important to follow the angle of the hairs to assure we did not cut the hairs.

Tips and tricks for onychoscopy

Prof. Luc Thomas (Pierre bénite, France)

Prof. Luc Thomas shared 11 **tips and tricks for onychoscopy**:

1. Have acetone.
2. Make a complete anamnesis and skin examination – the clue is outside the nail.

3. Check other nails- sometimes you find the “ugly duck”. Remember acral melanoma is the main melanoma in black people, and they usually have nail pigmentation.
4. Always use contact immersion dermoscopy
5. Use gel for immersion to see the whole surface of the nail.
6. Also look at the free edge- in pigmented lesions, you´ll see no hyperkeratosis and the level of pigmentation. Low pigmentation=distal matrix. In melanomas, generally pigmentation is in different levels of the free edge (never hiperkeratin plug). Onychopapilloma- nail plate thinner and hyperkeratotic plug underneath (similar to SCC, but SCC is usually not well limited and wider). Onycomatrichoma- nail plate thicker with holes.
7. Take good photos.
8. Consider digital follow-up. Nail biopsy is painful. Sometimes it is better to wait and be sure biopsy is mandatory.
9. Consider telexpertise consultation.
10. Bring your dermoscope in surgery room. According to the suspect, you can choose between shaving or incisional biopsy, with different evolution to scars.
11. Do not give an opinion without dermoscopy!

Clinical and histopathologic features of the Hutchinson sign

Prof. Dr. Iris Zalaudek (Trieste, Italy)

Prof. Dr. Iris Zalaudek presented **clinical and histopathologic features of the Hutchinson sign**, a periungual extension of pigment that may affect the nail folds and/or hyponychium. Hutchinson sign is suggestive for vertical growth phase of melanoma, so it associated with the diagnosis of advanced melanoma. Biopsy of Hutchinson sign should be avoided. It may lead to misdiagnosis in this special area. Longitudinal excision that includes the nail matrix is preferred, particularly the center of the pigmentation. Predicting factors for subungual melanoma:

1. **Age** (peak 5-7th decade), Asian or African
2. Brown/black and **width >3mm**
3. Change of nail morphology (late)
4. **Digit** (first more commonly involved)
5. Extension to proximal, lateral or distal nailfolds
6. Family history of melanoma or multiple nevi

Gray/black nail plate and granularity of pigment, regular bands BUT with triangular in the nail plate, shape are also predictive findings for melanoma. Recently described free edgefibrillar pattern appears insufficient to reliably distinguish congenital nail matrix nevi from advanced melanoma.

DERMOSCOPY IN INFLAMMATORY DISORDERS

Speakers: Prof. Dimitrios Ioannides, Prof. Harald Kittler, Dr. Josep Malvehy, and Prof. Aimilios Lallas

Report written by Dr. Ricardo Limongi Fernandes

Dermoscopy features of psoriasis and lichen planus

Prof. Dimitrios Ioannides (Thessaaloniki, Greece)

Prof. Dimitrios Ioannides presented the **dermoscopy features of psoriasis and lichen planus**.

The main features of Plaque Psoriasis are: white scales, dotted vessels (uniform distribution), erythematous base, Auspitz sign (blood extravasation). Trichoscopy shows clusters of red dots and globules (which tend to align into a linear pattern), glomerular or coiled vessels arranged in a linear or circular pattern. In treated psoriatic lesions, vessels tend to merge with the erythematous background and their structure is not clearly defined. In severe acute rashes, dotted vessels are visible around the pustules. Dermoscopy differentiates guttate psoriasis from a mimicker pityriasis rosea.

The hallmark of lichen planus is pearly-whitish (and less commonly yellow or blue-white) structures, possibly displaying several morphological patterns, including reticular, annular, round, mimicking the crystal structure of snow, or "starry sky" (clustered, follicular white dots) aspect.

Infectious diseases

Prof. Harald Kittler (Vienna, Austria)

Prof. Harald Kittler presented **infectious diseases**, dividing in the following categories:

- Viral- peripheral scales suggest pityriasis rosea, erythema (brownish in skin of color) probably associated to HHV, rainbow pattern found in Kaposi´s Sarcoma (and many other patterns. Papilloma with loop vessels in the center are typical in warts. Dermoscopy in these cases are good to differentiate from seborrheic keratosis, clavus. Moluscum, with vessels that don´t cross the central umbilication.
- Bacterial- orange structures suggest granulomas, like cutaneous tuberculosis.
- Fungal- white scales in skin furrows, perifollicular white scales, perifollicular white color suggest pityriasis versicolor. Pigmentation in the ridges, reticular pattern suggests tinea nigra. Inverted pigmented triangle is typical in onychomycosis, and helps differential diagnosis to melanoma.
- Protozoa- central yellow scales with white perilesional circle, or diffuse structureless white area pattern are features of leishmaniosis.
- Infestations- it is helpful to visualize pityriasis pubis, myiasis, pediculosis, lice agents. White-colored noduled with black-centered pore is typical for tungiasis. Also, for scabies, dermoscopy is very helpful

Inflammoscopy of the scalp

Dr. Josep Malvehy (Barcelona, Spain)

Dr. Josep Malvehy showed the importance of **inflammoscopy of the scalp**. It helps differentiation between seborrheic dermatitis (arborizing red lines and yellow dots), contact dermatitis (irregularly distributed twisted red loops and comma vessels), tinea capitis (corkscrew hairs, morse code-like hairs, zig-zag hairs, bent hairs, diffuse scaling) and scalp psoriasis (regularly distributed simple red loops, twisted red loops and globules), helps differentiating alopecia areata and tricothilomania, and define prognosis for alopecia areata treatments, helps differenciating lichen planopilaris (perifollicular vessels, perifollicular erythema, loss of vellus hairs) and discoid LE (keratin plugs).

Do we need inflammoscopy?

Assoc. Prof. Aimilios Lallas (Thessaloniki, Greece)

Prof. Aimilios Lallas answered the question "**Do we need inflammoscopy?**" and talked about the change of paradigm. A few years ago, in 2005, dermoscopy of inflammatory disorders was considered useless. Nowadays, things have changed, lots os studies in many different conditions were published, and inflammoscopy is strongly recognized as a very important tool for taking decisions in Dermatology. He showed some clinical situations where inflammoscopy clarified diagnosis.

ACNE

Speakers: MD, PhD Ediléia Bagatin, Prof. Dr. Falk Ochsendorf, Prof. Dr. Alberto Mota, and Dr. Hassan Galadari

Report written by Dr. Ricardo Limongi Fernandes

Prepubertal acne

MD, PhD Ediléia Bagatin (Sao Paulo, Brazil)

Dr. Ediléia Bagatin presented **prepubertal acne**. She began explaining the role of sebaceous glands in humans: in intrauterine life, as an evolutionary adaptation focused on protecting the bipedal human beings from dystocia. After birth, key role in androgen homeostasis, paracrine effect, antimicrobial, immune and inflammatory activities. Acne generally occurs later, when glands are pathologically stimulated due to a combination of factors that lead into inflammation (DHT, cutaneous barrier damage, microbiome changes, diet, lifestyle).

Steroidogenesis begins at adrenarche (8yo. Girls and 9yo. Boys), with the production of DHEA and DHEAS, that can be peripherally converted in DHT, which activates sebaceous glands. It is a process independent from ACTH and different from gonadarche. Prepuberal acne is a rare disease (infantile, midchildhood or preadolescent) related to premature adrenarche, not gonadarche. It iss not an endocrinopathy, as the plasma androgens level is normal. It is related to peripheral conversion in DHT. Therefore, history, physical examination hands X-ray for bone age and growth curve are sufficient, with no need of an extense evaluation, except if signs of advanced puberty. In this case, lab tests should be performed (LH/FSH/DHEA/DHEAS/Testosterone total/free/17 α-hidroxiprogesterone/prolactin).

There are no guidelines to manage this disease, but clinical practice shows that usually light topical treatment is enough. Skincare (gentle cleanser + moisturizer + photoprotection) and dermocosmetics can be an effective treatment, preventing scars and hyperpigmentation. Prescription products like adapalene, azelaic acid, fixed combination, antibiotics (the less, the better) and oral isotretinoin (0,3mg/kg/day until complete resolution + 1 month, many cycles as necessary) can be used. Treat to cure! Maintenance and follow up are mandatory.

How to manage acne during pregnancy

Prof. Dr. Falk Ochsendorf (Frankfurt, Germany)

Prof. Dr. Falk Ochsendorf explained **how to manage acne during pregnancy**.

Up tp 43% of pregnant women are affected by acne, typically at 2nd/3rd trimester. Background risk for malformations of any kind is 3-6/1000, and theses malformations are usually connected to treatments performed during pregnancy.

Labeling is different when we compare the European Medical Association and the FDA, In EMA, drugs go from 1 to 8, while for FDA, we have X, D, C, B, A. Prof. Ochsendorf thinks the site 'www.embryotox.de' is useful to assist doctors in clinical practice.

Topical Clascoterone, Retinol and Salicylic acid are not recommended. Topical azelaic acid, BPO, Clindamycin, Dapson, Erythromycin, Metronidazol, Glycolic acid are possible.

Systemic isotretinoin, Spironolactone, Trimethoprim- Sulfamethoxazol are not recommended. Macrolides (except estolate), Amoxicilin, Cefalexin, Clindamycin are possible. Tetracycline is possible until the week 16. Corticosteroids are considered safe, specially in low doses. Oral Zinc is also possible.

Intralesional corticosteroids and blue light are possible. PDL, other lasers and PDT are not recommended.

Choice depends on acne severity.

Truncal acne: from the diagnosis to the treatment

Prof. Dr. Alberto Mota (Porto, Portugal)

Prof. Dr. Alberto Mota presented **truncal acne from diagnosis to treatment**. Half of patients with acne have truncal involvement. Up to 1/3 of them don´t mention truncal involvement (importance of examination!). It can be isolated in 2% of cases. Male patients, severe forms, family history and androgen exposure are risk factors. Scars risk is lower than in face. It is associated to psychosocial burden. Hyperseborrhea might not play a major role in the truncal acne. Truncal Acne Severity Scale (TRASS) guides the treatment:

- Truncal Acne Severity Scale (TRASS) guides the treatment:
- Mild: topical retinoids, benzoyl peroxide 9,8% emulsion foam – short contact, azelaic acid 15% foam
- Moderate: Trifarotene, topical fixed combination, Clascoterone, +/- Zinc, +/- oral cyclins. Spironolactone/oral contraception is also an option for female patients.
- Severe: oral cyclins + Trifarotene or topical fixed combination or Clascoterone, oral isotretinoin. PDT is an alternative.

Prevention and treatment of atrophic scars?

Dr. Hassan Galadari (Dubai, United Arab Emirates)

Dr. Hassan Galadari ended the session, presenting **prevention and treatment of acne scars**. Scarring can happen in all forms of acne. True scars can be atrophic (Ice peak – V-shaped and deep, box – wide, shallow/deep or rolling – the widest) or elevated (keloid or hypertrophic scar). Different types of scars respond to different kind of treatment:

- For ice peak scars, punch excision has great efficacy, CROSS technique is good and ablative lasers, fair.
- For box pick scars, ablative lasers, non-ablative lasers, needling, CROSS and punch excision are good.
- For rolling scars, ablative lasers, non-ablative lasers, needling, fillers and subcision are good.

AESTHETIC DERMATOLOGY FOR MEDICAL INDICATIONS

Speakers: Prof. Dr. Klaus Fritz, Prof. Dr. H.A. Martino Neumann, Dr. Hassan Galadari, and Dr. Peter Velthuis

Report written by Dr. Ricardo Limongi Fernandes

Microneedeling and microneedle RF for medical indications

Prof. Dr. Klaus Fritz (Landau, Germany)

Prof. Dr. Klaus Fritz talked about **microneedling and microneedling RF (radiofrequency) for medical indications**. According to him, sometimes in Dermatology it is very difficult to separate medical and cosmetic indications. Microneedling is a collagen induction therapy, and it takes time… from 3-12 months. He recommends not to perform a 2nd treatment before 6-8 weeks and a 3rd, only after 6-12 months. The main medical indications are: acne scars, atrophic scars, scars resulting from trauma or injury, burn scars and stretch marks. In general, 1,5mm needles are indicated, except mild scars in thin skin (0,5mm), light scars (1mm) and burn scars (2,5mm).

According to him, it is a gentle and safe method, activates collagen and elastin production, improves thickness of epidermis, clinically improve scars, is associated to mild side effects, is safe, easy to perform and cost effective method.

Lasers for psoriasis

Prof. Dr. H.A. Martino Neumann (Banholt, Netherlands)

Prof. Dr. H. A. Martino Neumann defended the **treatment of Psoriasis with 585nm pulsed dye laser**. PDL has direct effects on blood vessels, and also indirect effects in nearby structures (ablation of free nerve endings and perivascular nerves around the vessels, impairing its functions). Additional long-term effects, thank to the poor regeneration of nerves and brings remarkable long remission time.

Dermatologist's guide on the uses of botulinum toxin for medical indications

Dr. Hassan Galadari (Dubai, United Arab Emirates)

Dr. Hassan Galadari presented **medical indications for botulinum toxin**. Starting with Hyperhydrosis, he suggests 50U each axilla (up to 100), high efficacy. For palmar, he suggests same doses, remembering it is more painful and more risk for muscular impairment. For migraine, criteria are well defined (at least 15 episodes a month, minimum 8 typical), 155-195units in a very well-known protocol. For TMJ (temporomandibular joint) pain/bruxism, around 100U in 10 points od Masseter and temporalis muscles. For scars, no consensus about doses (about 10U/cm) and moment to inject. For depression, mechanism may be related to Positive Feedback, social feedback, neurotrophic factor, serotonin, etc.

Fillers for medical indications

Dr. Peter Velthuis (Rotterdam, Netherlands)

Dr. Peter Velthius ended the session, presenting **medical indications for fillers**. The highlights were acne scars, lagophtalmus (injections in the ROOF makes upper eyelid heavier), ectropion (high G´filler injected in the lower lid to improve the stiffness of the eyelid, also in Ichthyosis patients), nose (improving internal nasal valve opening), cheilitis angularis, keloids (HA filler pneumatically injected leads to massive hydration, softening and flattening the tissue), scars, defects after steroids atrophy.

ALOPECIA AREATA

Speakers: Prof. Dr. Annica Vogt, Prof. Dimitrios Ioannides, Dr. PhD Jovan Lalosevic, and Dr. Maryanne M. Senna

Report written by Dr. Lucija Vanjaka-Rogošić

Clinical spectrum and severity of alopecia areata

Prof. Dr. Annika Vogt (Berlin, Germany)

In this lecture, Prof. Vogt suggests that the best way to achieve correct diagnosis of alopecia aerata (AA) is by detailed medical history, examination of the patient, and dermatoscopy as essential tool

Additional helpful information come from the evaluation of the extent of the lesions at the scalp, using the SALT score (Severity of ALopecia Tool) and other body regions (eyebrow, eyelashes, beard), activity of the disease, which is tested by hair pull test, and the special pattern of the lesions. Sometimes changes are also visible on nails (46% of pediatric patients, and 15% of adults).

Severe alopecia is described when SALT score is 50% or more. Predictors are diffuse hair loss, like ophiasis –a type of alopecia, duration of the disease for over a year, onset in early childhood and positive family history. Also, some comorbidities are seen with AA, such as atopic dermatitis, associate autoimmune diseases like Hashimoto thyroiditis, vitiligo, SLE (systemic lupus erythematosus) and rheumatoid arthritis.

AA also has bih psychosocial impact on patient, so more than 50% of patients have severe depressive disorders, and 39-62% of patients have anxiety disorders. Children and adolescents can have stigmatisation, mobbing and bullying, so Prof. Vogt suggest, when we have patients with AA, we have to think, that hair is not just a hair- it is symbol of gender, age, beauty anfd health.

At the summary Prof. Vogt pointed that severity and burden of AA is multidimensional. It affects physical dimension, comorbidities and psychosocial dimension.

The main aim is to assess the treatement strategies as soon as possible, and the treatement choices have to be as individual decisions for each patient.

Trichoscopy in alopecia areata

Prof. Dimitrios Ioannides (Thessaloniki, Greece)

Trichoscopy is a very useful tool to guide the diagnosis of alopecia aerata (AA) , and for the follow up through the treatment. It is a non-invasive, inexpensive, and easy to perform method.

First step is to exclude the developement of scarring alopecia, in diagnosis, by looking at the presence or absence of the follicular openings. The severity of the inflammation will show various trichoscopic features which could be observed.

- The inflammatory insult against the hair bulb will lead to formation of hair shafts with increased fragility, so called *zig zag* hairs, *moniletrix like hairs*, or *black dots*, where the breakage takes the place.
- In Trichotillomania we can see on trichoscopy all degrees of broken hair shafts with regular tips.
- *Exclamation mark hairs* can suggest rapid transmision from anagen to telogen phase and narrowing of the proximal shaft.
- In chronic AA, the telogen phase is prolonged, so hair follicules are devoid of shafts, and in the trichoscopy we can see yellow dots.

Prof. Ioannides gave the tips which can be useful while performing trichoscopy:

Tips which can be useful while performing trichoscopy

DOWNLOAD

Active disease	Inactive disease	Hair regrowth
Zig zag hairs Moniletrix-like hairs Broken hairs Black dots Exclamation mark hairs Tulip hairs Tapered hairs	Yellow dots Vellus hairs	Upright regrowing hairs Pigtail hairs- oval or circular Vellus hairs

Alopecia areata comorbities

Dr. PhD Jovan Lalosevic (Belgrade, Serbia)

In this lecture, Dr. Lalošević describe connection of AA with other autoimmune and inflammatory diseases.

Etiopathogenesis of AA is still not completely clear, but in recent publications, it is seen that AA patients have a higher prevalence of autoimmune and inflammatory diseases.

Known associations are with Autoimmune thyroiditis, Vitiligo, SLE, Rheumatoid arthritis, Pernicious anemia, Psoriasis, Atopy spectrum, Psychiatric disorders, Zinc and vit.D deficiency. The comorbities can have influence on therapy. It is important to make screening for comorbidities like tests for IgE, antinuclear antibodies, anti TPO, Anti Tg antibodies, Rheuma factor, Serum Zn and vit. D, HDL cholesterol, Triglyceride and fasty blood sugar, for metabolic syndrome.

If AA appears as early onset, usualy it will be connected with atopic dermatitis. If AA has late onset, it is usually connected with autoimmune thyreoiditis.

At the end of lecture, Dr. Laloševic has described their expirience. Their results shows that severe form of AA were more frequently associated with Thyreoid disease, and there is also higher incidence of Metabolic syndrome. Also, patients with Autoimmune thyreoiditis who were treated with i.v. pulse corticosteroids, had significantly worse treatement response.

Are new treatments for alopecia areata a real breakthrough?

Dr. Maryanne M. Senna (Winchester, United States)

At the beginning of her lecture Dr. Senna pointed, that she will review the current therapeutic lanscape of AA, and she will also discuss about the challenges and opportunities for more targeted and personalised aproaches for treatement of AA.

There is an insuffitient acceptance of hair loss, as an important medical problem, and disease is highly vissible and different to conceal, so patients have to share their problem with public, which further lead to loss of privacy. To get AA cumulative lifetime risk is of 2%, it affects all ages, races and sexes, and initially onset is typically before age 30.

The pathogenesis of AA is not still completely clear, but it is known that cytotoxic T cells penetrate the proximal anagen hair bulb and initiate an autoimmune attack on still unrecognised antigen. T- helper cells are in peribulbar location and they also play role in AA pathogenesis.

In 2014., 25- year old male with extensive psoriasis and AA, was treated with *oral Tofacitinimib*, which led to improvement of psoriasis and hair regrowth. From that moment, new directions in treatement of AA with Jak inhibitors are open and investigated in many clinical trials. At the moment, AA clinical trials with efficacy data

with use of Baricitinimib and Ritlecitinimib vs placebo are on-going. It is reccomended for very severe AA patients with SALT (Severity of ALopecia Tool) of 50% or more. This patients have to know warnings about the side effects of this medications, like cardiovascular and cancer risk, malignancy and seriuous infections risk.

The better results are achieved, when therapy is performed in less severe patients and with shorter duration of current episode (less than 4 years). For some patients, better results are achieved with adjuvant oral *minoxidil* therapy. Also, good results can be achieved with *dupilumab* (Th-2 inhibitors), for patients who also have severe Atopic dermatitis.

In conclusion, Dr. Senna pointed that JAK ihibitors have revolutionised our ability to care fot these patients, and it is important to improve diagnostic techniques which will hopefully allow us to better understand to adjust targeted treatements.

ROSACEA

Speakers: Dr. Linda Stein Gold, Prof. Dr. Martin Steinhoff, Prof. Eszter Baltas, and Dr. Lucero Noguera

Report written by Dr. Lucija Vanjaka-Rogošić

New data in pathophysiology

Dr. Linda Stein Gold (michigan, united states)

In this lecture Dr. Stein Gold indicate, that rosacea may be thought as a systemic disorder, which can be associtated with comorbidities as neurologic disorders, cardiovascular disorders or gastrointestinal disorders.

Most patients with rosacea have more than one subtype of rosacea (erythemato-teleangiectatic, papulo-pustular, phymatous or ocular subtype). To evaluate and diagnose Rosacea, Dr. Stein Gold, suggest that it is better to make transition from subtypes to phenotypes of rosacea.

The phenotypes are divided in 3 groups of symptoms:

- Diagnostic: fixed centro facial erythema, phymatous changes)
- Major: flushing, papules and pustules, teleangictasia, ocular manistation)
- Secondary: burning sensations, stinging sensations, edema, dryness)

Positive diagnosis of rosacea is performed by **one diagnostic phenotype** alone or **at least two major phenotypes**.

Also, there is a different amount of facial rednes in rosacea, and even, erythema can progress over the time from intermittent facial erythema (because of altered blood flow), early persistent facieal erythema (because of structural vascular changes) to advanced facial erythema (because of permanent dilatation of superficial vessels).

The sensitivity of rosacea skin is result of diminished skin barrier, with severe dryness, elevated pH, transepidermal water loss and decreased hydratation level, which is similar to that of affected skin in Atopic Dermatitis.

Rosacea is an inflammatory neurovascular disease with abnormalities in innate immune response with higher amount of Cathelicidin, and LL37 peptides, which have together pro-inflammatory chemotactic and angiogenic activities. Clinical picture of rosacea is also complicated by Demodex mites, and *Demodex folliculorum* was

detected in inflammatory rosacea, and *Demodex brevis* in mild rosacea. Demodex has influence on activation on specific receptors like TRPV-1, which promote cutaneus neurogenic inflammation.

Mast cells also participate in the pathophysiology of rosacea- in innate immune response, neurogenetic tranformation, vasodilatation, angiogenesis and fibrosis.

Use of tetracycline drug has antibiotic and non antibiotic influence, because they also have impact on inflammation and oxidative stess, and understanding of the pathogenesis of Rosacea is important to achieve better ways of rosacea treatment.

Rosacea, not just a skin disease

Prof. Dr. Martin Steinhoff (Doha, Qatar)

In rosacea patients, there are usually more comorbidites like neurological, psychiatric, gastro, endocrine, autoimmune, cardiovascular and rheumatological comorbidities.

Still, there is no sufficient diagnostic tool for rosacea patients.

The therapeutic challenges are:

- Pathohysiology based therapies
- Early control
- Prevention of phymata
- Improved laser and medical therapies.

Pathophysiology of rosacea is very complex, composed of genetic predisposition and trigger factors, which lead to inflammation. There are still many studies, which are *pro* or *contra* against the impact of Helicobacter pylori on rosacea.

It is very important to have better understanding of pathomechanisms and pathways of rosacea, so Prof. Steinhoff suggests more multicenter high scale studies which are still lacking.

Managing facial erythema in 2023

Prof. Eszter Baltas (Szeged, Hungary)

Prof. Baltas introduces that she will discuss about differential diagnosis of patients with facial erythema, and also about the treatment of facial erythema in rosacea. Erythema of the face can be persistent, as diagnostic feature, or transient (flushing), as major feature. Also it can be as perilesional erythema.

Persistent facial erythema can have many possible causes, like physiological (photoaging), or infectious, chronic inflammatory diseases, external factor triggered and autoimmune.

Rosacea like erythema can be also drug induced, se we have to think about the use of topical corticosteroids, topical calcineurin inhibitors and *dupilumab*.

It is suggested to look patient at all, if they have diseases of LE group or dermatomyositis.

In the treatment for Rosacea, it is recommended to use phenotype approach:

- For persistent erythema- topical *brimonidine*
- For moderate erythema- topical *oxymetazoline*

- For low-moderate erythema and teleangiectasia- laser and IPL
- For low erythema- tetracycline and low dose *minocicline*.

When patients use *brimonidine* or *oxymetazolin*, they have to be informed, that the results lasts about 12 hour after the applications. Sometimes, adverse reactions are possible like, paradoxical erythema, exaggered reccurence of erythema and allergic contact dermatitis occuring several months after the initiation of therapy.

For the treatment of the papules and pustules, it is reccomended to use local *ivermectin* 1% cream, because of antiinflammatory effect.

At the end of the lecture, Prof. Baltas concluded that current modalities provide symptomatic relief and there are no new drugs in the last few years. Energy and light-based devices are used widely and they are reliable.

Phenotype led combination treatment remain as gold standard, in the treatment of facial erythema in rosacea.

Emerging therapies in rosacea

Dr. Lucero Noguera (Madrid, Spain)

Dr. Nougera has discussed about new terapies in rosacea and especially in childhood rosacea. There is connection between skin and gastrointestinal tract, and new therapeutic options are still in trials .

Topical 10% *tranexamic acid* is used in erythemato-teleangiectatic rosacea, as plasmid inhibitor. It reduces mast cells count in the skin and supresses inflammatory biomarkers and angiogenesis.

In some trials there is a use of *botulin toxin* A as mesotherapy.

For papulopustular rosacea there is a trial with use of 1,5% *minocycline* foam.

From new therapies, there is an oral therapy with *sarecycline*, which is narrow spectrum third generation tetracycline class, and also antimalaric drug *hydrochloroquine* with anti-inflammatory actions.

There are also new clinical trials with new biologic therapy with *erenumab*.

For childhood rosacea diagnosis and treatment is challenge, and periorificial dermatitis are difficult to treat. 1% *ivermectin* cream is applied for 3-4 months, with good results and it is safe.

In conclusion, Dr. Nougera add that there are new options available for erythemato-teleangiectatic and papulopustular rosacea, topical and systemic. The combination approach should be the goal. For children, younger of 9 years of life, there are less options for treatment.

ECZEMAS: ATOPIC DERMATITIS

Speakers: Prof. Dr. Jan Gutermuth, Dr. Melinda Gooderham, Assoc. Prof. Valeria Aoki, and Dr. Bruno Duarte

Report written by Dr. Lucija Vanjaka-Rogošić

Pathophysiology of atopic dermatitis

Prof. Dr. Jan Gutermuth (Brussels, Belgium)

Atopic dermatitis (AD) is defined as chronic inflammatory dermatosis, characterised by phases of relapses and remissions. It is elicited by epidermal barrier abnormalities and chronic (Th2) inflammation. 10-15% of patients with AD (moderate to severe forms) require systemic treatment.

AD starts as combination of multiple dysregulated immune pathways. At the beginning we have barrier dysfunction, innate immune system activation and Th2-driven and Th22- driven inflammation, and variable Th 1 and Th 17 activation. Type 2 inflammation affects multiple organ involution, so in AD patients there is a possibility of food allergy, eosinophilic esophagitis, chronic rhinosinusitis, allergic rhinitis, asthma and eosinophiolic COPD (Chronic Obstructive Pulmonary Disease). Itch in AD is induced by cytokines, and increased expression of pruritogens like TSLP, Il-4, IL-13 and IL- 31is most important for induction of itch in AD.

Skin microbiome works as biomarker in AD. Diversity is good and prediction of healthy skin, so new attempts should be to therapeutically diversify skin and gut microbiome.

Phenotypes of atopic dermatitis

Dr. Melinda Gooderham (Peterborough, ON, Canada)

The goal of this lecture is to identify distinct atopic dermatitis (AD) phenotypes, subtypes and endotypes, depending on the approach.

AD is heterogeneous inflammatory skin condition and the diagnosis is clinical. Understanding AD phenotypes will help and lead to personalised treatments and achieve optimal outcomes.

Clinical phenotypes can be stratified by age of onset, race, morfology and topography.

Age of onset:

- Very early onset 60-80%
- Early onset
- Childhood onset 10%
- Adolescent onset less than 10%
- Adult onset 20%
- Very late onset

Race/ Ancestry: In all groups of races Th2 and Th 22 are positive, but in patienst with black skin Th1 and Th17 was absent.

Morphology:

- Classic presentation
- Nummular
- Papular/ follicular
- Lichenoid
- Prurigo nodularis
- Dishydrotic
- Erythrodermia

Topography of lessions:

- Classic distribution (flexural)
- Hand and foot
- Head and neck

- Facial/scalp
- Sensitive areas (eyelids, areolae, lips)

At the end, Dr. Gooderham concluded, that AD is a heterogeneous condition, which can be subtyped based on many factors. Understanding AD phenotypes and using biomarkers will aid in prognosis and individualized treatment approaches.

Topical and conventional systemic treatment for atopic dermatitis

Assoc. Prof. Valeria Aoki (Sao Paulo, Brazil)

In this lecture Assoc Prof. Aoki suggest when we will treat our patients with topical or systemic treatment for AD patients.

Initial treatment should be topical treatment with corticosteroids, before switching to a topical calcineurin inhibitors (TCI), to reduce risk of skin stinging and burning symptoms.

Proactive therapy (twice weekly application of TCI) is suggested to reduce risk of relapse and better disease control. Topical treatments with CPI are safe, only we can have worse response in those patients with low IgE levels.

For systemic tteetment of AD it is usually prescribed *cyclosporine* or *methotrexate*. *Cyclosporin* is most commonly prescribed, but *methotrexate* and oral corticosteroids are also frequently prescribed and used as first line systemic agents.

Cyclosporin has faster response, but *methotrexate* has better maintanance response after the treatment.

At the end of the lecture Assoc Prof. Aoki concluded that new target therapies are promising (monoclonal antibodies, small molecules JAK-is), and that ciclosporine and systemic corticosteroids are not indicated for AD long term treatment.

Managing atopic dermatitis with biologics and JAK inhibitors

Dr. Bruno Duarte (Lisbon, Portugal)

From 2017. there are new targeted and pathogenesis -based treatments. We can didvide them in biologics (*dupilumab* and *tralokinumab*), and JAK inhibitors (*baricitinib, upadacitinib, abrocitinib*).

Biologics blocks biologic actions of one or two cytokines. They are quite safe. Mild to moderate side effects are ocular surface disease- conjunctivitis and *dupilumab* associated head and neck erythema.

JAK inhibitors blocks a broader array of cytokines, and as side effects, we can find acne, hyperseborrhea, abdominal dysfunction and Herpes zoster.

Biologic prefered patients are those with greater risk for infections and malignancy, elderly, patients who have some other comorbidities, and females who have pregnancy plan. JAK inhibitors are suggested for those patients where we need very fast onset of actions.

At the conclusion it is suggested to choose together with your patient the systemic agent, that fits better to patients personal preferences and disease characteristics.

NON-ATOPIC ECZEMA

Speakers: Dr. Richard Brans, Md, PhD Marie-Louise Shuttelaar, Prof. Suzana Ljubojevic, and Prof. Luca Stingeni

Report written by Dr. Lucija Vanjaka-Rogošić

Hand eczema

Dr. Richard Brans (Osnabrück, Germany)

Hand eczema (HE) is non-contagious, inflammatory skin disease, located on the hands and covers different aethiologies and morphologies.

Hand eczema can be *acute* (last less then 3 consecutive months or occurs only once per year), and *chronic* (last more than 3 consecutive months or relapsesd more then 2 times per year).

Still there is no clear consensus about the clasiffication of HE. HE can have ***aetiology*** from atopic dermatitis, irritant contact dermatitis, allergic contact dermatitis and protein contact dermatitis. If we look ***morphology***, it can be hyperkeratotic HE, acute reccurent vesicular HE, nummular HE and pulpitis sicca (scaling and fissures on fingertips).

Average onset of HE is early to mid- twenties and it is more often seen in women. Occupational HE is the most common occupational disease, because hands are usually exposed to skin hazards (hairdressers, healthcare workers or construction and metal workers).

Dr. Brans suggests to take careful medical history including a search for personal and occupational exposures and also clinical examination of entire skin (feet!). The patch test should be performed in all patients with HE of more than 3 months duration, those who are nonresponsive to adequate treatment and those with clinical suspicion of contact allergy.

Biomarkers of HE are important to identify new targets of therapies, or predictive markers of treatment response.

In ***standard therapy of HE*** it is suggested to avoid clinically relevant allergens, to wear protective gloves, use of emolliens and health education. In ***almost clear HE*** it is recommended use of moderate topical corticosteroids, or tacrolimus ointment. In ***moderate HE*** it is reccomended to use moderate to potent topical corticosteroids, and as suggestion, also, tacrolimus ointment or photo-therapy. In ***severe/very severe HE***, it is reccomended to use moderate and potent topical corticosteroids, or Alitretinoin, which is only systemic drug licenced for HE, but not in all countries.

New therapeutic drugs like IL-4/IL-13inhibitors (*dupilumab*), and topical JAK inhibitors, like *degolcitinib, ruxolitinimib* and *tofacinitib*, are still in studies/trials.

In conclusion Dr. Brans suggest that managing of hand eczrema includes preventive measures and treatment depending on the severity of the disease.

Clinical spectrum of allergic contact dermatitis

Md, PhD Marie-Louise Shuttelaar (Groningen, Netherlands)

Allergic contact dermatitis (ACD) usually develops at the site of exposure, and in most obvious cases it is direct contact with allergen.

- In *bullous ACD* there are the episodes of blisters on exposed parts of the skin.
- In *airborne ACD* the allergens are transfered from the air and deposed on the skin. They are usually plant derived allergens, fragrances, colophony and epoxy.
- In *ectopic ACD* allergens are transmited form one side of the body to another (for example: nail polish can influence eyelid ACD).
- There is also *connubial/proxy dermatitis*, which has typical unilateral pattern, which we can use as indicator.
- *Fixed drug eruptions* are very common for some medications, like tetracyclines, NSAIDs, paracetampol, Sulphonamides, Barbiturates, Benzodiasepines).
- ACD- fingers in florist or dental tehnicians are typical as occupational ACD.
- Cheilits as ACD can be induced by toothpaste or cosmetics, and it is very frequent too.
- Shoe ACD has clinical features on the dorsum of foot and toes. Common allergens in shoes are rubber allergens, preservatives, shoe adhesives and leather materials.

ACD does not always present as eczema, so we have to think about it, if we have patients with bullous ACD, angioedema-like ACD, lichenoid ACD, ACD with pustular reaction, erythema multiforme-like ACD, ACD with purpuric or granulomatous reaction. Because of that, it is always suggested to perform patch testing.

Most relevant alleregens in 2023

Prof. Suzana Ljubojević (Zagreb, Croatia)

Contact sensibility and Allergic contact dermatitis (ACD) are not the same thing.

To have ACD we have to have a patient with contact sensitivity, dermatitis, **and** clinically relevant exposure to postive contact allergen. Patients medical history is very important.

Today we have lots of hypersensitivity reactions to home made products, because, lots of pepole think if they made cosmetics by themselves, it is healthier and with no chemicals. Lots of ACD comes from contact with lanolin, nickel, aluminum, acrylates/methacrylates as most common allergens in 2023.

We have to think about allergens which can be found in medical devices (Freestyle glucose sensor), or allergens in facial masks.

Also very common are Gaming/electronics dermatitis, which can be found in younger populations, who are in contacts with rubber compounds and plastics in gaming equipments.

It is important to point out the significance of patients history and allergen exposure, and big importance of the "patch" test.

Pitfalls of patch testing

Prof. Luca Stingeni (Corciano (PG), Italy)

Patch testing is gold standard in diagnosis of ACD. It is highly user dependent and many steps can influence final results.

Pitfalls of patch testing can be:

- false negative reactions
- false positive reactions
- patch test morphology

- special populations (children, pregnancy, breastfeeding).

The choice of patch test vehicle and patch test concentration are very important to perform good patch testing. Also, it is important to have at least two readings of tests, at D2, D3, D4 and D7. A second reading between D3 and D7 is essentia,l to detect most of the allergic reactions.

Use of topical corticosteroids, metals, neomycin, some dyes, acrylates and some preservatives can delay reactions in patch testing. The interpretation of positive reactions beyond day 7 is tricky, because it can reflect newly acquired sensitisation, rather than a delayed reaction to an existing allergy.

It is important too to thing about immunosupressive drug, because it is still not defined, how long is the duration of inhibition. Immunotherapies which targets TNF alfa and IL-12/IL-23, does not show inhibitory effect on patch testing.

If there is an active dermatitis, patch testing should be performed when dermatitis is quiescent, at least for one week. Chronic dermatitis of hands, feet and face, generally does not interfere with patch test results.

Excited skin syndrome or *Angry back syndrome* is defined as multiple concomitant positive reactions to patch testing. It is often induced by concomitant dermatitis, and pre-treatment with low dose of Cyclosporine for 7 days, may be used before further testing.

It is not reccomended to do patch trest in pregnant or lactating women for medico-legal reasons.

At the end, Prof. Stingeni conclude, that everybody can apply patch test, but for correct interpretation of test- an expert is required.

DERMOSCOPY PIGMENTED LESIONS

Speakers: Prof. Danica Tiodorovic, and Prof. Caterina Longo

Report written by Dr. Lucija Vanjaka-Rogošić

Early diagnosis of superficial spreading melanoma

Prof. Danica Tiodorović (Niš, Serbia)

Superficial spreading melanoma (SSM) is the most common type of melanoma, which usually affects younger demographic group of population and it participate as 60% of all cutaneous melanoma.

The risk location of SSM for males is back, and for females are lower extremities.

Dermoscopic pattern in SSM is multicomponent pattern with multiple colours (3 or more).

- Atypical pigment network
- Irregular dots or globules
- Blotches
- Irregular streaks/radial streaming
- Regression structures – white like-scar area/ peppering
- Blue white veil
- Homogenous structures

Dermoscopic features on early SSM:

- Atypical pigment network
- Irregular dots and globules
- Irregular streaks
- Homogenous areas

Prof. Tiodorović suggests that for early diagnosis of SSMwe should not focus on diameter. ABCD rule does not always work. It is suggested to perform complete body examination and try to look for subtle dermoscopy features.

Digital dermoscopy and total body photography in clinical practice

Prof. Caterina Longo (Modena, Italy)

At the beginning Prof. Longo suggest how to choose which type of patients are candidates for total body photography. It is recommended to follow up the patients with atypical mole syndrome (AMS) or Familiar melanoma multiple mole (FAMM).

We have to monitor lesions which shows:

- Asymmetric enlargement
- Occurence of regression structures
- Developement of new structures
- Small flat reticular lesions
- Lesions with globules which tend to grow and change faster

These patients should be followed the lifetime, beacuse of higher risk of developing of melanoma. On the other side, it is the fact, that the majority of melanomas occur "de novo" in 70% of the cases, and there were no precursor lesions.

New medical devices are really helpful, but still we have to bi critical to artifitial intelligence.

For conclusions, Prof. Longo pointed, that total body photography and digital monitoring should be offered to patient group, like AMS patients, Fammm syndrome patients and MN patients with a history of melanoma. New tools might help to standardize the procedure, and be faster in our offices.

For the end, life long regular surveillance is a key issue in the management of high risk patients.

BRAIN-SKIN AXIS: ITCH AND BEYOND

Speaker: Prof. Sonja Ständer

Report written by Prof. Mirjana Milinković Srećković

Prof. Sonja Ständer (Germany)

Prof. Ständer talked about the connection between scratching and brain. To illustrate the feeling induced by scratching, she has mentioned the experimental design they had previously done: two groups were formed, one group of people who were scratching without itch (no itch induced) and second group of patients who were scratching with itch (exp. cowhage-induced itch) in chronic pruritus patients (CP) and healthy controls (HC). The result was that CP group perceived scratching as pleasurable irrespective of the presence or absence

of cowhage-induced itch. Scratching alone has significantly elevated brain activity in CP *vs.* HC. In CP higher activity in brain regions involved in the reward system was detected by MRI. She has raised the question of addictive scratching observed in CP patients that was possibly inducing or contributing to neural hypersensation. She has shown the cycle of itch and scratching in which the addictive scratching is causing the activation of reward system, increases spinal pruritogen receptor expression, induces neuronal hypersensitivity and alters cutaneous neuroanatomy.

Dr. Ständer has also talked about the systematic review about brain and verbal instructions and concluded that verbal instructions may strongly influence the outcome expectations. Placebo and nocebo effects may modulate itch. Then she explained the brain and physiological parameter and gave the example of pharmacological conditioning, published in another systematic review that has shown the strong evidence that immune functions could be modulated through behavioral conditioning. For example, if cyclosporine was given with the taste stimulus (conditioning), re-exposure to the same taste stimulus only, has significantly reduced IL-2 levels (in PBMCs) even several days after the conditioning. Another example, that was recently published, involved brain and verbal instructions:

- Placebo effects: associated with brain regions involved in planning and emotion regulation can be evoked by expectations regarding treatment outcomes.
- Nocebo effects: associated with brain regions responsible for somatosensory itch processing.

Itch itself is stress, causes sleep loss and quality of life loss. Stress activates the hypothalamic-pituitary-adrenal (HPA) axis. It has been recently found that keratinocytes produced stress hormones (CRH, ACTH), which is exacerbated in psoriasis, for example. Then, Dr. Ständer explained the circle between mind and skin, exploring the links between inflammation, sleep disturbance and neurocognitive function in patients with atopic dermatitis. Placebo and nocebo provoke itch, which causes stress, HPA-axis and inflammation, influencing itch, depression and anxiety, scratching and reward system activation. Scratch itself, by neurosensitization and pruritogen upregulation, also influences reward system activation in the brain. And the circle geos on…

FOCUS ON NEW TECHNOLOGIES

Speakers: Dr. Josep Malvehy, and Prof. Marco Romanelli

Report written by Prof. Mirjana Milinković Srećković

Applications of artificial intelligence to dermatology

Dr. Josep Malvehy (Barcelona, Spain)

As the topic is modern and most probably, unknown to many dermatologists, firstly, some definitions were presented:

- Artificial intelligence (AI): study of intelligent agents; any device that perceives its environment and takes actions that maximize its chance of successfully achieving its goals. AI is program that can sense, reason, act and adopt.
- Machine learning (ML): field of study that explores the construction of algorithms that can learn from data. ML – algorithms whose performance improve as they are exposed to ore data over time.

- Deep learning (DL): subset of machine learning algorithms composed by neural network which learn from vast amount of data.

Then, impacted fields from the use of AI technologies in medical applications were presented:

1. Image-based diagnoses for radiology, dermatology, ophthalmology and pathology
2. Genome interpretation
3. Biomarker discovery
4. Inferring health status through wearable devices
5. Autonomous robotic surgery
6. Clinical outcome prediction
7. Patient monitoring

On site, in practice, the following procedures were suggested: natural language processing, avatars and deep imaging, sensors and biometrics, ML for complex analytics, generative AI, robotics for surgery and laser, drug delivery by nanotechnology, AI for monitoring the patients, AI for support for patients.

Deep phenotype and precision medicine are used in: demographics, clinical data, imaging, biosensors, genomic, transcriptomics, proteomics, metabolomics, microbiomics, epigenomics, exosomics, radiomics and dermatomics: "deep" imaging phenotype.

Many pictures of clinical and new combining multiple imaging techniques presentation of pigmented lesions were shown. After that, measurement of photoageing by linear confocal-OCT (LC-OCT) was presented in several different techniques. Then, non-invasive scoring of cellular atypia in keratinocyte cancers in 3D LC-OCT images using Deep learning was shown. Fascinating presentation of medical devices using non-invasive molecular analyses – adhesive patch biopsy easily performed was enough for objective gene expression assessment (not skin cancer *versus* skin cancer). Analyses of RNA in stratum corneum and epidermal genomic information retrieval (EGIR). Based on expression profiles of the long intergenic non-protein RNA 518 gene and the preferentially expressed antigen in melanoma gene (PRFAME) in skin tissue sample obtained *via* adhesive patch biopsies, can accurately classify pigmented skin lesions with a sensitivity of 92% and a specificity of 69%. All of this was not possible to imagine until recently. Natural language processing seems to become everyday simple use in near future.

Five current areas of applications for machine learning (ML) in dermatology are:

1. Disease classification using clinical/dermoscopy images
2. Disease classification using dermatopathology images
3. Assessment of disease using mobile applications and personal monitoring devices
4. Facilitating large-scale epidemiology research
5. Precision medicine

Machine learning comprises of deep learning – convolutional neural network (CNN), and statistical learning – natural language processing, support vector machine and random forest.

Then the experiment Man against Machine was described. Man against machine: diagnostic performance of a deep learning convolutional neural network for dermoscopic melanoma recognition in comparataion to 58 dermatologists. Also, comparation of the accuracy of human readers *versus* machine-learning algorithms for pigmented skin lesion classification, as and open, web-based, international, diagnostic study, with very good results.

There is as Task Force of AI of the EADV. "The mission of the AI Task Force is to influence, promote and develop this field within Dermatology and Venereology, to provide a mechanism for greater engagement of EADV

members in AI and links to existing subspecialty and other scientific and professional societies including the area of Health, Digital Health and other specialties". The aims are:

1. Creation of communication tools for the management of the Task Force, projects and dissemination
2. Education in AI for dermatologists, students, residents, patients, general public, computer scientists
3. Radar of AI groups/projects in Dermatology in Europe and worldwide
4. Collaborative research sand innovation in AI in Dermatology and Venereology
5. Position papers on AI in Dermatology. Analyses of the regulatory policies of software using AI (European directives set forth by the European commission)

At the end of the presentation, the skinScan medical device was shown. It is class 1 medical device (CE mark) for providing assisting information about pigmented skin lesions and skin self-examination. TeleSkin ApS aims to help people self-examine and track their moles. Proprietary algorithm helps users to identify atypical moles, with 90% sensitivity. It is available in Scandinavia for more than one year and it has been recently launched in Australia and New Zealand. There was a feedback from multiple users that the app helped them identify atypical moles which were problematic and further assessed by doctors as melanomas.

On the other hand, the paper that has been recently published in *JEADV - Position statement of the EADV Artificial Intelligence (AI) Task Force on AI-assisted smartphone apps and web-based services for skin disease*, has given the following key considerations: risk associated with inaccuracy and improper user education, decline in professional skills, the influence of non-medical commercial interests, data security, direct and indirect costs, regulatory approval and the necessity of multidisciplinary implementation. The main recommendations of the EADV AI Task Force are:

1. To ensure users trust, app developers should prioritize transparency in data quality, accuracy, intended use, privacy and costs
2. Apps and web-based services should ensure a uniform user experience for diverse groups of patients
3. European authorities should adopt a rigorous and consistent regulatory framework for dermatology apps to ensure their safety and accuracy for users.

When the use of AI will become widely accepted in practice, doctors could potentially be held liable for failing to use available software as and aid to diagnosis. Decisions of liability may become complex in situations where the clinician and software come to contradictory conclusions. So, these are important legal issues to think of, liability and responsibility.

Ultra-high-frequency ultrasound in hidradenitis suppurativa and wound management

Prof. Marco Romanelli (Pisa, Italy)

Prof. Romanelli has first divided the HS management into disease specific management and comorbidities specific management. He has shown the ultrasound skin lab in Pisa, Italy. They have high-frequency ultrasound (HFUS) 18-22 MHZ and ultra-high-frequency ultrasound (UHFUS) >30 MHz (48-70 MHz) devices. The ultrasound criteria for diagnosing HS were given (at least 3 findings are needed):

1. Widening of hair follicles
2. Thickening and/or abnormal echogenicity of the dermis
3. Dermal pseudocysts nodules
4. Fluid collections
5. Fistulous tracts

He reminded the public of the clinical-sonographic scoring system (SOS-HS):

- Stage I - single fluid collection and dermal changes (hypoechogenic of anechoic pseudocysts, widening of hair follicles, altered dermal thickness); involvement of a single body area i.e. axilla, groin, breast, buttock (unilateral or bilateral); no fistulous tracts.
- Stage II - between 2 and 4 fluid collections or a fistulous tract with dermal changes; involvement of 1 or 2 body areas (unilateral or bilateral).
- Stage III – five or more fluid collections or at least 2 fistulous tracts, with dermal changes or involvement of more body areas (unilateral or bilateral).

Then, Prof. Romanelli has shown many pictures of the clinical, ultrasound and histopathology correlation, using different frequencies of both HFUS and UHFUS devices for early diagnosis of HS. After that, he discussed the objective HS assessment and compared the clinical and ultrasound evaluation. Underestimation of severity and challenging descriptions of the lesions are seen by clinical evaluation. On the other hand, ultrasound evaluation shows a higher inter-rater correlation than clinical scores such as Hurly staging, modified Sartorious scoring and abscess and nodule counts. Restaging form Hurly I to stage II or III in 44, 7% of patients was found, leading to change of treatment plans. Considering ultrasound and the plan for HS treatment, it was shown that there was a change in clinical treatment in 82% and switch for medical to surgical management in 24%. Also, Color Doppler US can modify HS management in more than 80% of patients. Patients should not have their treatment suspended on the basis of clinical examination alone. So, the role of US is important in medical treatment monitoring. Finally, he has shown the significance of US in pre surgical / laser mapping. In US-guided surgical excision the recurrences risk was lower.

In conclusion, Prof. Romanelli noted: clinical examination alone can underestimate the severity of HS; US criteria give us early and more precise diagnosis and staging of HS; US drives treatment choice and treatment monitoring; US makes the HS therapy more effective; US is operator dependent and requires specific training in HS.

PSORIASIS

Speakers: Prof. Wolf-Henning Boehncke, Prof. Carle Paul, Prof. Paolo Gisondi, and Prof. Evangelia Papadavid

Report written by Prof. Mirjana Milinković Srećković

Early detection and prevention of psoriatic arthritis

Prof. Wolf-Henning Boehncke (Geneva, Switzerland)

Psoriatic arthritis (PsA) is a multi-facetted disease, making diagnosis difficult. Prof. Boehncke first talked about GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) criteria and treatment schema for PsA. It is important to consider which domains are involved, what is patients preference, what are previous or concomitant therapies that patient has… and to make a choice of therapy that should address as many domains as possible. The domains are: Peripheral arthritis, axial disease, enthesitis, dactylitis, psoriasis (skin/scalp), nail disease, inflammatory bowel disease (IBD) and uveitis. Comorbidities and associated conditions may impact choice of therapy and/or guide monitoring. The advice is to treat, periodically re-

evaluate treatment goals and modify therapy as required. PsA and axial disease can affect one or more or the six clinical domains recognized by GRAPPA.

It is important to psoriatic patients for PsA. The question is whom to screen most attentatively. He gave 3 answers:

1. patients with increased risk for PsA,
2. psoriasis with asymptomatic synovio-entheseal imaging abnormalities, and
3. psoriasis with MSK symptoms not explained by other diagnosis.

Increased risk factors for PsA are: nail psoriasis, first-degree relative with PsA, severe psoriasis, arthralgias, history of uveitis, obesity, scalp psoriasis, second-degree relative with PsA, ≥ 1 validated susceptibility gene.

MRI signs of asymptomatic synovio-entheseal imaging abnormalities are: enthesitis, bone marrow edema, synovitis, tendonitis, erosions and new bone formation. Ultrasound (US) signs are: ehthesitis, synovitis, tendonitis and erosions.

Symptoms not explained by another diagnosis are: heel pain, stiffness and arthralgias.

He discussed the use of ultrasound (US) by dermatologist. Despite the wide use of US in PsA, more research is needed to identify predictive factors of progression to PsA in patients with psoriasis, as well as to determine most specific US features that differentiate PsA from other conditions. Establishment and validation of a didactic musculoskeletal US course for dermatologists using an innovative handheld ultrasound system – the MUDE study (Musculoskeletal ultrasound in dermatology). Then, he showed the fluorescence-optical imaging as a promising easy-to-use imaging biomarker to increase early PsA detection in patients with psoriasis.

The evolving EULAR (European League Against Rheumatism) concept is to define clinical and imaging features of patients suspicious to progress from PsO to PsA. The objective if to find a therapeutic intervention to attenuate, delay, or prevent PsA development. Biologics have been shown to delay PsA when compared to topicals, phototherapies, and csDMARDs (published 2023).

In summary, Prof. Boehncke pointed out the following:

1. Presence and type of PsA directly influence therapeutic decision-making
2. PsA is a multi-facetted disease, making diagnosis difficult
3. Early diagnosis and initiation of treatment improve the prognosis
4. There is currently no alternative to clinical assessment when it comes to diagnosing PsA early
5. Preventing PsA remains “science fiction” at this point in time (but should remain the ultimate goal)
6. **Call for action:** to screen your PsO patients regularly for PsA (questionnaires); do initiate evidence-based therapy early (see GRAPPA or EULAR recommendations); look out for “red flags” (nail involvement, PsO severity, obesity, positive family history)!

Approach to psychological burden of psoriasis

Prof. Carle Paul (Toulouse, France)

Dr. Paul talked about psychological suffering of patients with psoriasis. They have been stigmatized all around the world, in all societies, both adults and children. How do patients verbalize their suffering? They feel anxious and ashamed, fatigue, low self-esteem, emotionally puzzled, they feel like thy are in the war with their skin, disfiguring, difficult to cope with, restriction to clothing, leisures and other activities, social isolation, they avoid

intimate relationships… He has shown the results of the research of higher psychological burden to patients with PsO comparing to various other skin diseases. Recent large European research reviled the highest level of stigmatization with psoriasis, vitiligo and alopecia areata. Considering impact of psoriasis on social relationships, patients reported feeling stared at (84%), worry and feel guilty about possibly passing PsO on their children (76%), prefer not to be seen in public during a flare (74%), reported covering PsO with long clothing (64%), reported feeling like an outcast (48%), reported reluctance to engage in casual physical contact (eg. shaking hands, embracing) (30%), even reported being asked to leave public pools or gyms (20%). Then, Dr. Paul gave a very instructive example from his practice.

He raised the question how to approach the psychological burden of psoriasis. Important things are:

1. physician caring attitude,
2. patient education programs,
3. motivational interview, and
4. psychotherapeutic approach.

Elements of a caring consultation are:

- to practice mindfulness: center yourself and be "fully present",
- to sit down and maintain eye contact and smile,
- to listen with focus attention,
- to be positive and avoid negative words,
- to be prepared to be vulnerable and human,
- to inquire about the patient goals and aspiration,
- to seek to understand the social context of the patient and what give them joy and meaning.

Patient education programs for psoriatic patients should be individual and /or group sessions to address disease mechanism, clinical course, impact, treatment, coping strategies, comorbidities; physicians, nurses and psychologists should be involved; programs should be variable in content and intensity; they can improve patient-well-being, quality of life, self-confidence and disease knowledge. Empowering patients to take responsibility for psoriasis control is of high importance. Structured patient educational programs improve their knowledge, confidence and adherence to treatment.

Motivational interview should have the following principles: listening to the patient, avoiding the righting reflex, supporting the patient, exploring and understanding the patient's motivation and ask open questions.

Psychotherapeutic approach to psoriasis patients comprise of: psychodynamic approach, cognitive-behavioral therapy and mindfulness-biofeedback relaxation. There are the evidence from randomized controlled trials that mindfulness and meditation or cognitive and behavioral therapy leads to:

- improvement of PASI/SaPASI and DLQI *versus* control in some trails;
- improvement of stress, anxiety only in a minority of trials;
- no significant effect on depressive symptoms. The issue is with small sample size, methodological heterogeneity and attrition rate.

In conclusion, Prof. Paul pointed out that psychological burden of psoriasis consists of: grief and loss, impaired quality of life and well-being, stigmatization; anxiety, depression, sleep disturbance, alexithymia, social isolation; addictive behavior (smoking, alcohol, eating disorders). As caring physicians, we have the power to support the patient positively and to empower them to restore hope and self-confidence, regaining freedom and happiness.

At the end, there was a fruitful discussion on the need of dermatologist to gain proper education to help their patients to properly cope with their burden of psoriasis.

Management of cardio-metabolic comorbidities

Prof. Paolo Gisondi (Verona, Italy)

Prof. Gisondi started his presentation with psoriatic patient from his practice who had serious metabolic syndrome and depressive disorder. He defined metabolic syndrome (MS) as having at least 3 of the following components: elevated waist circumference (>88 cm for women and > 102 cm for men), elevated triglycerides (> 150 mg/dL), low HDL cholesterol (< 40 mg/dL for men and < 50 for women), arterial hypertension, elevated fasting glucose (≥ 100 mg/dL). Prevalence of MS in patients with PsO is at least double at the age from 30 to 60 years, compared to controls. Non-alcoholic fatty liver disease (NAFLD) encompasses a wide range of fatty liver disease in the absence of significant alcohol intake (2-3 drinks or fewer daily) and other common causes of hepatic steatosis (viral hepatitis medications). It is idiopathic, associated to insulin resistance and metabolic syndrome or secondary to gastrointestinal disease, drugs, infection or environmental toxic agents. Prevalence of NALFD is 15-25% in the general population, but > 40% in obese or diabetic patients. Prof. Gisondi has also mentioned a new definition for metabolic dysfunction-associated fatty liver disease (an international expert consensus statement) in the context of obesity, or normal weight, or type 2 diabetes, leading to metabolic dysfunction-associated fatty liver disease (MAFLD). It is important to detect hepatic steatosis early by imaging techniques, blood biomarkers/scores or by liver histology. The studies have shown nearly two times higher odds of prevalent NAFLD in PsO patients compared to non-PsO individuals, as well as higher prevalence in PASI≥10 than PASI<10.

Then, Prof. Gisondi has raised the question Why this association and has shown the insights in the pathogenesis. Inflammatory mediators released from psoriatic lesions may have systemic effects. Cytokines (TNF-α, IFN-α, IFN-γ, IL-1, IL-6, IL-17) influence the liver (homocystein, CRP, fibrinogen increase), adipose tissue (chemerin, leptin, resistin, LDL, TG increase, but adiponectin and HDL decrease) and skeletal muscle (insulin resistance), which all leads to endothelial dysfunction and atherosclerosis. Psoriatic inflammation could favor the progression from normal liver to NAFLD.

The next question has raised was about the influence of MS to the treatment selection for psoriasis. Prof. Gisondi talked about adverse effects of different systemic therapeutics on dyslipidemia, arterial hypertension, obesity, glucose intolerance/diabetes, liver disorders, ulcerative colitis… What are preferred systemic agents in obese patients? Infiximab and ustekinumab are dosed based on weight and are ideal to treat PsO in obese patients. IL-17 inhibitors are highly effective regardless of a patient's weight, but are shown to have even better clearance rates in non-obese patients. Apremilast can be used favorably in obese because weight loss is noted side effect of this drug. Methotrexate carries a higher risk of fatty liver and hepatic fibrosis in obese patients. Acitretin and cyclosporine need to be used in higher doses in obese, leading to a higher incidence of side effects and potential toxicity.

In conclusion, Prof. Gisondi has noted that moderate to severe PsO is frequently associated to metabolic disorders that represent a cardiovascular risk factor. Making the clinical decision of selecting the treatment should consider several factors including: PsO severity and localization; comorbidities including cardiometabolic; impact of PsO on quality of life.

Management of challenging sites

Prof. Evangelia Papadavid (Athens, Greece)

Prof. Papadavid pointed the prevalence of PsO at special/important/challenging sites: scalp 45-56% (itching, bleeding, embarrassment and limited choice of clothing), face 50% (highly visible, may lead to impaired vision,

hearing and chewing/swallowing), intertirginous regions 21-30% and genital 30-40% (itching, irritation, soreness and decreased sexual health), palms and soles of feet 12-16% (pain, difficulty in walking and using hands), nails 23-27% (pain, physical impairment and cosmetically disturbing). Additionally, psoriasis in nails, scalp and intertriginous regions correlates with increased risk of psoriatic arthritis (PsA). All of those are associated with symptoms and decrease quality of life. They have disproportionally higher physical and psychological burden.

Psoriasis in challenging sites can be under or misdiagnosed. Initial diagnosis of regional PsO can be difficult. There are low physician awareness and patient reluctance. Misdiagnosis for other dermatoses is not uncommon (scalp – seborrheic dermatitis, face – rosacea, intertiginous regions – dermatitis, erythrasma, palms and soles – eczema, genital area – infection, nails – onychomycosis).

Prof. Papadavid showed recommendations on management of challenging sites. First, practical treatment algorithm for scalp PsO, published in 2021. Irrelevant to the severity of scalp PsO, when topical treatment fails, we should upgrade to systemic therapy. Then she has shown GRAPPA clinical treatment algorithm of nail PsO. They now promote biologics as a fist-line-option in patients with nail psoriasis. She showed examples form her practice and talked about real world evidence from the use of secukinumab in specific sites. After that, she presented the study showing guselkumab demonstrating higher long-term efficacy in skin clearance by body regions *versus* secukinumab. Again, she presented cases from clinical practice. Then she demonstrated the efficacy of risankizumab in treatment of nail, scalp and palmoplantar PsO. Optimum results are achieved in bio naïve patients. This is very important for early treatment optimization. In conclusion, from RWE the best treatment options for challenging sites seem to be IL-17 and IL-23 inhibitors.