6th INDERCOS ONLINE CONGRESS

11 - 14 March 2021

Integrative Dermatology and Technology in Dermatology

FULL TEXT CONGRESS BOOK

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Integrative Dermatology and Technology in Dermatology

11 March Thursday		12 March Friday		13 March Saturday		14 March Sunday	
09:00-09:15	OPENING SPEECH & LECTURE	**09:00-09:50**	INFECTIVE SKIN DISEASES	**09:00-10:10**	DERMATOSCOPY SESSION-2	**09:00-10:40**	SESSION: ADVANCED TECHNOLOGIES IN DERMATOLOGY
09:30-11:10	ERCIN OZUNTURK SESSION (AESTHETIC DERMATOLOGY)-1	**10:05-11:45**	INVESTIGATIVE DERMATOLOGY-2	**10:25-10:45**	TRICHOSCOPY COURSE	**10:55-12:25**	SESSION: GENERAL DERMATOLOGY 3
11:25-12:45	INVESTIGATIVE DERMATOLOGY-1	**12:00-13:00**	DEBATABLE TOPICS FOR DERMATOLOGIC THERAPY	**11:00-12:00**	SESSION: ORPHAN DISEASES IN DERMATOLOGY	**12:25-12:55**	LUNCH
12:45-13:15	LUNCH	**13:00-13:30**	LUNCH	**12:15-12:45**	LUNCH	**12:55-14:05**	INVESTIGATIVE DERMATOLOGY-3
13:15-14:25	DERMATOSCOPY SESSION-1	**13:30-14:50**	SESSION: SYSTEMIC TREATMENT IN DERMATOLOGY-1	**12:45-14:15**	TOPICAL TREATMENT IN DERMATOLOGY	**14:20-15:30**	DIET AND ALTERNATIVE THERAPY FOR DERMATOLOGIST
14:40-15:40	SATELLITE NOVARTIS | Reimagining Medicine	**15:05-16:05**	SATELLITE Pfizer Pfizer PFE İlaçları	**14:30-15:30**	SATELLITE NOBEL	**15:35-16:35**	BREAK
15:55-17:35	ERCIN OZUNTURK SESSION (AESTHETIC DERMATOLOGY)-2	**16:20-17:50**	ERCIN OZUNTURK SESSION (AESTHETIC DERMATOLOGY)-3	**15:45-16:25**	NAIL SURGERY SESSION	**16:40-17:20**	PSORIASIS
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				20:05-21:55	ERCIN OZUNTURK SESSION (AESTHETIC DERMATOLOGY)-4	**20:45**	CLOSING SPEECH AND LECTURE WHAT'S NEW IN VITILIGO 2020

11 March Thursday

09:00 - 09:15	**OPENING SPEECH & LECTURE** ***A new era in Integrative Dermatology / Katlein Franca***	
09:30 - 11:10	**ERCIN OZUNTURK SESSION (AESTHETIC DERMATOLOGY)-1** ***Chairs: Pertevniyal Bodamyalı, Sadiye Kuş***	
	Survivin in dermatology	*Elif Cömert*
	Exosoms in dermatology	*Sevda Önder*
	Microneedling combined procedures in aesthetic dermatology	*Mehmet Can Emeksiz*
	Inflamm-aging in skin: Update	*Sadiye Kuş*
	Liquid collagen: Where are we now for dermatology?	*Semahat Alp*
	Ceramides and skin	*Semahat Alp*
	Beta-carotene/Astaxanthin/CoenzymeQ10 and dermatology	*Seray Külcü Çakmak*
	Zinc/Selenium and skin	*Deniz Demirseren*
	Shock waves in aesthetic dermatology	*Pertevniyal Bodamyalı*
	HIFEM in aesthetic dermatology	*Pertevniyal Bodamyalı*
11:25-12:45	**INVESTIGATIVE DERMATOLOGY-1** ***Chairs: Özgür Gündüz, Habibullah Aktaş***	
	Mitochondrial DNA and dermatology	*Özgür Gündüz*
	Aquaporins in dermatology	*Özgür Gündüz*
	Integrins / HIF1alpha / VEGF / PAI1 in dermatology	*Yasemin Yuyucu Karabulut*
	Cytokines and chemokines in dermatology	*Birgül Özkesici Kurt*
	Differences between B and T cells	*Seçil Vural*
	Nod2: The intestinal gate keeper in dermatology	*Büşra Altun Deniz*
	Transepidermal elimination in dermatology	*Gökşen Ertuğrul*
	Nobel Prize of Aziz Sancar and Dermatology	*Habibullah Aktaş*
12:45-13:00	**RATIONAL USES OF MEDICINE**	*Özgür Gündüz*
13:00-13:15	**LUNCH**	
13:15-14:25	**DERMATOSCOPY SESSION-1** ***Chairs: Mustafa Turhan Şahin, Fezal Özdemir***	
	Inflamoscopy: Basics and beyond	*Paweł Pietkiewicz*
	Dermoscopy in acral lesions	*Fezal Özdemir*
	Facial pigmented lesions: Make it simple!	*Ömer Faruk Elmas*
	Dermoscopy in melanoma: What's new?	*Tuğba Kevser Uzunçakmak*
	Mucoscopy: What we know ?	*Mustafa Turhan Şahin*
	Dermoscopy in adnexal lesions	*Aylin Türel Ermertcan*
	Onychoscopy in non-pigmented nail lesions	*Herman Mayısoğlu*

11 March Thursday

14:40-15:40	**SATELLITE SYMPOSIUM**	
	How AWARE are we about chronic urticaria treatment? NOVARTIS | Reimagining Medicine **Moderators:** *Emek Kocatürk, Kemal Özyurt*	
	24-month outcomes from the multicenter observational study AWARE	*Marcus Maurer*
	Real world outcomes with omalizumab treatment in CSU from Turkey	*Nida Kaçar*
15:55-17:35	**ERCIN OZUNTURK SESSION (AESTHETIC DERMATOLOGY)-2** ***Chairs: Gaye Sarıkan, Filiz Kuşak***	
	Face shapes and cosmetical approaches	*Gökçe Işıl Kurmuş*
	Off-label uses of HA fillers in aesthetic dermatology	*Hilal Gökalp*
	Ageism in aesthetic dermatology	*Ayşe Ferzan Aytuğ*
	Diet and aesthetic dermatology	*Gaye Sarıkan*
	BDDA: Myths and facts in aesthetic dermatology	*Pelin Üstüner*
	Botulinum toxins for nasel area problems	*Filiz Kuşak*
	The skin aging exposome	*Selda Pelin Kartal*
	Epidemiology of cosmetic procedures in dermatology	*Selda Pelin Kartal*
	A Holistic approach to skin aging	*Şükran Sarıgül Güdük*
	Periorbital hyperpigmentation: Etiology, medical evaluation and treatment	*Filiz Kuşak*
17:50-18:40	**SESSION: SUN, LIGHT, VITAMIN D AND THE SKIN** ***Chairs: Işıl İnanır, Mustafa Tunca***	
	Sunscreens: What's new?	*Işıl Bulur*
	Do sunscreens prevent vitamin D sythesis?	*Armağan Kutlay*
	New vitamin D analogues in dermatology	*Mustafa Tunca*
	Does phototherapy cause cancer?	*Algün Polat Ekinci*
	What's new in phototherapy?	*Işıl İnanır*
	Discussion	
18:55-19:25	**ATOPIC DERMATITIS** ***Chairs: Marcus Maurer, Kemal Özyurt***	
	Type II inflammation and its role in atopic dermatitis and beyond	*Marcus Maurer*
	Emerging treatments of atopic dermatitis	*Torsten Zuberbier*
	The role of allergens in atopic dermatitis	*Maryam Khoshkhui*
19:40-21:10	**SESSION: PIGMENTATION DISORDERS AND SKIN CANCERS** ***Chairs: Rafet Koca, Emine Çölgeçen***	
	Integrative approaches of vitiligo	*Abdullah Demirbaş*
	Integrative approaches of melasma	*Emel Hazinedar*
	Integrative approaches of skin cancers	*Mahmut Sami Metin*
	Lipoma: Causes, symptoms, diagnosis and treatment	*Gözde Emel Gökçek*
	Piezogenic pedal papules: Etiology and treatment	*Emine Müge Acar*
	Xanthelasma: What is new?	*Gözde Emel Gökçek*
	Bowen disease: Update	*Aslı Şahin*
	Novel modalities in keloid and hypertrophic scars	*Pelin Ertop Doğan*
	Discussion	

12 March Friday

09:00-09:50	**INFECTIVE SKIN DISEASES** ***Chairs: Bengü Gerçeker Türk, Belkız Uyar***	
	COVID-19 and skin	*Bengü Gerçeker Türk*
	COVID-19 and urticaria	*Emek Kocatürk*
	Molluscum contagiosum: What's new?	*Ayşin Köktürk*
	Integrative approaches of superficial fungal infections	*Belkız Uyar*
	Discussion	
10:05-11:45	**INVESTIGATIVE DERMATOLOGY-2** ***Chairs: Ömer Kutlu, Betül Şereflican***	
	Mechanoreceptors in dermatology: An overview	*Emin Gündüz*
	Skin aging and epigenetics (Anti-aging genes)/SIRT1: As antiaging	*Emin Gündüz*
	Cellular oxygen sensor systems in skin	*Begüm Ünlü*
	Follistatin/activin a and skin/hair	*Begüm Ünlü*
	Biological rhythms in the skin	*Pelin Ertop Doğan*
	Human 3D skin models	*Neslihan Fişek İzci*
	ELISA in dermatology	*Betül Şereflican*
	Free fatty acids in dermatology	*Hülya Süslü*
	TGF-beta and Dermatology	*Ömer Kutlu*
	CCR-5 in dermatology	*Ömer Kutlu*
12:00-13:00	**DEBATABLE TOPICS FOR DERMATOLOGIC THERAPY** ***Chair: Arzu Kılıç***	
	How long should biologics treatments be used?	*Zeynep Topkarcı*
	Do biologics cause cancer?	*Nida Kaçar*
	Whats the new approach for antifungal therapy?	*Arzu Kılıç*
	If superbugs are monster, how can we prevent them when using antibiotics?	*Melek Aslan Kayıran*
	Discussion	
13:00-13:30	**LUNCH**	
13:30-14:50	**SESSION: SYSTEMIC TREATMENT IN DERMATOLOGY-1** ***Chairs: Özlem Su Küçük, Didem Didar Balcı***	
	Postmodern treatments in dermatology	*Tuğba Özkök Akbulut*
	Does metformin really works in dermatology?	*Asude Kara Polat*
	Adaptive immunotherapy in dermatology	*Sibel Doğan*
	Immun checkpoint inhibitors and dermatology	*Didem Didar Balcı*
	EGFR inhibitors and skin	*Sezgi Sarıkaya Solak*
	Dupilumab in dermatology: Indications and adverse events	*Özlem Su Küçük*
	Discussion	

12 March Friday

15:05-16:05	**SATELLITE SYMPOSIUM**	*Pfizer PFE İlaçları*
	A Comprehensive Approach to Superficial Fungal Infections	*İlteriş Oğuz Topal*
16:20-17:50	**ERCIN OZUNTURK SESSION (AESTHETIC DERMATOLOGY)-3** ***Chairs: Zehra Aşiran Serdar, Berna Aksoy***	
	Periorbital wrinkles: Etiology and treatment	*Zehra Aşiran Serdar*
	Acoustic waves in aesthetic dermatology	*Zahide Eriş*
	Low-level laser treatment in dermatology	*Zahide Eriş*
	Cryolipolysis: What is new?	*Hasan Mete Aksoy*
	Smoking and skin aging	*Berna Aksoy*
	Endermologie in aesthetic dermatology	*Hasan Mete Aksoy*
	Alpha-and beta-hydroxy acids in dermatology	*Aslı Tatlıparmak*
	Fractional photothermolysis in aesthetic dermatology	*Filiz Canpolat*
	Hyaluronon and skin	*Filiz Canpolat*
18:05-19:05	**SESSION: ALLERGY AND PRURITUS-1** ***Chairs: Ümit Şahiner, Oktay Taşkapan***	
	Nocturnal pruritus in children	*Ümit Şahiner*
	Nocturnal pruritus in elder	*Oktay Taşkapan*
	Integrative approaches of pruritus	*Zafer Türkoğlu*
	Integrative approaches of urticaria and drug allergy	*Murat Türk*
	Integrative approaches of atopy	*Murat Türk*
	Discussion	
19:20-20:00	**DERMATOLOGIC SURGERY SESSION** ***Chairs: Emel Fetil, Amor Khachemoune***	
	Skin biopsy techniques	*Tamer İrfan Kaya*
	Advanced surgical suturation techniques in dermatological surgery	*Eckart Haneke*
	Basics of flaps and grafts in dermatological surgery	*Amor Khachemoune*
	Cryosurgery and electrosurgery: Widen your horizon	*Tuğrul Dereli*
20:15-21:25	**POPULAR** ***Chairs: Emel Erdal, Meltem Önder***	
	Physician burnout and mental stress in pandemia	*Emel Erdal*
	Panel or manel/sex discrimination in dermatology congress	*Meltem Önder*
	Predatory publishing and congress in dermatology	*Vildan Manav*
	Myths and facts in dermatology	*Müge Göre Karaali*
	Pioneers in dermatology	*Mahmut Can Koska*
	Financial toxicity in dermatology	*Gonca Saraç*
	Discussion	

13 March Saturday

09:00-10:10	**DERMATOSCOPY SESSION-2** ***Chairs: Şirin Yaşar, Ercan Arca***	
	Dermoscopy in non-melanoma skin cancers: What's new?	*Ercan Arca*
	Black, red and green: Siascopy	*Ahmet Metin*
	Dermoscopy: widen your horizon!	*Cüneyt Soyal*
	Dermoscopy: A game changer in management of multiple nevi	*Gamze Erfan*
	Onychoscopy in pigmented nail lesions	*Şirin Yaşar*
	Dermoscopy in infectious skin diseases	*Ersoy Acer*
	Discussion	
10:25-10:45	**TRICHOSCOPY COURSE** ***Chairs: Ömer Faruk Elmas, Haitham Donia***	
	Trichoscpy of patchy alopecia (clues & algorithms)	*Haitham Donia*
11:00-12:00	**SESSION: ORPHAN DISEASES IN DERMATOLOGY** ***Chairs: Deniz Yücelten, Aslı Kaptanoğlu***	
	Syndromes associated with palmoplantar keratoderma	*Deniz Yücelten*
	Syndromes associated with ichthyosis	*Deniz Akkaya*
	Orphan drugs in dermatology	*Nazan Emiroğlu*
	Orphan tests and diagnostic approaches in dermatology	*Aslı Kaptanoğlu*
	Syndromes associated with hair and nail problems	*Aslı Bilgiç*
	Discussion	
12:15-12:45	**LUNCH**	
12:45-14:15	**SESSION: TOPICAL TREATMENT IN DERMATOLOGY** ***Chairs: Aslı Hapa, Göknur Kalkan***	
	Topical "jump start" therapies in dermatology	*Pelin Eşme*
	Are they immortality formulas: Resveratrol and rapamycin	*Şule Güngör*
	Hypericin-the facts about a controversial agent	*Gülşen Tükenmez Demirci*
	Topical brimonidine in dermatology	*Burçe Can*
	Vinegar in dermatology	*İlteriş Oğuz Topal*
	5-FU in dermatology	*Esra Ağaoğlu*
	Topical timolol and nifedipine in dermatology	*Hasan Aksoy*
	Topical JAK inhibitors and skin	*Aslı Hapa*
	Discussion	
14:30-15:30	**SATELLITE SYMPOSIUM**	
	Görünenin Ötesindeki Güçlü Seçenek Beksar JEL **Moderator*: Dilek Bayramgürler***	NOBEL *İlkin Zindancı* *Dilek Bayramgürler*
15:45-16:25	**NAIL SURGERY SESSION** ***Chairs: Eckart Haneke, Necmettin Akdeniz***	
	Ingrown nail: Non-surgical approach	*Gülru Erdoğan*
	Ingrown nail: Surgical approach	*Necmettin Akdeniz*
	Biopsy in nail disorders: When and how?	*Fatih Göktay*
	Surgical principles in nail unit tumors	*Eckart Haneke*

13 March Saturday

16:40-17:40	**PSORIASIS-1** ***Chairs: Sibel Alper, Tomasz Hawro***	
	Psoriasis and itch	*Tomasz Hawro*
	Stigmatization in patients with psoriasis	*Tomasz Hawro*
	Social and psychological impacts of psoriasis	*Sibel Alper*
	Psoriasis and alopecia	*Filiz Topaloğlu Demir*
	Nail-lacquers in dermatology	*Mahmut Sami Metin*
	Discussion	
17:55-18:35	**SESSION: UCARE** ***Chairs: Luis Felipe Ensina, Kemal Özyurt***	
	Emerging therapies in urticaria: What's new?	*Emek Kocatürk*
	Urticaria and comorbidities: What's new?	*Luis Felipe Ensina*
	Biologic markers in urticaria: What's new?	*Andaç Salman*
	Following the latest guideline in 2021: What's new?	*Ragıp Ertaş*
18:50-19:50	**SEBACEOUS GLAND DISEASES: DEBATABLE ISSUES FOR DERMATOLOGIST** ***Chairs: Bodo Melnik, Ayşe Serap Karadağ***	
	Which came first? The chicken or the egg?: The rosacea or the demodex situation	*Seray Külcü Çakmak*
	Which is better for HS: The surgery or the medical treatment	*Algün Polat Ekinci*
	Is diet important for acne?	*Sezgi Sarıkaya Solak*
	What is discussed in 2021 on isotretinoin therapy	*Ayşe Serap Karadağ*
	The role of FoxO1-GATA6 signaling in acne pathogenesis and treatment	*Bodo Melnik*
	Discussion	
20:05-21:55	**ERCIN OZUNTURK SESSION (AESTHETIC DERMATOLOGY)-4** ***Chairs: Ahu Birol, Ömür Tekeli***	
	Laser, HIFU and RF treatments in hyperhidrosis	*Ahu Birol*
	Inflammatory skin diseases (psoriasis, acne and seborrhea) and botulinum toxins	*Melike Kibar Öztürk*
	Understanding the differences of emollient, moisturizer and humectant in dermatology	*Melike Kibar Öztürk*
	Picosecond lasers in dermatology	*Ömür Tekeli*
	Gummy smiles and treatment	*Hüray Hügül*
	Visual loss in aesthetic dermatology	*Hüray Hügül*
	Tears trough problems and fillers	*Hüray Hügül*
	Retaining ligamants of face in aesthetic dermatology	*Filiz Kuşak*
	Fat pads of face and aesthetic dermatology	*Zekai Kutlubay*
	Can we analyse skin aging by blood markers?	*Mehmet Melikoğlu*
	Blepharoplasty for dermatologist	*Alp Kayıran*

14 March Sunday

09:00-10:40	**SESSION: ADVANCED TECHNOLOGIES IN DERMATOLOGY** ***Chairs: Tamer İrfan Kaya, Emin Özlü***	
	Simulation models in dermatology education	*Emin Özlü*
	eHealth technologies in dermatology	*Duygu Erdil*
	Best dermatology software	*Ozan Erdem*
	Industry 4.0/5.0 and dermatology	*Cahit Yavuz*
	Flow-cytometry in dermatology	*Emine Müge Acar*
	Blue light and skin health	*Cahit Yavuz*
	Elastography in dermatology	*İlkin Zindancı*
	Continuous-wave laser hyperthermia in dermatology (thermotherapy)	*Abdullah Demirbaş*
	Thermography in dermatology	*Ozan Erdem*
	Confocal, USG, imaging methods in dermatology	*Sümeyre Seda Ertekin*
10:55-12:25	**SESSION: GENERAL DERMATOLOGY-3** ***Chairs: Aylin Türel Ermertcan, Zennure Takcı***	
	Colours in dermatology (white, black, brown, purple, yellow, green, redness)	*Aylin Türel Ermertcan*
	Diagnostic criteria in dermatology	*Ayşenur Botsalı*
	Hypo/hyper/absence (A)-conditions in dermatology	*Banu Taşkın*
	Red scrotum syndrome and male genital dysaesthesia	*Amr Abdelhamed*
	Jolly roger sign in dermatology	*Bachar Memet*
	Intestinal bacterial overgrowth in dermatology	*Amr Abdelhamed*
	Cutibacterium in dermatology	*Elif Cömert*
	Black box sigs for dermatologic therapies	*Zennure Takcı*
	Discussion	
12:25-12:55	**LUNCH**	
12:55-14:05	**INVESTIGATIVE DERMATOLOGY-3** ***Chairs: Emel Bülbül Başkan, Kansu Büyükafşar***	
	IGF in dermatology	*Ufuk Kavuzlu*
	Ghrelin in dermatology	*Ufuk Kavuzlu*
	Histopathologic features of aesthetic applications on rats	*Recep Dursun*
	Ultrastructural and histopathological changes after cosmetic procedures in humans	*Özge Aşkın*
	Microchimerism and skin diseases	*Ahmet Metin*
	MRGPRX-2 and allergy	*Kansu Büyükafşar*
	AI in dermatology	*Emel Bülbül Başkan*

14 March Sunday

14:20-15:30	**DIET AND ALTERNATIVE THERAPY FOR DERMATOLOGIST** ***Chairs: Erdem Yeşilada, Hilal Kaya Erdoğan***	
	Healing plants for skin diseases	*Erdem Yeşilada*
	Ketogenic diet in dermatology	*Emine Ünal*
	Do vitamins work for skin diseases?	*Hilal Kaya Erdoğan*
	Does pyhtotheraphy real or not for skin therapy?	*Hatice Kaya Özden*
	Discussion	
15:35-16:35	**BREAK**	
16:40-17:20	**PSORIASIS-2** ***Chairs: Kemal Özyurt, Zafer Türkoğlu***	
	When? & which one? Biologics for psoriasis	*Leon Kırcık*
	Management of difficult to treat psoriasis	*Omid Zargari*
	Integrative approaches of psoriasis and psoriatic arthritis	*Şule Ketenci Ertaş*
	Discussion	
17:35-18:35	**SESSION: PSYCHODERMATOLOGY** ***Chairs: İlknur Kıvanç Altunay, Mohamad Jafferany***	
	How do we look at the skin and read the brain?	*Anthony Bewley*
	Management approach to psychocutaneous disorders	*Mohamad Jafferany*
	Tattoo and psychology	*Ezgi Özkur*
	How liyezon psychiatry works for dermatology?	*İlknur Kıvanç Altunay*
	Personality disorders in dermatology	*Mohamad Jafferany*
	Discussion	
18:50-19:50	**HOW CAN WE TREAT CHALLENGE CASES? (4 DIFFICULT/CHALLENGE CASES)** ***Chairs: Serap Öztürkcan, Ayşe Serap Karadağ***	
	Bullous diseases	*Ayşe Akman*
	Psoriasis	*Ayşe Serap Karadağ*
	Skin cancer	*Fatma Pelin Cengiz*
	Vasculitis	*Sibel Doğan*
	Pruritus	*Esra Pancar Yüksel*
	Discussion	
20:05-20:45	**HIGHLIGHTS OF THE CURRENT TOPICAL ANTIBIOTIC GUIDE** ***Chairs: Ayşe Serap Karadağ, Ümit Türsen, Belma Türsen***	
	In infection diseases	Göknur Kalkan
	In inflammatory diseases	*Andaç Salman*
	For cosmetologic and surgical and wounds	*Bengü Gerçeker Türk*
	Discussion	
20:45	**CLOSING SPEECH AND LECTURE WHAT'S NEW IN VITILIGO 2020** ***Chairs: Torello Lotti***	

LECTURE SUMMARIES

SURVIVIN IN DERMATOLOGY

Elif Cömert-Özer

Marmara University Pendik Research Hospital, Istanbul, Turkey

Survivin is smallest member of the inhibitor of apoptosis (IAP) protein family. Survivin has antiapoptotic functions and also regulates the cell cycle. Survivin is highly expressed in cancer cells, but it is expressed at a low level in normal adult tissues, including skin. It is mostly located in the nucleus of keratinocyte stem cells (KSCs), but it is also expressed in melanocytes and fibroblasts. Survivin has an important role in the regulation of cell cycle in keratinocytes, it protects these cells from anoikis and UV-induced apoptosis and low levels of survivin might be necessary to preserve the regenerative potential of epidermal stem cells. In the skin, surviving has been implicated in several pathological conditions such as psoriasis and tumors of melanocytic and epithelial origin. In both, melanocytic and epithelial skin tumors, survivin expression has further been associated with tumor aggression, decreased patient survival and metastasis.

Survivin is a small protein with multifunctional domains. Its N-terminal two-thirds comprise a globular baculovirus inhibitor of apoptosis repeat (BIR) domain and it is defines survivin as an IAP. Although IAPs are generally considered antiapoptotic proteins, survivin not only inhibits apoptosis but also regulates cell division. And also, unlike other IAPs survivin is not able to inhibit apoptosis by directly binding to caspases. Under apoptotic stimuli involving mitochondria, surviving forms a complex with X-linked inhibitor of apoptosis protein (XIAP), thus increasing the stability of XIAP and its inhibitory activity against caspases. The gene encoding for survivin, named BIRC5 located on the long arm of chromosome 17 (q25). BIRC5 encodes ten splice variants by alternative splicing, six with known function: wild-type (WT)-survivin, survivin-2B, survivin-DEx3, survivin-3B, and survivin-2a, survivin-3a. It is not yet fully known how these different variants are regulated and how they function in comparison with the WT-survivin. Survivin is the only member of IAP family that can interact with the mitotic apparatus, by binding to microtubules, thus ensuring correct cell division.

Survivin is expressed in normal human skin, and it is mostly localized in the few cells located in the basal layer of the epidermis. It is thought that survivin is protecting the viability of epidermal stem cells. Various studies have confirmed that survivin expression in a subpopulation of keratinocytes in the basal cell layer of normal human interfollicular epidermis where stem cells reside. Survivin is markedly upregulated during UVB-induced keratinocyte cell cycle arrest and protects human keratinocytes against UVB-induced apoptosis. Together, these data provide evidence that survivin is important for both cell cycle progression and resistance to apoptosis of human keratinocytes. In human melanocytes, survivin expression and functions are controversial. In some reports, melanocytes do not seem to express survivin. In contrast, some studies detected survivin in normal melanocytes in culture. Survivin is also detected in skin endothelial cells. It is expressed in capillaries of normal epithelium, while it is upregulated in endothelial cells of granulation tissue. Survivin was also found to be expressed in sebocytes of normal human sebaceous glands, mainly in reserve cells Hence, survivin might have a similar pro-survival role in sebocytes. Consequently, survivin is important for both resistance to apoptosis and cell cycle progression of keratinocytes.

Clearly, with roles in mitosis, apoptosis suppression, autophagy, migration, metabolism and angiogenesis, survivin can promote tumor cell survival and cancer metastasis. Mitochondrial survivin seems to have an important role in cancer biology, it protects cancer cells from apoptosis and promotes tumor formation. In cutaneous tumors, both nonmelanoma and melanoma skin cancers, survivin is overall highly expressed compared with normal skin. In addition to cancer, survivin has been implicated in psoriasis, acne and acne scars, alopesia areata, vitiligo, lichen planus, rheumatoid arthritis and multiple sclerosis.

In human cutaneous tumors, survivin is expressed in both premalignant and malignant neoplasms, as well as in some benign tumors. Survivin is overexpressed in human SCCs as compared with normal skin, and it is levels correlates with tumor aggressiveness and lymph node metastasis. Also, in head and neck SCCs, survivin overexpression correlates with tumor progression and resistance to therapy. Survivin is expressed both in precancerous lesions, such as actinic keratosis, and in the SCC, although in SCCs its expression is more pronounced. In contrast, basal cell carcinomas weakly

express surviving. Merkel cell carcinoma, a rare and highly aggressive malignant tumor, recent studies showed that survivin expression is upregulated in this tumor and it is expression correlate with tumor recurrence and metastasis. Survivin is overexpressed in melanoma cells as compared with normal melanocytes, and this seems to be a promoting factor for early-step melanoma formation and prognostic factor for metastasis.

A role of survivin in inflammatory skin disorders has also been studied. Survivin is expressed in 70–80% of psoriatic lesions, and it is overexpressed in lesional skin than normal epidermis. Although in normal human skin survivin is located only in few cells of the basal layer, in psoriasis survivin is expressed in nearly all layers of epidermis. In psoriatic skin, survivin thought to role in prolonged keratinocyte survival as well as in angiogenesis, which are the key pathogenetic events in this disease.

In conclusion, further studies are needed to better understand the exact functions of survivin in healthy skin. In skin pathologies, survivin is proposed to be a useful cancer biomarker, as well as a reliable predictive marker of skin tumors with a direct correlation with resistance to radio- and chemotherapy. Although different treatment strategies targeting survivin have been studied, more research are needed at the skin level to develop new treatments for inflammatory and neoplastic skin diseases.

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EXOSOMES IN DERMATOLOGY

Sevda Önder

Cell to cell interaction is vital for human life and development. Although the intercellular interaction is regulated with many hormones, mediators, cytokines or direct cellular interactions, the important roles of extracellular vesicles (EVs) have attracted the attention of researchers in recent years. EVs have been divided into three categories; exosomes, microvesicles and apoptotic bodies. They include specific cargos like messengerRNAs (mRNA) microRNAs, long noncoding RNAs, mitochondrial DNAs, DNA, protein ligands, receptors and transcription factors (1).

What are exosomes?

Exosomes are nano-vesicles with sizes ranging from 30 to 150 nm, released by all known cells. These vesicles can be obtained from all body fluids (such as serum, plasma, urine, amniotic fluid, synovial fluid, breast milk, saliva, cerebrospinal fluid) in both healthy and diseased conditions. Studies have shown that they play important roles in many biological functions such as intercellular communication, signal transmission, genetic material transfer and regulation of immune response (2). Understanding that exosomes have such functions has led to the different uses of these nanoparticles (1).

Structure and Cargo of Exosomes

Exosomes are formed when the endosome membrane folds into itself during the maturation of the endosomes. This formation, which contains many nanovesicles, is called multivesicular bodies (MVB). Exosomes spread to body fluids as this MVB combines with the cell membrane of the endosome and releases the cargo inside. Studies show that the exosome content varies from cell to cell and according to the current state of the cell (1-2). However different cell origin exosomes also express certain common proteins. Among these proteins, CD9, CD37, CD53, CD63, CD81 and CD82 stand out. Exosomes also express Alix and TSG101 (tumor susceptibility gene 101), Rab11, HSP70 (heat shock proteins 70) and 90, Annexin 1 and 2 and ICAM-1 (intercellular adhesion molecule 1) proteins that play a role in the formation of MVB. Cholesterol, phosphatidylcholine, phosphatidylserine and diglycerides in lipid barrier that are found in the membrane structure of exosomes are common lipid molecules found in all exosomes. What makes exosomes so popular is that they contain mRNA, miRNA and sometimes DNA (3). This functional mRNA and miRNA can be transferred from cell to cell via exosomes. Exosomes play an important role in the pathogenesis of diseases due to their very different functions. Considering all these functions, exosomes can be used both for diagnosis as a biomarker and for the treatment of diseases due to their specific properties in many branch of medicine

Exosomes in dermatology

In recent years there is increasing literature about exosomes roles in the dermatology field. It is known that exosomes have important roles in skin homeostazis, pathology and repair. Recent studies showed that exosomes play roles in the physiological processes of the skin and have pathological roles in the process of skin diseases. Among the pathologic process of the skin diseases exosomes regulate the secretion of pro-inflammatory cytokines , promote angiogenesis, deposite collagen in skin defects and regulate the proliferation and differentiation of skin fibroblasts in the cutaneous tissue. Exosomes regulate microenvironment of skin by releasing their spesific cargos and thus they promote the occurrence of skin diesases such as psoriasis, atopic dermatitis, melanoma and some other skin diseases (4,5,6). Thus, exosomes may act as potent drug carriers that can selectively infiltrate skin lesions for the treatment of various skin diseases. Exosomes have important physiological roles in skin homeostazis, such as inflammatory response, cutaneous wound healing, the immune response, and skin immunity (7). The specific contents carried by the exosomes reflect the physiological or pathological conditions of the cells from which they originate. Many studies have reported that the RNA profile of exosomes derived from pathological cells or diseases is different from exosomes derived from healthy cells, therefore, exosomes are potential candidates for diagnostic biomarkers and treatments for a variety of diseases (1,7).

Exosomes have also become an area of interest in cosmetic dermatology in recent years (8) Exosomes can originate from many different tissues, both immune and non-immune. According to the tissues they originate from, their contents and therefore their functions may also change. In cosmetic dermatology, there is increasing literatur about the roles of the adipose tissue-derived exosomes. Adipose tissue has important functions in immune modulation, wound healing,

and tissue regeneration. Removing stromal cells from the adipose tissue can create complex application possibilities. Thus, adipose-derived stem cells(ASCs) and ASC-derived exosomes (ASC-exos) become important derivatives of fat tissue. The ASC-exos can be used as tools for repairing and regenerated activation of damaged cells, have roles on skin regeneration, skin homeostazis, anti-inflammation and immune function (9).

As a result, the increasing literature knowledge of exosomes shows us they will continue to be the focus of researchers in the field of dermatology in such as pathogenesis, diagnosis and treatment of many diseases and cosmetic dermatology in the coming years.

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MICRONEEDLING COMBINED PROCEDURES IN AESTHETIC DERMATOLOGY

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Orentreich first described the use of a skin needling as "subcision" in In 1994.

Furthermore, the first modern dermaroller was introduced in 2006. Main devices using microneedling technology can be summarized as 1. Dermaroller, 2. Derma pen 3. Fractional radiofrequency microneedling 4. Superficial home-care rollers 5. Devices combining microneedling and vacuum-assisted infusion such as DermaFracTM (Genesis Biosystems, Lewisville, TX, USA) 6. LED microneedling rollers 7. Others such as Fluzone® Intradermal influenza virus vaccine (Sanofi Pasteur, Swiftwater, PA, USA)[1]

The basis of microneedling relies on physical trauma which penetrates the dermis to a uniform depth, creating a controlled skin injury. The natural wound healing cascade is induced as platelets and neutrophils are recruited to release growth factors such as TGF-alpha, TGF-beta, and platelet-derived growth factor (PDGF). This ultimately results in the deposition of collagen by fibroblasts. This controlled skin injury induces rapidly-healing micropunctures with subsequent stimulation of collagen and elastin fiber production, resulting in skin remodelling.[1,2]

Microneedlng is a non-ablative alternative for many cosmetic procedures. Although initially developed as a tool for skin rejuvenation, it is now being used for many indications, such as scars, acne, melasma, photodamage, skin rejuvenation, hyperhidrosis, alopecia, and facilitation of transdermal drug delivery.[1,2]

Despite its common use and a wide variety of indications, strong evidence for the efficacy of microneedling is not still evident in the literature.[1,2]

Although being used as a routine in near and middle-east countries for a longer time, it has gained popularity in the USA and other western countries in the last few years.[2]

Microneedling can be used alone and combined with many procedures. At least two different and unrelated modalities, which can be combined depending on the patient's condition, needs, and goals are employed to consider as a combination treatment.[2]

Some microneedling combined procedures are:[1-8]

1.Platelet-rich plasma (PRP): for facial rejuvenation, androgenetic alopecia, alopecia areata, stria, atrophic acne scars, also telogen effluvium, pigmentation, melasma, skin laxity, wrinkles etc.

2.TCA 15% peeling: for pigment tx, or facial rejuvenation,

3. Minoxidil treatment: alopecia

4. Mesotherapy: for facial rejuvenation, alopecia, stria, melasma, periorbital melanosis

5. Lasers: such as 1927 nm thulium laser and fractional Er:YAG laser for facial rejuvenation; 1064-nm Q-switched Nd:YAG laser for hyperpigmentation.

6. Radiofrequency (RFMN): for facial rejuvenation, aging, acne scars, inflammatory acne, axillary hyperhidrosis, cellulite, stria, alopecia, rosacea, postinflammatory erythema etc.

7. Chemical peeling (glycolic acid, Jessner's solution) for atrophic acne scars

8. Stem cell: amniotic fluid mesenchymal stem cell-derived conditioned media (AF-MSC-CM): for facial ageing

9. BotulinumtoxinA: post-operative facial scars, mesobotox

10. Drug delivery: lidocaine for local anaesthesia, 5-fluorouracil (5-FU) and bleomycin for SCC and warts; Topical glycopyrrolate for eccrine hidrocystomas, and vitamin C, tranexamic acid for melasma etc.

11. Photodynamic therapy (PDT) utilizing the photosensitizers aminolevulinic acid (ALA) or methyl aminolevulinate (MAL) for actinic keratosis, superficial BCC, SCCs, and other sun-related skin damage.

Advantages:[1,3]

Easy application

Low cost, a relatively short recovery period (two to three days) and

A very low risk for postinflammatory hyperpigmentation that is a potential side effect of other collagen remodeling treatments.

Disadvantages:[1,3]

A bit painful

Mild transient erythema and edema is expected

Scar formation, very rare

Risk of granuloma formation (if combined with topicals)

Although, microneedling is generally a well-tolerated, safe procedure. Contraindications are limited, but include the following:[2]

1. Active acne, especially inflammatory lesions

2. Active herpes labialis or other localized infection in the treatment area, including warts.

3. Moderate-to-severe chronic skin diseases such as eczema or psoriasis

4. Patients with extreme keloidal tendencies

5. Immunosuppressed patients, including patients on chemotherapy

6. Care should also be taken in patients near concomitant chemodenervation (botulinum toxin) injection sites to avoid unwanted toxin diffusion

Adverse effects:

The use of topical medications with or immediately after a microneedling procedure may increase the incidence of adverse effects because of the creation of channels within the epidermis and dermis that acts as a gateway into the body allowing for the development of an immune response to immunogenic particles. Avoidance of non-prescribed skincare products for the first week after the microneedling procedure as these may potentially induce a local or systemic hypersensitivity reaction.[1,4]

Since the microneedling procedure is often used in combination with other treatments such as injections of hyaluronic acid filler and chemical peels and various dermatologic lasers, no “wash out” period is necessary before initiation of treatment. However, it is recommended the order of treatments be applied from deep to superficial (e.g., injectables before micro-needling and/or laser irradiation) to maintain visual landmarks and prevent diffusion of injectables caused by tissue edema or bleeding. [1,4,5]

What’s new?

Nanofat micro-needling:[9]

Nanofat is prepared by a 2-step emulsification technique followed by filtration. It is a highly concentrated solution of progenitor cells and has no viable adipocytes with no filling capacity. Grafting can be performed by a microneedling delivery pump system called Hydra Needle 20 microneedling device (Guangzhou Ekai Electronic Technology Co Ltd, Guangzhou, China).

Meso-botox by microneedling[9,10]

Botox can be applied through a very superficial and uniform injection technique into the dermis via the same microneedling delivery system. The botulinum toxin acts by decreasing sweat, oil, and sebum production and superficial wrinkles.

Skin booster (as a combination of all) [9,10]

The mixture with nanofat, botulinum toxin, and vitamin C can be delivered in the same session. Striking improvement on the skin quality is perceived 6 to 8 months after nanofat grafting. Association of hyaluronic acid, botulin toxin, and vitamin C provides shorter-term enhancement of skin quality.

In conclusion, microneedling is a safe, minimally invasive, and effective aesthetic treatment modality for numerous dermatologic conditions, including acne and other scars, rhytides, and striae. With its fast post-treatment recovery, limited side effect profile, and impressive clinical results, microneedling is a valuable alternative to more invasive procedures such as laser skin resurfacing and deep chemical peeling. Moreover, the combination of microneedling with another procedure is found to increase the success, and decrease the complication risk in the recent literature.

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keywords: collagen induction therapy, microneedling, dermarolling, or skin needling

LIQUID COLLAGEN: WHERE ARE WE NOW FOR DERMATOLOGY?

Semahat Alp Erdal

Collagen is the one of an essential components of connective tissue and present abundant in various fibrous tissues, such as skin, bones, ligaments, tendons, blood vessels, muscle, cornea and dentin. This fibrous protein composed of the characteristic triple helix of three polypeptide α chains containing repetitive triplets of the amino acids glycine, proline, and hydroxyproline accounts for ˜30% of total protein mass in the mammals body, and may constitute >70% of the dry weight of the normal human skin dermis.

Having the same basic amino acid building blocks collagens differe in according to their α-chain composition, and there are 28 different unique types of collagen. The skin contains mostly Type I, and Type III collagen (Natural ratio of type I:III collagen is 4:1). Collagen type II is mainly present in the cartilages. Collagen loss in the body starts about 29 years of age, after 40 years the human body can lose around 1% per year.

According to 2019 industry reports, with rising of collagen demand in the healthcare area and medical industry, Collagen Market size has exceeded USD 3.5 Billion, globally in 2019 and it is antipicated to register more than 8% CAGR between 2020 and 2026. We see that it is common to use collagen supplements in population through advice or advertising without dermatologist advice. It is no wonder that rising globally coronavirus issues and improvements in health awareness among people have led to increasing nutraceuticals demand to boost immunity and to remain healthy. For these and similar reasons oral collagen supplements have recently become more popular due to various beneficial e□ects, such as improving muscle strength, bone density, and skin health. Though widely marketed to consumers via alleged benefits, these expected effects have still not precisely elucidated in the literature. However, data regarding its affirmative effects on wrinkle reduction, skin rejuvenation, skin aging reversal, besides data directed to its possible long term adverse impacts on body are not yet enough. According to common opinion of supporters, based on their in vitro/ in vivo experimental or clinical trials, orally intaking protein peptides can maintain and increase the collagen in the skin. They claim that these products induce fibroblast migration and increasing hyaluronic acid production of dermal fibroblasts, promote stronger collagen fibrils, increase the water content of the stratum corneum, and additionally protect the skin against UV induced melasma.

Collagen has long been used in food supplements and pharmaceutical industry. It can be isolated from several sources, mainly bovine (because of its availability and biocompatibility), porcine byproducts, which they have a di□erence in its chemical and thermal properties. Collagen extraction can be carried out from their different tissues such as tendons, bones, lung tissue, or even connective tissue. Alternative sourche of collagen are fish tissue such as bones, skin, and scales, ovine tendon and skin, jellyfishes or sponges or others sources such as chicken, duck, and rabbit skin. Collagen peptides obtained these sourches, are offered in pill, powder, liquid or topical forms on market.

Oral collagen supplementation is usually in the form of hydrolyzed collagen (HC, collagen peptides). Collagen is considered to be an antioxidant in its hydrolyzed form. HC is composed of small peptides with low molecular weight 3-6 KDa. There have been different types of extraction of HC. It can be obtained by thermal treatment with/without pressure, enzymatic reaction by use of chemical products, or by use of high intensity ultrasound. Low-molecular-weight collagen hydrolysates are generally thought to perform better bioactivities than their larger counterparts. Many clinical studies performed to show benefits, such as bioavailability, rapid absorption in the digestive tract, passage into the bloodstream as small peptides and accumulation in the skin. Hydrolyzed collagen has to cross the intestinal barrier and to enter the bloodstream to be reach to the skin. The rate of transport across the intestinal barrier is an controlling factor that affects these compounds bioavailability in the skin. For this reason, it is important to determined better absorbed in what quantity and form of collagen peptides. It is claim that beverages with HC have more advantage of easy digestion, high assimilation (about 80%), and good absorption at the intestinal level.

Digestion process involving in several proteases consists of degradation of hydrolyzed collagen to form dipeptides and tripeptides or free amino acids. However, before they are absorbed, peptides are hydrolyzed in the gastrointestinal tract, in order to predominantly free amino acids can enter the circulation. Hydroxyproline is absorbed in two forms, with an

amino acid form and a peptide form. The free amino acids provide building blocks for the formation of collagen and elastin fibers. Collagen oligopeptides stimulates the production of new collagen, elastin, and hyaluronic acid. Most of oral collagen peptide supplementation products also include vitamins like A, C, E, biotin to provide bioactivity in these process.

Some studies have shown, by histological analysis, that the structural architecture of dermal collagen fibers and stratification of epidermal layers improves when HC supplements are taken orally. Common alleged benefits include wrinkle reduction, skin rejuvenation, skin aging reversal, and skin fullness. Hydrolyzed collagen has been presumed to be safe and non toxic. It has generally mild advers effects including diarrhea, heaviness in the stomach, and rashes, yet there have been reported high levels of cadmium, a toxic heavy metal in all collagen products. In 2016 the FDA prohibited the use of bovine products in dietary supplements to avoid bovine spongiform encephalopathy, except gelatin.

Despite claims of manufacturers, many benefits of liquid collagen seems to be anecdotal. Most of research are performed about HC. Persuasive scientific research with high level of evidence is needed to say that oral collagen supplement is the best way to get collagen. The best way to boost collagen seems to be dietary intake of protein-rich foods such as beef, poultry, fish for now.

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BETA-CAROTENE/ASTAXANTHIN/COENZYME Q10 AND DERMATOLOGY

BETA-CAROTENE

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Beta-carotene is a yellow pigment found in chlorophyll-containing plants, bacteria, and food. It is the most abundant and most efficient precursor of vitamin A and most nutritionally active carotenoid. Its' consumption does not lead to hypervitaminosis A because of a feedback mechanism in the mucosa of the gut.

Beta-carotene is derived from natural dietary sources such as carrots, pumpkin, spinach, sweet potatoes, other yellow and green vegetables and fruits.

Besides direct light-absorbing properties, carotenoids provide endogenous photoprotection and contribute to the prevention of UV damage in humans mostly by their well-known antioxidant effects. It prevents UV-induced erythema, increases minimal erythema dose (MED) and decreases the rate of mitochondrial mutation in human dermal fibroblasts after UV irradiation. Systemic photoprotective effects of beta-carotene depend both on the dose and the duration of treatment. In most of the interventional studies with carotenoids, photoprotection was observed only after a minimum of 10 weeks of dietary intake or supplementation, with doses >12 mg/day. It was found especially useful in the treatment and prevention of some photodermatoses, like erythropoietic protoporphyria and polymorphic light eruption.

It has also been shown to prevent and repair effects of photoaging; improve facial wrinkles and elasticity by O2 quenching and decrease in MMP5 -1, -3, and MMP-10 and MMP-9.

There are also some studies on mice showing the effectiveness of beta-carotene in atopic dermatitis.

Though protective effects of beta carotene from some cancers like esophagial and breast cancer has been shown, long-term beta-carotene supplementation has been associated with an increased risk of lung cancer in smokers and also a higher beta-carotene status may increase risk of prostate cancer. So further studies are needed to determine the optimal daily allowance for supplementation.

ASTAXANTHIN

Astaxanthin (ASX) is a ketocarotenoid first isolated by Kuhn and Sorensen from a lobster. It is found extensively in the aquatic environment primarly in the microalgae *Haematococcus pluvialis* and multiple marine species, as an orange pigment.

Astaxanthin is related to other carotenoids, however, it is more bioactive than zeaxanthin, lutein, and beta-carotene. ASX is not converted into vitamin A. It has a higher antioxidant activity than other carotenoids.

Recently, ASX has attracted considerable interest because of its potential pharmacological effects, including anticancer, antidiabetic, anti-inflammatory, and antioxidant activities as well as neuro-, cardiovascular, ocular, and skin-protective effects.

The mechanisms involved in the protection of skin are antioxidant and antiinflammatory activities and altering the DNA repair kinetics. The effects of ASX on hyperpigmentation suppression, photoaging inhibition, and wrinkle formation reduction have been reported in several clinical studies. The reported effects of astaxanhine in skin are; decrease in fine wrinkles, increase in moisture content, improvement in skin elasticity, reduction in visible signs of aging, improvement of skin elasticity, antioxidant effect leading to facial rejuvenation, suppression of inflammatory response on UV-B–exposed skin, decrease in corneocyte desquamation and microbial presence in skin, increase in MED andimprovement in skin texture. Benefical effects of ASX also have been reported in wound healing, atopic and contact dermatitis.

FDA has approved ASX from H. pluvialis for direct human consumption dosages up to 12 mg per day and up to 24 mg per day for no more than 30 days. Researches have also shown that astaxanthin is a safe compound, without adverse effects.

COENZYME Q10

Coenzyme Q10 (CoQ10) is an essential compound found naturally in virtually every cell in the human body. It is necessary for cellular respiration and ATP production. It also functions as an intercellular antioxidant and recognized to have an effect on gene expression that might account for its effects on overall tissue metabolism.

It is naturally found in dietary sources, with large amounts present in heart, chicken leg, herring and trout.

In the skin CoQ10 acts as an antioxidant with 10-fold higher levels in the epidermis than in the dermis. The amount of coenzyme Q10 in skin decreases with age. Additionally, UV-irradiation, which leads to oxidative damage, significantly reduces skin's Q10 levels. Therefore, in the cosmetic industry the antioxidant CoQ10 is widely used in anti-aging products.

Topical application of coenzyme Q10 to human skin was found to be effective in reducing the depth of wrinkles. Daily supplementation with 50 and 150 mg of CoQ10 has also been shown to significantly reduce wrinkles and microrelief lines and improve skin smoothness. CoQ10 is able to suppress the UVR- or IL-1-induced inflammatory response in dermal fibroblasts. It can block the UVR induction of the matrix-eroding enzyme, MMP-1.

Other effects in dermatology are; suppression severity of dermatitis in mice and cutaneous healing effects in vivo.

CoQ10 dosage guidelines, which appeared to be safe and well tolerated, were suggested for adults (up to 1,200 mg/day) and for children (up to 10 mg/kg/day).

Drug-nutrient interactions may be observed with cholesterol-lowering drugs, beta blockers, propranolol and metoprolol, phenothiazines and tricyclic antidepressants, antiplatelet drugs, warfarin and antihypertensive drugs.

Gastrointestinal effects such as abdominal discomfort, nausea, vomiting, diarrhea, and anorexia may occur and CoQ10's antiplatelet effect may increase the risk of bleeding.

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ZINC / SELENIUM AND SKIN

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Zinc is a nutritionally essential trace element. It plays an important role in the regulation of lipid, pro-tein and nucleic acid metabolism .It supports healthy immunologic system and plays an important role in wound repair. Zinc, has antioxidant eect and prevents ultraviolet damage. Unfortunately, no ideal method exists to measure the body zinc level. Measurements of zinc in serum, plasma, erythrocyte , hair and urine can be done. Normal plasma zinc level range is considered as 70-250 mg/dL. Daily zinc is 5-9 mg for females and 7-14 mg for males. There is no standard regiment for the dosage and period. The main source of zinc taken in diet is meat. As we all know, acrodermatitis enteropathica is an autosomal recessive disease characterised by a deffect in zinc absorbtion. Symptoms start with the delactation. In contrast to severe deficiency, there is no evidence of the effect of moderate zinc defici-ency on wound repair. There are studies showing that serum zinc level in patients with Behçet Disea-se and recurrent aphthous stomatit is low. Consequently; despite contradictory studies; zinc therapy; can be considered as encouring in recurrent aphtous stomatitis and Behçet diseases. There are studies showing a positive correlation between zinc deficiency and hair loss. Al-Refu K. suggested that zinc deficiency might be the reason of cronic hair loss in children. However, there are studies not binding alopecia and zinc deficiency. Harrison and Sinclair claimed that zinc deficiency in telogen effluvium couldn't be the reason of alopecia without other dermotological signs. In the systematic review of Cochrane database in 2012, it is noted that there are not a convincing evidence about the effective-ness of dietary supplements in atopic dermatıtıs about the effectiveness of of dietary supplements in atopic dermatıtıs .As a conclution; there are studies about zinc deficiency in dermotological diseases, there is not enough scientific evidence for recommending its therapatic usage. In order to prove its efficacy in dermotological diseases, more plecebo controlled, double blind and randomized studies should be done with large group of patients and then, treatment algoritms should be prepared. For now, it can be recommended as adjuvant medications in addition to current approved therapies.

Selenium is an essential trace element in human nutrition being the component of selenoproteins which have antioxidant functions in cardiovascular disease and cancer prevention. Selenium, though present in meat, may be found in higher values in seafood. Selenium has an important role in glutathi-one peroxidise activity, a crucial enzyme in detoxification processes.

Basic research has further clarified the role of selenium in skin aging. Selenium preserves keratinocyte stemness and delays senescence by maintaining epidermal adhesion . Besides, after oxidative damage to keratinocytes by ultraviolet A, young keratinocytes treated with low doses of selenium attenuate the cytotoxicity of ultraviolat A by promoting DNA repair of 8-oxoguanine. Nevertheless, for aged kerati-nocytes, a higher concentration of selenium is needed , suggesting that selenium supplementation strengthens the DNA repair activities of keratinocytes to fight aging and prevent photoaging in skin tissue. As a conclusion, there are many beneficial effects of selenium on human skin health involving its antioxidant properties along with various other biochemical actions.

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Mitochondrial DNA and Dermatology

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Mitochondrium (pl. mitochondria); is an double membrane-surrounded organelle, which is, with a few exceptions (i.e., erythrocytes), found in most of the eukaryotic cells.[1] Number, shape, and form of mitochondria may differ from cell to cell.[2] Hundred to thousands of mitochondria can be found in most human cells, depending on their metabolic activity. Mitochondria generate most of the much-needed cellular energy in the form of ATP through a process called oxidative phosphorylation (OXPHOS), which takes place in its inner membrane. In addition to that, mitochondria play essential roles in Ca homeostasis, heme synthesis, steroid synthesis, heat generation.

Recent mitochondrial genetic and ultrastructural studies showed that the functions of mitochondria are not limited to biosynthetic processes, energy generation. New data indicate that mitochondria possibly have a crucial role in the regulation of cellular proliferation and apoptosis. A good example is the discovery of the mitonucleon. Although mitochondrium has initially been believed to be an individual, isolated organelle, in recent years, it has been found out that mitochondria may fuse into the superstructures, called mitonucleons, which are thought to take part in endometrial differentiation, spermatogenesis, and also synthesis and excretion of steroid hormones.[3]

Mitochondrial DNA

Mitochondrial functions are regulated by mitochondrial (mtDNA) and nuclear genomes (nDNA). mtDNA includes 16,569 base pairs and encodes 13 proteins.[4] Unlike diploid nDNA, mtDNA is a multi-copy genome transmitted and maternally inherited through oocyte. Point mutations or rearrangements of mtDNA may lead to mitochondrial dysfunction and multisystem diseases through compromising OXPHOS function.[5] The multi-copy nature of mtDNA easily causes the heteroplasmy as a unique aspect of mtDNA, making mitochondrial diseases more complex and heterogeneous. mtDNA-, and nDNA-associated mitochondrial dysfunction play a critical role in the development of multisystemic primary mitochondrial diseases, neurodegeneration, and various cancers.[5]

Mitochondrial Diseases

Mitochondrial diseases are genetic disorders, which are caused by mutations in the nuclear DNA (nDNA) and mitochondrial DNA (mtDNA) encoding the structural mitochondrial proteins or proteins participating in mitochondrial function, and which usually lead to defective oxidative phosphorylation. These disorders may manifest in childhood or later in life. While some mitochondrial disorders may manifest as a single organ disease (e.g., the eye in Leber hereditary optic neuropathy [LHON]), others may affect multiple organ systems and are often characterized by neuromuscular symptoms. Mitochondrial diseases may manifest at any age. Many individuals with a mutation of mtDNA may present with typical clinical features of a discrete clinical syndrome, such as the Kearns-Sayre syndrome (KSS), chronic progressive external ophthalmoplegia (CPEO), mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS), myoclonic epilepsy with ragged-red fibers (MERRF), neurogenic weakness with ataxia and retinitis pigmentosa (NARP), or Leigh syndrome (LS). But, considerable clinical variability exists, and many patients can not be classified easily into one particular category, which is well-illustrated by the overlapping spectrum of disease phenotypes (including mitochondrial recessive ataxia syndrome (MIRAS) resulting from mutation of the nuclear gene POLG, which has emerged as a major cause of mitochondrial disease. Common clinical features of mitochondrial disease are ptosis, external ophthalmoplegia, proximal myopathy, exercise intolerance, cardiomyopathy, sensorineural deafness, optic atrophy, pigmentary retinopathy, and diabetes mellitus. Common central nervous system findings are encephalopathy, seizures, dementia, migraine, stroke-like episodes, ataxia, and spasticity. A high incidence of mid-and late pregnancy loss is a common occurrence that often goes unrecognized.

The prevalence of childhood-onset mitochondrial disorders is reported to range from 5 to 15 cases per 100,000 individuals. With a prevalence of 2,5 cases per 100000 births, Leigh syndrome is the common mitochondrial disease of childhood. Adult-onset mitochondrial diseases are estimated to have a prevalence of 20 cases per 100000 individuals globally. mtDNA mutations seem to be more frequent in adult-onset mitochondrial disorders (about 80% of all cases), where they are observed only in 20-25% of childhood mitochondrial diseases.[6]

Dermatology and Mitochondrial Genetics

As the outermost layer of the human body, the skin is continuously in contact with numerous environmental stimuli, many of which can be quite detrimental. Constant mitosis at the level of stratum basale, the passage of keratinocytes directed to the skin surface from basal layer to the stratum corneum, and transformation of basal keratinocytes into the

corneocytes, presenting antigenic structures to immune cells are some of the crucial means by which our skin deals with these harmful stimuli. Each one of these processes requires a constant energy flow, which is supplied by numerous mitochondria. Recent research show that, in addition to acting as power generators, mitochondria play more critical roles in the metabolism and differentiation of keratinocytes[7,8]. It is reasonable to speculate that any disturbance in mitochondrial functions may also manifest as skin problems.

Skin manifestations such as poikiloderma, acrocyanosis, vitiligo, hair abnormalities, hirsutism, petechiae with cutis marmorata, brownish discoloration of skin were reported in 16 of 271 patients with mtDNA disorders.[9] Moreover, mutations in mtDNA have been detected in specific dermatological diseases. Powers et al. reported mtDNA^{3895} and mtDNA^{4977} deletions in sun-exposed human skin.[10] Berneberg et al. reported 10-fold 5000bp deletion in the mtDNA of photodamaged skin compared to sun-protected skin cells. Singh et al. observed that ubiquitous depletion of mtDNA in mice results in skin wrinkling and hair loss and speculated that restoration of mtDNA could reverse these conditions.[11] Another research group, Villavicencio et al., studied the pigmentation changes in mtDNA depleted mice's ears and observed cutaneous and pigmentary changes similar to age-related cutaneous changes in humans such as senile lentigines.[12] Various research groups also found out that radiation and other carcinogenic stimuli damage mtDNA directly, indicating the possible role of mtDNA damage in cutaneous carcinogenesis. Furthermore, dose-dependent changes in mitochondrial membrane potential and function in SLE and pemphigus Vulgaris patients treated with glucocorticoids have been observed.

All things considered, mitochondrial dysfunction seems to play a crucial role more than imagined before. New therapeutic approaches targeting the defective or dysfunctional mitochondria may prove effective in various dermatological conditions, particularly in skin-aging, pigmentary problems.

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AQUAPORINS IN DERMATOLOGY

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Aquaporin(AQP)s, also known as water channels, are a group of intrinsic membrane proteins that form pores in biological cells' membranes, mainly facilitating water transport between cells.[1] Aquaporins possess six membrane-spanning alpha-helical domains with both carboxylic and amino terminals on the cytoplasmic side. Due to their diminutive size, water molecules can pass through the cell membrane through simple diffusion. However, simple diffusion is relatively slow because of the polarity of water molecules, and the majority of water passes through aquaporin.[2] In recent years, it has been found out that, in addition to water, AQPs also transport other molecules, such as glycerol.

The first aquaporin, 'aquaporin-1' (known initially as CHIP 28), was reported by Peter Agre of Johns Hopkins University in 1992, who also won The 2003 Nobel Prize in Chemistry for his discovery.[3,4] Further studies using supercomputer simulations identified the pathway of water as it moved through the channel and demonstrated how a pore could allow water to pass without the passage of small solutes.[5]

Aquaporins in Humans

Thirteen aquaporin types have been identified (AQP0-12) in humans and divided into three subgroups according to the primary sequences: water selective AQPs (AQP0, 1, 2, 4, 5, 6, 8), aquaglyceroporins (AQP3, 7, 9, 10), and superaquaporins (AQP11, 12 - aquaporins found inside the mammalian cells). Due to the lack of specific inhibitors, functions of AQPs are hypothesized from the observations of AQP null mice and humans. Abnormal water metabolism was observed with AQP1, 2, 3, 4, 5 null mice, particularly with AQP2 null mice: leading to death at neonatal period due to diabetes insipidus. Abnormal glycerol transport was detected in AQP3, 7, 9 null mice, despite their normal phenotypes. Ctaracts are observed in AQP0 null mice suffer. AQP11 null mice are reported to die from uremia as a result of polycystic kidneys. AQP6, 8, 10, 12 null mice are healthy. AQP null humans have been reported with AQP0, 1, 2, 3, 7. Among them, AQP2 null humans manifest diabetes insipidus.6

Dermatology and Aquaporins

AQP3 is of particular interest to dermatologists. Aquaporin-3 (AQP3) is a membrane transporter of water and glycerol expressed in plasma membranes in the basal layer keratinocytes of the epidermis in normal skin.7 Altered expression of AQP3 has been detected in atopic eczema, erythema toxicum neonatal, squamous cell carcinoma, indicating their possible roles in inflammation and carcinogenesis.

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INTEGRINS / HIF1 ALPHA / VEGF/PAI1 IN DERMATHOLOGY

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Integrins

Integrins are heterodimeric proteins composed of noncovalently associated α and β subunits. Different combinations of 18 α and 8 β subunits make up the 24 integrin heterodimers encountered in mammals. The integrin structure is depicted as a molecule with a head and two tails. The head is the ligand-binding extracellular component made up of the ectodomains of the α and β subunits; intracellular domains represent the legs anchoring to cytoskeletal proteins, with other domains traversing the transmembrane region in between (1).

Integrins therefore function bidirectionally, meaning information can be transmitted from the outside environment to inside the cell and vice versa.This bidirectional signaling capability of integrins provides the cell with important information on its immediate extracellular environment and informs decisions on proliferation, apoptosis, or the remodeling of the ECM to facilitate metastasis (1, 2).

Integrins also are important for angiogenesis, providing both blood supply to the rapidly growing tumor cells and a pathway for hematogenous spread to distant organs. Integrins mediate angiogenesis by interacting with the tumor-secreted growth factors, specifically by promoting endothelial cell migration and survival. Integrins may contribute to signal transduction that promotes angiogenesis (3).

Hypoxia-inducible factor-1α (HIF-1α)

Skin, the first barrier against invading microorganisms, is hypoxic, even under baseline conditions. The transcription factor hypoxia-inducible factor-1α (HIF-1α, the principal regulator of cellular adaptation to low oxygen, is strongly expressed in skin epithelium. HIF-1α is now understood to play a key role in the bactericidal capacity of phagocytic cells such as macrophages and neutrophils (4).

More recently, HIF-1α has emerged as a critical regulator of immune cell function that couples shifts in cellular metabolism to cell type-specific transcriptional outputs. Activation of macrophages with inflammatory stimuli leads to induction of the metabolic program aerobic glycolysis and to HIF-1α stabilization, which reinforce one another in a positive feedback loop that helps drive macrophage activation. This activation of aerobic glycolysis and HIF-1α is important both for production of inflammatory cytokines, such as IL-1β, and for cell intrinsic control of infection (5).

Chronic infections are often associated with inflammation and tissue disruption. Inflamed tissues are characterized by low levels of oxygen and glucose, a microenvironment that triggers the stabilization of the hypoxia-inducible transcription factor HIF-1α. HIF-1α is the master regulator of the response to hypoxia (6).

Plasminogen activator inhibitor-1 (PAI-1)

PAI-1, also known as SERPINE1 (serpin peptidase inhibitor, clade E), is a member of the serpin family of protease inhibitors (7).

Fibrosis is defined as a fibroproliferative or abnormal fibroblast activation-related disease. Deregulation of wound healing leads to hyperactivation of fibroblasts and excessive accumulation of extracellular matrix (ECM) proteins in the wound area, the pathological manifestation of fibrosis. The accumulation of excessive levels of collagen in the ECM depends on two factors: an increased rate of collagen synthesis and or decreased rate of collagen degradation by cellular proteolytic activities (7). The urokinase/tissue type plasminogen activator (uPA/tPA) and plasmin play significant roles in the cellular proteolytic degradation of ECM proteins and the maintenance of tissue homeostasis. The activities of uPA/tPA/plasmin and plasmin-dependent MMPs rely mostly on the activity of a potent inhibitor of uPA/tPA, plasminogen activator inhibitor-1 (PAI-1). Under normal physiologic conditions, PAI-1 controls the activities of uPA/tPA/plasmin/MMP proteolytic activities and thus maintains the tissue homeostasis. During wound healing, elevated levels of PAI-1 inhibit uPA/tPA/plasmin and plasmin-dependent MMP activities, and, thus, help expedite wound healing. In contrast to

this scenario, under pathologic conditions, excessive PAI-1 contributes to excessive accumulation of collagen and other ECM protein in the wound area, and thus preserves scarring. While the level of PAI-1 is significantly elevated in fibrotic tissues, lack of PAI-1 protects different organs from fibrosis in response to injury-related profibrotic signals. Thus, PAI-1 is implicated in the pathology of fibrosis in different organs including the heart, lung, kidney, liver, and skin (7, 8).

Vascular endothelial growth factor (VEGF)

Vascular endothelial growth factor (VEGF, also referred to as VEGF-A), which plays a key role in normal and pathological angiogenesis, is a homodimeric, heparin-binding glycoprotein, with at least five isoforms of 121, 145, 165, 189, and 206 amino acids due to alternative splicing (9)

VEGF secreted by the cutaneous cells plays an important role in sustaining the skin development and maintenance and in wound healing . Overexpression of VEGF in skin could lead to pathologic angiogenesis observed in psoriasis and other chronic inflammatory skin diseases (10).

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CYTOKINES AND CHEMOKINES IN DERMATOLOGY

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The skin is the largest organ in the human body and forms a barrier against the entry of physical agents, chemicals and microbes. To maintain this function, keratinocytes undergo a differentiation (also called cornification) process. It is a highly complex process under the control of cytokines and intercellular signaling molecules. This differentiation program requires well-regulated cell communication processes. Alterations and disorganization of the differentiation process lead to weakening of the skin barrier (1). Atopic dermatitis and psoriasis are examples of immunologically well-defined inflammatory skin diseases that involve defects in skin barrier formation (2,3). Clarifying key pathogenic factors has changed our therapeutic practice (4-6).

Cytokines and chemokines are responsible for the control of cellular communication and trafficking. Cytokines are messenger substances that can be secreted by almost any cell type. They can act in an autocrine, paracrine or endocrine manner. Cytokines exert their biologic activities by binding to specific cell surface receptors (7). Cytokines and their receptors can be classified based on the three-dimensional structure of the receptors. Besides, due to structural similarities, some cytokines are grouped into families, e.g. the IL-10 family (IL-10, IL-19, IL-20, IL-22, IL-24, IL-26), and the IL-12 family (IL-12, IL-23, IL-27) (1). Cytokines influence the proliferation, differentiation, and activation of cells. Chemokines are a large superfamily of small cytokines that have chemoattractant activity. CC, CXC, C, and CX3C chemokines are the four main subfamilies (8). They play a crucial role in leukocyte migration. Advances in this area have provided clinical relevance. I will give this lecture in the light of current dermatological advances.

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NOD2: THE INTESTINAL GATE KEPER IN DERMATOLOGY

Büşra Altun Deniz

Nucleotide-binding oligomerization domain 2 (NOD2) is an intracellular protein recognition receptor and this intracellular surveillance protein detect bacterial peptidoglycan and stimulates host immune response.

There are hundreds of NOD2 gene mutations associated with diseases such as Crohn's disease, Blau syndrome, and NOD2-associated autoinflammatory disease (NAID). Its relationship with graft-versus-host-disease is controversial.

NOD2 gene mutations are associated with several diseases and shapes the gut commensal microbiota and pathogens. In this presentation, we present about the structure of NOD2, relationship with diseases and role of NOD2 in dermatology.

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TRANSEPIDERMAL ELIMINATION IN DERMATOLOGY

Gökşen Ertuğrul

Tranepidermal elimination (TE) is a mechanism whereby foreign or altered constituents can be removed from the dermis. There are 3 mechanisms whereby dermal foreign material can be transported to the surface of the skin. In type 1; nonmotile cells (eg,erytrocytes) or small inert particles (eg,hemosiderin) carried upward to the surface during epidermal turnover. In type 2; larger, motile cells (eg,leukocytes) or organisms such as Treponema pallidum may actively migrate into the epidermal spaces. Type 1 and 2 have been termed as "transmigration". In type 3; there is varying degrees of pseudoepitheliomatous hyperplasia of the epidermis or follicular epithelium. İrritant material partially or completely taken into the prolifering epithelium and moved upward by the force of maturing keratinocytes. As a result, transepithelial perforating channels are formed (1,2).

Perforating disorders of the skin are group of uncommon diseases which are histopathologically characterised by transepidermal elimination of material from the upper dermis. Perforating dermatoses have a common clinical appearance; umbilicated papules with hyperkeratotic plug and unigue histopathologic findings (1). Due to the fact that perforating dermatoses are quite rare, little is known about their pathogenesis.

Perforating dermatoses may be divided into in primary and secondary forms. In primary perforating dermatoses, the main disease process consists of perforation of the dermoepidermal junction and transepidermal elimination of collagen or elastic fibers. In secondary perforating dermatoses, perforation and elimination of connective tissue fibers or other materials is an occasional phenomenon which occurs in another dermatosis with a different pathogenesis (3).

Primer Perforating Diseases;

1. Elastosis perforans serpiginosa (EPS)
2. Reactive perforating collagenosis (RPC)
3. Kyrle disease (Hyperkeratosis follicularis et parafollicularis in cutem penetrans) (KD)
4. Perforating folliculitis (PF)

Secondary Perforating Dermatoses

- Non-infective granulomatous disorders; Granuloma annulare, Necrobiosis lipoidica diabeticorum, Rheumatoid nodule, Sarcoid
- Dermatoses with calcification; Pseudoxanthoma elasticum, Calcified tumor of hair follicle origin (pilmatricoma), Calcinosis cutis, Osteoma cutis
- Infectious agents; Botryomycosis, Schistosomiasis, Chromoblastomycosis, Tuberculosis, Leishmaniasis, Rhinosporidiosis, Lobomyosis, Histoid leprosy
- Others; Chondrodermatitis nodularis chronica helicis, Collogenome perforant verruciforme, Lichen nitidus, Papular mucinosis, Melanoma, Amyloidosis, Vitiligo, Nevocellular nevus, Porokeratosis of Mibelli, Hidradenitis Suppurativa, Eruptive vellus hair cyst, Gout crystals, Tattoo pigment

Rapini et al suggested in 1989 that perforating dermatosis seen in people with diabetes mellitus (DM) or kidney disease should be named 'acquired perforating dermatosis'. However, many literature still use other terms such as acquired reactive perforating dermatosis, acquired perforating disorders, and perforating dermatoses (4).

Elastosis perforans serpiginosa

Elastosis perforans serpiginosa is a rare skin disease characterized by transepidermal elimination of abnormal elastic fibers. This condition classically presents as small papules arranged in serpiginous or annular patterns on the neck, face, arms, or other flexural areas (5). We can distinguish three subtypes of EPS. The first one, known as reactive one, is associated with connective tissue diseases such as Ehlers-Danlos syndrome, cutis laxa, Marfan syndrome, acrogeria, Rothmund-Thomson syndrome, osteogenesis imperfecta, Down's syndrome and pseudoxanthoma elasticum. The second form of the disease is a drug-induced one which is caused by treatment with D-penicillamine. The last

subtype, idiopathic one, may be associated with genetic basis of the autosomal dominant type of inheritance (6). It is believed that 90% of EPS cases are patients before the age of 30. EPS more often affects men and only 25% of cases are women. The prevalence of the disease is not known exactly (6). EPS etiopathogenesis has not been fully elucidated. Differential diagnosis should include granuloma annulare, dermatophyte infections, sarcoidosis, skin calcinosis, Mibelli porokeratosis (5).

In the biopsies an increased amount of elastic fibers can be found. There is no 'gold standard' therapy. Numerous treatment modalities have been described. The pinhole method using a carbon dioxide laser showed complete clearing in one case. Topical tazarotene and topical imiquimod therapy is reported to improve EPS skin lesions. Discontinuing penicillamine therapy does not guarantee preventing further development of EPS lesions in patients undergoing penicillamine therapy (5).

Reactive perforating collagenosis

Reactive perforating collagenosis is a rare skin disease that has transepidermal elimination of altered collagen through the epidermis. While there is epidermal hyperplasia in new lesions, degenerated basophilic collogen fibers and invagination of the epidermis with keratin plug will be observed in advanced lesions (7). The inherited form begins in infancy as papules located on the extensor surfaces of the hands, elbows and knees, most likely after superficial trauma to the area. Fewer than 50 cases have been reported in the literature so far (7). Reactive perforating collogenous lesions gradually turn into larger, umbilicated papulonodules with central adherent keratin plugging. The acquired form found in adults is more common and a underlying systemic disease mostly detected (8). DM, chronic renal failure and hyperuricemia are the most common diseases associated with acquired RPC. Other rare reasons are; thyroid and liver diseases, myeloproliferative and solid malignant neoplasms and some drugs (eg, clopidogrel, indinavir, sirolimus) (8). Acquired RPC is most common between the 3rd and 5th decades (7). Acquired form predilection sites are; trunk, shoulder girdle, gluteal region and extensor aspects on the upper and lower extremities (8). Lesions can often be itchy and heal within 6-8 weeks with hypopigmentation or scarring. Koebner phenomenon of the lesions can ocur. The sex distribution is generally considered to be equal. Most patients will experience a relapsing and remitting course of the disease throughout their life (7). At the pathophysiological level, RPC is characterized by hyaline degeneration of collagen fibers. The metabolic products obtained remain in proteins with a long half-life and change their physical / biochemical properties. Elimination of metabolites is impaired in chronic renal failure. The microtrauma to the skin may trigger the elimination of altered collagen fibers (8).

The treatment of ARPD is primarily the treatment of internal or oncological diseases with which it is associated. This includes the treatment of metabolic disorders, optimal management of diabetes mellitus, effective dialysis, and, if possible, the curative treatment of existing solid or hematopoietic neoplasms (8). Avoiding trauma is important. In topical treatment, first the application of keratolytic agent (5-7% concentration of salicylic acid, 10-15% urea and 0.01-0.1% tretinoin in Vaseline) after which the detacment of crusts and curettage is performed. Topical corticosteroids, antiseptic agents can be added to the treatment. Intralesional injections of the triamcinolone suspension can be tried. In addition, corticosteroids and retinoids can be used as systemic therapy. Systemic antihistamines and phototherapy are used to treat pruritus. Different responses have been reported regarding allopurinol treatment (8).

Perforating folliculitis

In perforating folliculitis; necrotic and modified dermal material is incorporated into the follicular lumen and slowly eliminated to the surface. Here, a dilated follicular infundibulum filled with a parakeratotic plug and a basophilic nuclear debris is seen (1). PF lesions are characterized by erythematous follicular papules with a central keratotic plug, several millimeters in diameter (3). PF persists for years with periods of remission, age of onset is between 2nd and 4th decades (1). Perforating folliculitis is usually associated with underlying conditions such as chronic renal failure, diabetes mellitus, arterial hypertention, primer sclerosing cholangitis, vitamin A deficiency, juvenile acanthosis nigricans , human immunodeficiency virus and drugs. Drugs which are reported to be associated with perforating folliculitis include infliximab, etanercept, bendamustine nilotinib, sorafenib and vemurafemid.

Kyrle disease

Histopathologically there is characteristic transepidermal elimination of abnormal keratin. Kyrle disease usually manifests as multiple, discrete, eruptive papules with a central keratotic plug on the lower extremities. Although few hereditary cases have been reported, most of the cases develops secondary to systemic chronic diseases (10). Kyrle disease typically occurs between the age of 30 and 50 years. Female-to-male ratio of up to 6:1. Kyrle disease is most commonly associated with chronic renal disease and diabetes mellitus. In rare cases, it has been seen in tuberculosis, pulmonary aspergillosis, scabies, atopic dermatitis, AIDS, neurodermatitis, malignancy, hepatic disorders, congestive heart failure, and endocrinological disorders. There are also authors who consider kyrle disease as a variant of prurigo nodularis representing end-stage excoriated folliculitis(10).

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Nobel Prize of Aziz Sancar and Dermatology

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Aziz Sancar won the 2015 Nobel Prize in Chemistry for his research mapping how cells repair damaged DNA and preserve their genetic information.

The DNA structure is faced with the attack of thousands of toxic internal and external agents every day. In response to these attacks, human cells have tried to develop many repair pathways to maintain their integrity. Absence or insufficiency of these repair mechanisms led to many diseases including cancer and genetic disorders.Some types of colon and breast cancer along with several genetic disorders including Ataxia Telangiectasia , Bloom and Werner syndrome have been reported in individuals with repair defects in cells (1).

Skin cancer is the most common form of cancer across the world. The main cause of this cancer is DNA damage induced by the ultraviolet component of sunlight. Ultraviolet radiation produces major lesions in DNA, which are mutagenic and carcinogenic in animal model systems and are thought to be the primary cause of skin cancer in humans (2).

Exposure of cells to ultraviolet light from the sun causes the formation of pyrimidine dimers in DNA that have the potential to lead to mutation and cancer.In humans, the single way for removing pyrimidine dimers from the genome is nucleotide excision repair (3).

Aziz Sancar studied the first DNA repair pathways, an enzymatic photoreactivation which is the process of converting ultraviolet-induced pyrimidine dimers back to monomers by photolyase enzyme (4).

Photolyase is a member of cryptochrome/photolyase protein family which perform different functions such as DNA repair, circadian photoreceptor, and transcriptional regulation. This enzyme repairs DNA photoproducts formed due to ultraviolet exposure through the absorption of blue light (5).

Several products are now commercially available that contain the specific ingredient, photolyase, one of the DNA repairing enzymes shown to have clinical effect on human skin.

Ultraviolet-induced skin cancers are caused by mutagenic replication of epidermal keratinocyte DNA. The same ultraviolet dose is more carcinogenic in early morning hours compared to exposure in the early evening hours.Sancar et al found that maximum repair capacity was in the morning hours. Thereby, restricting ultraviolet exposure to morning hours would reduce the risk of skin cancer in humans (6).

Besides skin cancers, there are many other diseases characterized by hypersensitivity to ultraviolet and are often precipitated or exacerbated by exposure to sunlight.So, excision repair is really an important issue for human health.

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THE RATIONAL USE OF DRUGS

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The Irrational Use of Drugs (IUD) is an ever-growing global problem. Due to non-compliance to the rules of rational use of drugs (RUD), many formerly unencountered economic and health-related problems have begun to arise, and the consequences of "irrational drug usage" make themselves more evident with each passing day. According to WHO, more than 50% of all medicines are incorrectly prescribed, dispensed, and sold, and more than 50% of patients take their drugs incorrectly.[1]

Rational Use of Drugs is defined by the World Health Organisation (WHO) 's experts as "Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.", in a meeting in Nairobi in 1985.[2]

The most common factors that may contribute to the incorrect use of medicines are indicated as follows;

1. Prescriptions based on the information from pharmaceutical companies rather than on evidence-based clinical guidelines;
2. Mis- or incomplete diagnosis of a patient's disease
3. Patients' budget limitations leading them to seek affordable but not-quality-assured versions of drugs on the internet.

CONSEQUENCES OF IRRATIONAL DRUG USE

One of the most well-known consequences of irrational drug use is the emergence of antibiotic-resistant bacteria. Overuse of antibiotics has led to the appearance of drug-resistant forms of various infectious diseases (e.g., multidrug-resistant forms of tuberculosis and staph. aureus). Other negative results of misuse include exhaustion of national health budgets, depletion of drug stocks, and increased drug prices. In addition to these global problems, incorrect use of drugs may also cause serious individual risks for patients, i.e., adverse events which may increase the illness period, cause death or reduce their faith in health-care providers.[3]

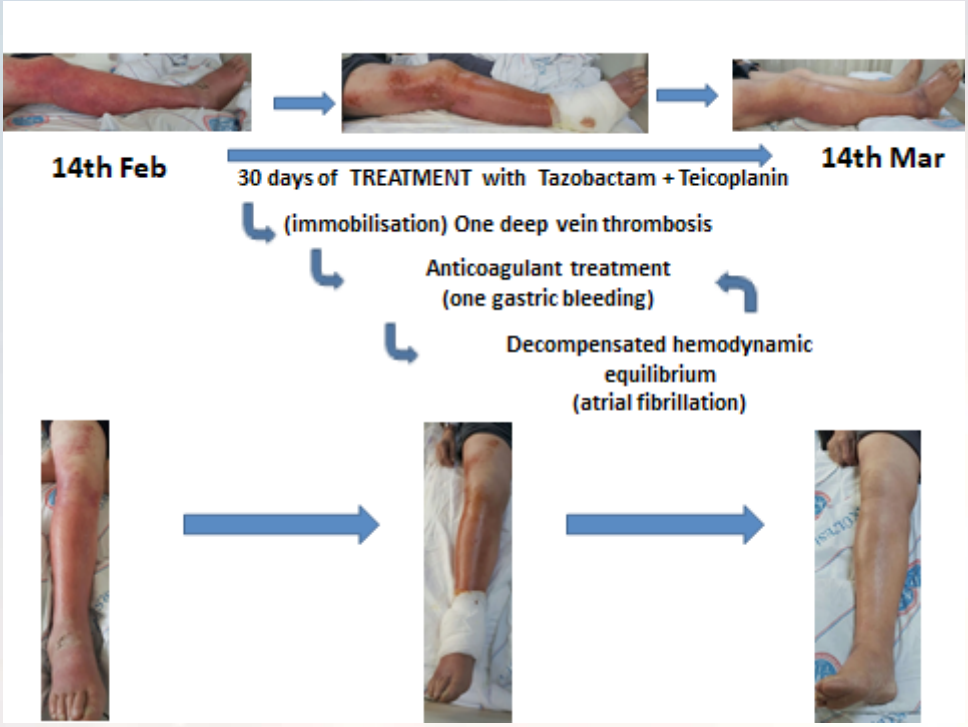
A PERSONAL EXPERIENCE

Like our many other colleagues, I have also experienced the effects of irrational use of drugs firsthand. At this point, I would like to present one of the cases followed-up in my clinic to emphasize the effects of "irrational use of drugs" on patients and doctors, to show how harder our lives are made by these antibiotic-resistant bacteria, the so-called "superbugs" by the mainstream media.

An 80-year man was referred to our clinic. This man was diagnosed with erysipelas and treated for 25 days with sulbactam + ampicillin combination (first ten days with tablet form and the remaining 15 days with iv form). Despite the worsening of the clinical situation, the patient's medications were not reviewed and changed. At the end of the 25 days, due to lack of clinical improvement, he was referred to our clinic. At the time of admission, the patient's right leg was edematous, covered with erythema, and painful to touch. After the admission and hospitalization, we performed multiple biopsies for cultures. Systemic antibiotherapy was started with tazobactam and teicoplanin without any further delay. All the bacterial cultures were negative, but there was a marked elevation in the Antistreptolysin O levels. After 30 days, there was a marked improvement in the patient's condition: to be precise in the condition of his right leg. However, during these days, we first had to struggle with the impaired renal function tests. Due to the persistent elevations in blood urea nitrogen and creatinine levels, we had to extend the intervals between the teicoplanin doses, leading to extended hospitalization and immobilization. On the 10th day (about after 40 days of immobilization), a deep vein thrombosis in the right leg manifested with intensified erythema and pain. The patient was heparinized (impaired renal function test), which was followed by gastrointestinal bleeding. Heparin dose was lowered, but then atrial fibrillation occurred, possibly due to thromboembolism. We had found ourselves in a situation similar to a "Mexican Standoff." We could

neither increase nor decrease the heparin doses safely. Finally, heparin doses were increased with closeup monitoring and with more intense gastrointestinal protective therapy.

As you can see, all the clinical and laboratory clues were pointing out to a streptococcal infection. Theoretically, this patient should be able to recover with simple aminopenicillins in 10 – 14 days. But it took him 60 days to heal, and during this period, he experienced many serious complications.



Probably, many of us have experienced similar situations and are familiar with this aspect of irrational drug use, antibiotic-resistant bacteria. World Health Organisation's 2014 surveillance report for global antimicrobial resistance (AMR) shows us that we are not alone, and the situation is far more critical.[4]

CONCLUSION

Irrational use of medicines is a global and multifaceted problem with severe consequences. Physicians may contribute to RUD by staying up to date with therapeutical guidelines.

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INFLAMMOSCOPY: BASICS AND BEYOND

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Even though the primary idea behind the introduction of dermatoscopy was an early skin cancer diagnosis, the method has become widely used in a number of situations. Considering how common are inflammatory diseases in everyday dermatology practice, inflammoscopy becomes an integrative part of the dermatologic clinical examination, along with taking medical history, visual inspection and palpation. The rudimentary knowledge on the origins of colours and vascular patterns in dermatoscopy, and the ability to combine all the clues is pivotal for making the diagnosis and to interpret the inflammoscopic images during the follow-up to monitor the outcomes of the treatment (monitoroscopy) [1]. This powerful auxiliary tool is not only potent to rule out many clinical differentials, confirm the tentative diagnosis or introduce new, dermatoscopic ones. This method limits the costs of care (unnecessary laboratory tests and medical procedures), saves patient's money, stress and time till the final diagnosis. Moreover, it may prevent the consequences of diagnostic error and subsequent therapeutic side-effects. The dermatoscope creates an invisible bond between the patient and the physician, and familiarizes him with the idea that the physician cares about the patient's well-being, is precise and eager to help, and has a broad knowledge on what he sees. International Dermoscopy Society consensus on inflammoscopy (2019) distinguished 5 parameters important for the diagnosis: vascular clues (morphology and arrangement), scale (colour and distribution), follicular clues, other clues and specific clues (unique to particular diagnoses) [2,3]. 4 clinical groups of inflammatory diseases were selected for this lecture (papulosquamous and maculopapular diseases, papulokeratotic diseases, erythematous facial diseases and granulomatous diseases) either due to their prevalence or for the presence of specific clues [4,5].

Keywords: dermatoscopy, inflammoscopy, monitoroscopy, inflammatory diseases

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FACIAL PIGMENTED LESIONS: MAKE IT SIMPLE!

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Dermoscopy significantly enhances the diagnostic accuracy of pigmented and non-pigmented cutaneous lesions. Nevertheless, the dermoscopic differential diagnosis of facial lesions may be challenging, due to the specific anatomic and histologic characteristics of facial skin. Solar lentigo, pigmented actinic keratosis, lichen planus like keratosis and lentigo maligna are the common pigmented flat facial lesions. The presence of four dermoscopic criteria has high sensitivity and specificity for the diagnosis of lentigo maligna when compared to solar lentigo or early seborrheic keratosis. These criteria include asymmetric pigmented follicular openings, dark rhomboidal structures, gray globules, and gray dots. Every single criterion can also be observed in solar lentigo or seborrheic keratosis but the presence of all four features together is indicative of lentigo maligna. In contrast, light brown curved lines, milia like cysts, scalloped borders and sharp demarcation have been linked with the diagnosis of seborrheic keratosis or solar lentigo. Recent studies showed that lentigo maligna and pigmented actinic keratosis show strikingly similar dermoscopic patterns. Any of the established criteria of lentigo maligna can be also observed in pigmented actinic keratosis. However; black blotches within the follicular opening, namely obliterated follicles appear quite specific to lentigo maligna while obvious follicular openings are indicative of pigmented actinic keratosis. The differential diagnosis between the two entities may be even histopathologically challenging when it is not clear whether the pigmented atypical cells in the basal layer are keratinocytes or melanocytes. Dermoscopic differentiation between lichen planus like keratosis and lentigo maligna is also not straightforward and can be made only if areas of the preexisting benign solar lentigo and seborrheic keratosis are yet preserved. Completely or nearly completely regressed lichen planus like keratosis is distinguished by diffuse brownish-gray granules, which may coalescence to create globules, streaks, or even structures similar to rhomboids. Because lentigo maligna may display the same dermoscopic features, a biopsy should constantly be done in a lesion exhibiting dermoscopic hints of regression.

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DERMOSCOPY IN MELANOMA: WHAT'S NEW?

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Melanoma is one of the most aggressive skin cancers and accounts for the vast majority of skin cancer deaths. Due to the rising incidence of cutaneous melanoma clinicians may need new diagnostic techniques and clues as well as the improvement of those that are already well known, such as dermoscopy. Since early detection and a proper technique for excising the tumor are crucial for patients' survival, early staging of the tumor is very important.

Multicomponent global pattern, including atypical network, regression, irregular dots/globules, irregular bloch, irregular streaks/pseudopods, shiny white streaks, blue white veil and atypical vessels is the most common and classical dermoscopic feature of melanoma. Most of the features above have been described in advanced melanoma cases and recently there are some new dermoscopic features that are described especially in diagnosis of melanoma in situ and small melanomas. Of course, classical features may be found in these tumors but irregular hyperpigmented areas, prominent skin markings, polygons/angulated lines and rhomboids or zig-zag lines may be the main clues of early melanoma. In nonpigmented thin melanomas the irregular blue structureless areas, shiny white lines, dotted vessels and serpentine vessels may be the clues for melanoma.

The presence of such dermoscopic structures should alert the examining clinician. From this point of view, dermoscopic examination is a very important method in the early diagnosis of cutaneous melanoma, especially in regard to early, non- metastatic tumors.

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MUCOSCOPY: WHAT WE KNOW?

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Dermoscopy is a noninvasive technique, which is widely used for the examination of pigmented and nonpigmented lesions of the skin, scalp, nails, palms, and soles. By using dermoscopy, the clinician's diagnostic accuracy increases, and may allow the recognition of malignant skin tumors at an early, curable stage. There is increasing evidence that dermoscopy may also be helpful to differentiate benign from malignant or suspicious lesions arising in the mucosa. Lips, oral cavity, and genital skin (perianal, penil, vulvar) are mucosal areas. Pigmented or non-pigmented lesions of these areas are rarely seen. Dermoscopic examination of mucosal lesions, namely Mucoscopy, reveals structural, color and pattern characteristics of these lesions. This presentation will review the dermoscopic features of pigmented and nonpigmented mucosal lesions and the dermoscopic criteria for differentiating benign from malignant tumors.

DERMOSCOPY IN ADNEXAL NEOPLASMS

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Introduction

Cutaneous adnexal tumors are classified to their adnexal differentiation as sebaceous, follicular, ecrine and apocrine. They often cause diagnostic difficulty. Dermoscopy is a noninvasive technique improves diagnostic accuracy of skin tumors.

Sebaceous tumors

They are classified as sebaceous nevus, sebaceous hyperplasia, sebaceous adenoma, sebaceoma and sebaceous carcinoma.

Sebaceous nevus; complex hamartoma presents at birth and commonly affects head and neck, particularly scalp. The natural history is divided into 3 stages: childhood, puberty and postpubertal stage. At the third stage 10-20% may be complicated by benign or malignant epidermal, adnexal or mesenchymal tumors (trichoblastoma, syringocystadenoma papilliferum and BCC).

Sebaceous hyperplasia; most common proliferative abnormality of sebaceous glands. It most often presents on the face of older adults, particularly men and characterized as whitish-yellow or skin colored, soft umblicated papules.

Sebaceous adenoma; solitary or multiple skin-colored, yellowish or reddish nodules, sometimes with multilobulated surface, particularly seen on head and neck area. Two patterns are observed on dermoscopy. One of them is opaque structureless ovoid white-yellow centre and embracing elongated radial telangiectasias (crown vessels) with central crater. The other one is branching but unfocussed arborizing vessels over a white-yellow bacground and few yellow comedolike globules without central crater.

Sebaceous carcinoma; a rare adenocarcinoma with variable degrees of sebaceous differentiation. Classified into periocular and extraocular subtypes. Clinical presentation is varied. It has a 30-40% for local recurrence, 20-25% distant metastases and 10-20% mortality. Dermoscopic pattern described only sporadically. It is composed of polymorphous atypical vessels, homogeneous yellowish background and ulceration.

Follicular tumors

These are a large and heterogeneous group neoplasms. They are classified as nevus comedonicus, basaloid follicular hamartoma, trichilemmoma, inverted follicular keratosis, pilomatricoma, trichofolliculoma, trichoblastoma, trichoepithelioma and fibrofolliculoma.

Nevus comedonicus; clinically characterized by multiple, grouped dilated follicular openings with dark keratin plugs resembling comedones. Dermoscopically, multiple, well-defined, light and dark brown, circular or barrel-shaped homogeneous areas with keratin plugs have been observed.

Basaloid follicular hamartoma; a rare acquired or hereditary benign adnexal tumor. Asymptomatic small lesion (macule, papule, nodüle, plaque) located on the head. Dermoscopically, structureless bluish macule or as a lesion with globular pattern; white, pink and gray areas; and the presence of comedolike openings and milialike cysts are seen.

Trichilemmoma; well-defined, asymptomatic, flesh-colored papules or verrucous growths located on head. On dermoscopy, radial linear vessels (occasionally hairpin vessels) with distal thickening adopting a triangular form in the periphery of lesion (red irislike structure), white shiny areas surrounding vessels, a whitish keratin mass, maybe with a central hyperkeratotic crust are seen.

Inverted follicular keratosis; a rare tumor originates from follicular infundibulum. Asymptomatic, solitary, white-pink nodular or verrucous lesion (small than 1 cm) located on head of older men. Dermoscopically, there are 2 main patterns: the most common «keratoacanthomalike pattern». Central keratin surrounded by hairpin vessels with a white halo in a

radial arrangement is seen. The other pattern is characterized by a yellowish-white,

homogeneous, amorphous central area surrounded by hairpin vessels with a white halo in a radial arrangement. Arborizing vessels, glomerular vessels, corkscrew vessels and milky-red globules may be seen. Vascular structures are commonly monomorphic.

Pilomatricoma; a benign tumor with tendency toward calcification that usually presents as a single, firm, dermal nodule, often on the head or neck of children or adolescents. White and/or yellow homogeneous areas shaped and distributed irregularly (calcification), white streaks, reddish homogeneous areas, hairpin vessels and linear irregular vessels are common. Ulceration, dotted vessels, structureless blue-gray areas are additional findings.

Trichofolliculoma; uncommon, benign hair follicle hamartoma of adults. Solitary facial or scalp papule with a central dilated pore with a small tuft of hairs. On «firework» pattern; central brown zone with radial, dark brown projections are observed. Pinkish papule with a central disruptor and fine peripheral serpiginous vascularization with centripetal disposition was described by Jegou-Penouil et al. Garcia-Garcia et al described a well-defined, firm, bluish nodule with a white-pink central area, shiny white structures, dotted vessels and a central scale.

Trichoblastoma; a benign tumor of rudimentary hair follicles characterized by solitary, skin-colored papule on the scalp or face. It developes in isolation or arise in sebaceous nevus. It is difficult to differentiate BCC by dermoscopy. Both have blue-gray ovoid nests, leaflike structures, and arborizing vessels. Arborizing vessels in trichoblastoma less branching than in BCC. Blue-gray globules and ovoid nests more frequent in BCC. Trichoblastomas are symmetric (BCC mainly asymmetric) and have large blue-gray ovoid nests.

Trichoepithelioma; considered as a superficial trichoblastoma with prominent infundibulocystic differentiation (cribriform trichoblastoma). There are skin-colored papules on the central face. Dermoscopically; small, thin, infocus arborizing vessels, shiny white areas/background and milialike cysts are observed.

Fibrofolliculoma; benign, clinically indistinguishable connective tissue tumors. Small (2-4 mm), white to flesh colored papules are seen on the head, neck and upper trunk. Dermoscopically, fibrofolliculomas show whitish globules with a central yellowish-brown spot and may present a prominent vascular component, such as curvilinear vessels connecting red dots and globules. Trichodiscomas reveal whitish globuler structures, blue-gray nests and blurred linear vessels.

Others

Pilar sheath acanthoma; benign tumor as an asymptomatic facial (upper lip) papule with a central opening. On dermoscopy: papillomatous projections toward the center of the lesion, linear vessels on the periphery, depressed central area with rests of yellowish keratin are observed.

Trichilemmal carcinoma; a rare malignant tumor frequently appears on the face and ears of elderly patients. Dermoscopically polymorphous vascular pattern, white-yellowish areas and ulceration have been observed.

Eccrine and Apocrine Tumors

Apocrine and ecrine hidrocystomas, syringocystadenoma papilliferum, nodular hidradenoma, cylindroma and spiradenoma, syringoma, poroma, hidroacanthoma simplex, porocarcinoma

Apocrine hidrocystomas are benign cystic lesions of apocrine sweat glands. Intradermal translucent nodule on the head and neck is seen. Dermoscopically; a central homogeneous area, translucent to opaque, occupied the whole lesion is observed. That area may be skin-colored, yellowish, blue, less frequently pinkish-blue or gray. Vascular structures usually as arborizing vessels and whitish structures may be observed.

Ecrine hidrocystomas are benign tumors of the ecrine sweat glands. Translucent, skin-colored vesicular-papular lesions, mainly localized on the face. Dermoscopically; a central homogeneous area with a skin-colored or bluish hue sometimes surrounded by a pale halo is seen.

Syringocystadenoma papilliferum; a benign sweat glandular tumor frequently seen in association with other adnexal tumors. Second most common benign neoplasm occuring in sebaceous nevus after trichoblastoma. Quite symmetric,

erythematous lesion with exophytic papillary structures, ulceration and vessels are observed. Flatter lesions have pinkish-white or yellowish structureless central area with irregular vessels were reported by Zaballos et al.

Nodular hidradenoma; is a benign, slowly growing benign tumor of mostly apocrine origin. It is characterized by solitary, nodular, cystic or pedunculated lesion. Serrano et al reported homogeneous area occupying the whole lesion with vascular and white structures on dermoscopy. Homogeneous area is pinkish in nonpigmented hidradenomas, bluish in pigmented hidradenomas and pink-bluish in the rest. Highly vascular; 3 most common

vascular structures are arborizing telangiectasias, polymorphous atypical vessels and linear irregular vessels. It is confused with BCC, melanoma, dermatofibroma.

Cylindroma; benign tumor of the head, characterized with slowly growing solitary pink or red dermal nodule.

Spiradenoma; solitary blue or pink dermal nodule. Dermoscopy of both are similar, homogeneous pink or pink-orange area with arborizing telangiectasias, sometimes blue globules and ovoid nests are seen.

Syringoma; common tumors present as multiple small papules on the lower eyelids, less frequently on other locations. Homogeneous pinkish or light brownish central area with multiple round yellow-whitish structures are seen.

Poroma; uncommon benign tumors clinically simulate other neoplasms. Solitary reddish nodule is seen on the soles or palms with a collarette. Multiple lesions, pigmented variants and different localizations have been described. It is called as «great dermoscopic imitator». Dermoscopic features associated with poromas are white interlacing areas around vessels, yellow structureless areas, milky-red globules. Vessels are poorly visualized.

Hidroacanthoma simplex; is a benign intraepidermal neoplasm derived from acrosyringium. It is usually misdiagnosed as a seborrheic keratosis, BCC or Bowen disease. As epidermal, special dermoscopic findings are pinkish, whitish or brownish background with black dots/globules, black lines, whitish globular structuress, scales and dotted vessels.

Porocarcinoma; most frequent malignant sweat gland neoplasm of elderly individuals commonly localized on lower extremities. It is characterized by pink nodule with occasional ulceration. Dermoscopically; pink, whitish, or brown background and vascular structures have been seen. White-pink halos around the vascular structures, round or oval structureless areas, hemorrhage and ulceration are seen.

Others

Accessory nipples; resemble dermatofibroma, peripheral delicate pigment network and a central white scarlike area.

Hidradenoma papilliferum; benign tumor with apocrine differentiation usually localized on anogenital area, diffuse homogeneous blue pigmentation.

Nipple adenoma; resembles mammary Paget disease, light red background with irregular vessels.

Tubular apocrine adenoma; red to brownish nodule of the scalp, oval bluish areas with short fine telangiectasias and large blue-gray ovoid nests very similar to BCC.

Microcystic adnexal carcinoma; locally aggressive malignant adnexal tumor of the head and neck, white or orange background with arborizing vessels and white small dots.

Malignant nodular hidradenoma (hidradenocarcinoma); only one dermoscopic description about a fast-growing facial nodule; whitish pink background and scattered around, pinpoint, linear irregular, hairpin and glomerular vessels. It resembles amelanotic melanoma, poroma or porocarcinoma.

Conclusion

Dermoscopy of adnexal neoplasms and the other skin cancers usually resembles to each other. So, excisional biopsy and histopathological examination is still gold standard for the distinct diagnosis.

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FACE SHAPES AND COSMETICAL APPROACHES

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Abstract

The concept of facial aesthetic has changed over time, for this reason it seems difficult to define ideal aesthetic characteristics and beauty. The face is the most important factor affecting the physical appearance. The most important factors of facial attractiveness are averageness, sexual dimorphism, youthfulness and symmetry.

In facial aesthetics, there is a specific mathematical proportion which is called golden proportion (GP). The GP is used to evaluate the aesthetic appearance of face in aesthetic surgery. Many authors have used the GP tool to measure and analyse facial aesthetic qualities in their own countries.

Facial analysis typically begins with examining the skeletal framework of the face for symmetry and proportion. This is traditionally done by dividing the face into horizontal thirds and vertical fifths. The horizontal thirds are measured from the hairline to the glabella, the glabella to the subnasale, and the subnasale to the menton. Each of these heights is exactly one-third of the facial height. Studies about facial height proportions reported that there is only 50% of equality. Facial height is higher in males than in females in all races. The face is also divided into vertical fifths, in which each part is equal to the width of the eye. Classically, the nose fits perfectly within the middle fifth, and the lateral fifth extends from the lateral canthus to the lateral most visible point of the helix of the ear on frontal view.

Although cosmetic interventions commonly are described based on a single anatomical unit, it is important to figure out the relationships between facial structures. Clinicians should be mindful of facial ratios when considering the introduction of filler materials. Augmentation procedures at the temples, zygomatic arch, jaw, chin, and lips all have the possibility to alter facial ratios. Changes should therefore be considered in the context of improving overall facial harmony, with the clinician's knowledge of the ideal vertical and horizontal divisions of the face. Understanding such concepts and communicating them to patients can help in addressing all target areas, thereby leading to greater patient satisfaction.

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OFF-LABEL USES OF HA FILLERS IN AESTHETIC DERMATOLOGY

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Injectable soft tissue filler procedures are becoming increasingly important for rejuvenating the aging face. Hyaluronic acid (HA) fillers appear to be ideal due to their low immunogenic potential.[1] They are medical device implants approved by the FDA for use in helping to create a smoother and/or fuller appearance in the face, including nasolabial folds cheeks, chin, lips, and back of the hands. However, glabella, nose, periorbital area, forehead, and neck have not been approved by the FDA. The FDA also recommends against using dermal fillers or any injectable filler for body contouring and enhancement to breast augmentation, size of the buttocks, fullness of the feet and bone, tendon, ligament, or muscle.[2,3]

As with any medical procedure, there are risks involved with the use of HA-fillers. It is important to understand their limits and possible risks. Any dermal filler can cause temporary side effects, permanent side effects, or both. Most side effects associated with HA fillers occur shortly after injection and many of them resolve in a couple of days. Swelling and pain after hand treatment may last a month or longer. In some cases, side effects may be lethal.[4-6]

Common risks include; bruising, redness, swelling, pain, tenderness, itching, rash and difficulty in performing activities (after hand filler).

Less common risks include; raised bumps in or under the skin (nodules or granulomas that may need to be treated with injections, oral antibiotics, or surgically removed), infection, open or draining wounds, a sore at the injection site, allergic reaction and vascular occlusion-necrosis.

Rare risks include; anaphylactic shock that requires immediate emergency medical assistance, late allergic reactions, filler migration, leakage or rupture of the filler material, chronic inflammation and infection, biofilm, hypertrophic or keloid scars, telangiectasia, the formation of permanent hard nodules, loss of function (Vascular occlusion, resulting in necrosis, vision abnormalities including blindness, stroke, or even death).[3-6]

It is crucial to manage complications of both approved or off-label uses of dermal fillers. Safety should be the first and most important consideration. Hyaluronic acid fillers can be delivered safely and efficaciously by either cannula or needle if used appropriately. However, the panel recommended that needles be used with caution in areas prone to vascular complications. Product selection is important, as the safety profiles of dermal fillers may vary. Importantly, the physical and rheologic properties of the filler should fit the intended intervention. For example, products with a higher elastic modulus (G′) are not recommended in delicate areas such as the tear trough. Appropriate injection techniques help to limit the risk of adverse reactions and contour irregularities.[7-8]

Insufficient experience is a contributory factor in the development of complications. Clinicians should seek appropriate product selection and practice proper techniques to minimize adverse reactions. Clinicians performing injections should have a thorough knowledge of injection-related anatomy and before treatment, elicit a full history of previous cosmetic procedures to determine whether relative or absolute contraindications exist. Vascular complications are statistically rare following the injection of dermal fillers, but these complications are still prevalent in the population because dermal filler products are used so often. The risk is higher for these events when large bolus injections are sent deeper into tissues for volume enhancement and when smaller needles are used. Treatment begins with diagnosis of the event and should continue with administration of hyaluronidase, aspirin, and topical nitropaste, along with the application of warm compresses and massage of the affected area. After initial treatment, if ischemia is still present, evidence, although weak, suggests that hyperbaric oxygen therapy may benefit some patients.[6-10]

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AGEISM IN AESTHETIC DERMATOLOGY

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Growing elderly population referred to as gray or silver tsunami are an increasingly serious health and socioeconomic concern for modern societies. Aging societies are no longer an interesting phenomenon but rather an inevitable fact[1].

Age discrimination is a widespread and insidious global issue with far reaching ramifications. But the tide is turning[2].

Ageism against individuals due to age negatively affects older adults, particularly women. Age discrimination has been shown to negatively affect self-esteem, cognition, behaviour, physiological function, health, willingness to live, and even mortality. This stress of rejection increases risk for psychological distress and physical health problems. Negative stereotypes of older adults as being incompetent may lead to different forms of social exclusion[3].

Such exclusion is also present in research, specifically in clinical research and randomised clinical trials. Many studies use upper age limits as an unjustified exclusion criterion[4].

Aging is a prominent factor in motivating patients to seek cosmetic treatments. A significant proportion of cosmetic surgery patients seek antiaging procedures due to negative societal views about aging and the appearence of aging signs[3].

84% of adults who undergo minimally invasive cosmetic procedures, and 81% of adults undergoing any cosmetic procedure, are ages 35 years and older![3]

However, few studies have investigated experiences of ageism and their relationship to health among patients seeking these and other cosmetic procedures[3].

'Looking younger' and **'as young as i feel'** were among the main reasons reported by patients for seeking their cosmetic procedure. patients reported seeking cosmetic treatment to look younger, but **not to 'conceal' their age![3]**

Perceived age discrimination was associated with poorer self-rated health, lower self-esteem, and greater anticipation of age discrimination in the future[3,5].

More research is needed to understand how older adults' use of anti-aging procedures, and the public's knowledge of these procedures, may or may not affect experiences of age-based discrimination. Also further studies are required to understand the relationship between cosmetic procedures and anticipated and perceived age based discrimination in aging patients to optimize patient outcomes[3].

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BDDA: MYTHS AND FACTS IN AESTHETIC DERMATOLOGY

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A myth is a popular belief or tradition that has grown up around something or someone. Besides, a fact is something that has actual existence. As acne vulgaris, skin aging problems and pigmentation disorders are the most common dermatological diagnostic skin disorders in the past year in my clinic, I would like to talk about the basic myths in these three popular topics. The myths and misconceptions about acne causation, exacerbating factors and treatment efficacies are common not just among the patients, but also among some family physicians (1). It was also seen that there is still a lack of knowledge about acne course, treatment outcomes, recurrences and isotretinoin therapy (1). The myth that "acne is just a teenager disease that will improve spontaneously" may have already caused some people refuse to go to a dermatologist (2). However, acne vulgaris is a chronic disease, that often starts at puberty and lasts long time after puberty. "Acne is not caused by cosmetics" is another common misconception, as some of the oily comedogenic make up products are the well known causes of a mild comedogenic acne known as "acne cosmetica" seen especially among young women (2). Besides, "acne doesn't affect psychosocial life, it's just only a skin disease" is another common myth (3). We have to accept that acne's psychological impact may affect social relationships, success in business life, sexual affair and friendship situations (4). Open comedones are thought to be blackheads that are made up of dirt. However, comedones are consist of oxidized sebum and keratin (2). Face wash with harsh soaps has just very little to do with acne and does not stop acne or cloging of the pores. Patients need to avoid frequently washing face because it will cause sebaceous gland hyperactivity to compensate skin lipid loss (2). Some people believe that sun exposure helps to eliminate acne vulgaris (2). In fact; although there is a little evidence that sunlight has a positive effect on acne, we also have to consider the possible long term carcinogenic effects of sun exposure (2).

Secondly when we have a look at the myths about skin aging; we may notice some people think that "Only genetic and age play a role in the formation of wrinkles" (4). But, in fact skin aging includes both intrinsic and extrinsic factors. Extrinsic factors include enviromental and behavioral factors such as sun exposure, smoking, dietary nutrients, body mass index, menopausal status (4). The myth that "skin aging can not be prevented by consistent skin regimen" is just a false belief (5). Retinoic acid, anti-oxidants, estrogens, growth factors and cytokines are some of the secondary measures against skin aging (5). Besides, cosmetic procedures such as chemical peels, microdermabrassion, laser, botulinum toxin and filler injections are the tertiary antiaging treatments that reduces and treats the signs of skin aging. While retinoids such as tretinoin and tazarotene are some of the evidence level A antiaging treatments, aminoacids, minerals, anti-oxidants such as vitamin C, vitamin E and Coenzyme Q10, alpha-Lipoic acid may also act with a level of evidence that differ from A to C (5).

There are also numerous other misconceptions regarding the use of botulinum toxin for aesthetic indications that have arisen (6). Botulinum toxin neurotoxin/protein complexes are irrelevant to the toxins's therapeutic indications. BONTA neurotoxin/protein complexes do not influence movement from injection site or immunogenecity (6). Any relationship between neutralizing antibody formation and clinical response is complex and clinicians should consider other factors that may induce an appereant loss of clinical response (6). Diffusion appears predominantely, perhaps exclusively, dose dependent (6). Careful placement and correct dosing optimizes likelihood of good outcomes. Manufacturers recommend reconstriction of products with sterile non-preserved saline. However, compelling evidence suggests that reconstriction using preserved saline dramatically improves patient comfort without compromising efficacy (7). Several posttreatment instructions/restrictions are widely used despite the lack of evidence, but muscle activity after injection may be beneficial (6). Cooling the treatment area might hinder BONTA translocation and should probably be abandoned (6).

Facial fillers that are used only for the elimination of wrinkles make the face look like frozen and they act exactly the same as botox are some of the common myths arisen about fillers. Besides, there are still lots of different myths and misconceptions about the aims, application protocols, treatment outcomes, patient expectations and adverse effects of cool sculpting, radiofrequency (RF), Thermage, high intensity focus ultrasound (HIFU) and laser hair removal treatments (7-8).

If we consider the most popular myths about the use of sunscreens, the myth that the higher SPF is better is not heard rarely (9). Besides, applying sunscreens with SPF 15 and SPF 30 will result in SPF45 is another common myth. There are also some other misconceptions about the use of sunscreens in cloudy weather and rainy seasons such as the sun exposure is not dangerous during winter (9). Moreover, some popular myths about skin pigmentation include darker complexion individuals are not likely to develop disorders of hyperpigmentation, using a skin-lightening treatment will permanently remove skin pigmentation and applying skin lightening products long term is safe (10).

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HOLISTIC APPROACH TO SKIN AGING

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Skin aging has two components. Intrinsic aging stands for the "normal" decay of the skin, associated with chronological age. Extrinsic aging is incurred through environmental causes of cell damage (exposome) and overlaps intrinsic aging. Both intrinsic and extrinsic inflammatory processes combine to manifest in the skin aging as fine wrinkles, loss of elasticity, dryness, and sallowness. Cosmetic dermatologists use many procedural interventions to diminish signs of aging. However the procedures alone are not enough for a successful antiaging treatment. A complete anti-aging treatment can consist of many strategies or combinations of them, such as avoiding exogenous factors of aging, changing one's lifestyle and habits (i.e. smoking, UV radiation, nutrition, physical activity, stress), and using topical cosmeceutical agents and/or oral nutraceuticals.

SUNSCREENS: WHAT'S NEW?

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Sunscreens are used to protect the skin against harmful effects of ultraviolet (UV) radiation. The history of sunscreen can be traced back to the Egyptians, they used ingredients such as rice bran, jasmine, and lupine to avoid the tanning effects of the sun.[1] Modern sunscreens were initially developed with the sole purpose of minimizing erythema after 1930s.[2] Nowadays, new sunscreens have the combination of a filter system (UVB, UVA, long-UVA) and antioxidant protection against infrared and pollution.[2]

The primary effect of sunscreens includes physical barriers that reflect and scatter light and chemical barriers that absorb light. Secondary factors include antioxidants, osmolytes, and DNA repair enzymes, which help to limit skin damage by disturbing the photochemical cascade that takes place by UV sunlight.

Antioxidants, photolyases or photoreactivation enzymes, and polyphenols or plant-derived aromatic compounds have been the newest area of research due to their anti-inflammatory and anticancer properties.[3, 4] Beside newest compounds delivery methods are also newly research area. Nanostructured lipid carriers (NLCs) have been highlighted for topical application due to their biocompatibility, owing to the presence of non-irritating and non-toxic lipids. They can provide controlled release for prolonged time and thus can potentially reduce systemic exposure. More importantly, these lipid nanoparticles present physical stability and produce the stabilization of labile substances against degradation. Additionally, the concentration of the incorporated sunscreen can be decreased, and the sunscreen effect is kept, which reduces the risks associated with high concentrations administered.[5]

In conclusion, together with the newly developed substances, sunscreens provide anti-inflammatory, anti-tumor, and antioxidant effects and the systemic side effect profile of sunscreens is reduced.

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DO SUNSCREENS PREVENT VITAMIN D SYTHESIS?

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Solar ultraviolet (UV) radiation contains UVB and UVA. While UVB makes up ~5% of solar radiation, it is responsible for most of the damaging effects of the sun. However, UVB also initiates cutaneous vitamin D synthesis, providing the mechanism responsible for ~80% of all the synthesized in the body (1). Sunscreen use is widely advocated to prevent the unwanted effects of sun exposure, such as skin aging, sunburns, and skin cancer. There are concerns that widespread use of sunscreens may lead to vitamin D deficiency.

In theory, effective use of sunscreens should limit UVB-dependent conversion of 7-dehydrocholesterol in the skin to pre-vitamin D3, which is later hydroxylated in the liver to form 25 hydroxyvitamin (25-OH-D), the primary circulating form of vitamin D. However, vitamin D production is dependent on various factors, such as the surface area of the body exposed to sun, exposure time, and previous vitamin D status.

Several experimental studies reported a reduction in vitamin D synthesis with sunscreen use (2,3). These studies utilized artificial UV radiation sources with spectra different from sunlight and measured the change in vitamin D levels in a short time span. On the other hand, large field trials with longer periods of observation reported that sunscreen use was not associated with lower levels of circulating 25-OH-D. However, the sunscreens used in these studies had a moderate sun protection factor (SPF) (4,5). There are not any field trials with high SPF sunscreens used. Most abundant data on the subject is present in observational studies, with discrepant results. In a systematic review, it was found that 65% of observational studies reported no association between sunscreen use and serum 25-OH-D levels, while 25% reported an increase and 10% reported a decrease (6).

In summary, it can be concluded that there is insufficient evidence that sunscreen use decreases 25-OH-D levels. There is still a need for large field studies with high SPF sunscreens. Considering the importance of sun protection in preventing skin cancers, and the low likelihood of sunscreens causing reduced 25-OH-D levels, their benefits seem to outweigh their risks.

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DOES PHOTOTHERAPY CAUSE CANCER?

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Phototherapy, ultraviolet (UV) light-based therapy, is characterized by controlled administration of non-ionizing radiation to the skin. Phototherapy is widely used in the treatment of various skin diseases including, psoriasis, mycosis fungoides, atopic dermatitis, vitiligo, pityriasis lichenoides chronica, eczema, chronic pruritus, lichen planus, and polymorphous light eruption.[1-3]

The commonly used phototherapy types are ultraviolet A-1 (UVA-1) spectrum, UVA spectrum with a photosensitizing agent (psoralenes) (PUVA), and ultraviolet B (UVB) spectrum as broad-band (BB)-UVB or narrow-band (NB)-UVB.[4]

Being the most often used phototherapy type, UVB phototherapy shows anti-inflammatory, immunosuppressive, and cytotoxic effects through of cis-urocanic acid induction, Langerhans cell depletion, decreased activity of natural killer cells, and apoptosis of both T lymphocytes and keratinocytes.[4] NBUVB therapy is known to be more effective and less carcinogenenic as compared with BBUVB therapy.

PUVA phototherapy shows its efficacy by forming the cross-linking of deoxyribonucleic acid (DNA), thus inhibiting DNA replication. Increased production of reactive oxygen species via PUVA leads to cell membrane damage followed by cell death. The other effects are depletion of Langerhans cells and suppression of T-lymphocyte functions and migration.[4]

UVA-1 phototherapy penetrates into the deeper parts of the dermis. Its mechanism of action occurs via inducing interstitial collagenase and cytokines, which provides softening of the sclerotic skin.[4]

Along with therapeutic effects of ultraviolet light, various damages to the skin, including mutations in the DNA of keratinocytes and fibroblasts, chronic oxidation and inflammation, and changes in the expression of tumor suppressor genes may result in carcinogenic skin lesions. [2]

The risk of nonmelanoma skin cancers (NMSC) with PUVA in patients with psoriasis has been well investigated in the literature. A systemic review by Archier[1] et al. showed controversial results of PUVA therapy concerning the risk for squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) in patients with psoriasis. Overall, the majority of large-scaled studies showed that the risk of SCC was significantly higher for patients exposed to more than 200 sessions or 2000J/cm^2 of PUVA than those exposed to less than 100 sessions or 1000J/cm^2 of PUVA. Moreover, SCC may develop in non-exposed skin areas such as the genital region. SCC risk increases linearly with cumulative UV dose. Moreover, despite to cessation of treatment, the risk continues to persist.[1] The risk of BCC was also found to be increased in patients exposed to very high doses of PUVA. The risk of melanoma among psoriatic patients treated with PUVA was reported to be increased, particularly in patients who were exposed to at least 200 sessions of PUVA treatments and after 15 years of time from the first treatment. Merkel cell carcinoma (MCC), a rare type of skin cancer, was investigated in only one study, which showed an increased risk in PUVA-exposed skin sites in patients with psoriasis.

NB-UVB related skin cancers were evaluated in fewer studies compared to PUVA therapy. A recent population-based retrospective cohort study investigated the risks of skin cancers and precancerous lesions among patients who had undergone NBUVB to treat vitiligo.[5] The authors reported that the risks of Bowen disease, nonmelanoma skin cancers, and melanoma did not increase even after more than 200 sessions of NBUVB. However, the risks of actinic keratosis increased significantly in patients who received 200 or more sessions of NBUVB phototherapy.[5]

There is not a large-scale study evaluating the risk of skin cancers following UVA1 phototherapy. Only two cases were reported with the development of skin cancers like melanoma and MCC after UVA1 phototherapy. But these two patients also had other risk factors as follows; concomitant bath PUVA therapy in the first case and immunosuppressive comorbidities in the second case.[6]

In conclusion, the increased risk of skin cancers particularly NMSC is well-documented in patients undergone more than

200 sessions of PUVA. On the other hand, NBUVB seems to be not associated with the increased risk of skin cancers. There is the lack of data on carcinogenic risks of UVA-1 and other phototherapy types.

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WHAT'S NEW IN PHOTOTHERAPY?

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Phototherapy has been widely used in dermatology since early 20th century. Conventional phototherapy modalities are UVA, broadband UVB, narrowband UVB and UVA1. The disadvantages such as frequent clinic visits, difficulty in some areas, risk of photoaging and carcinogenesis, caused development of newer targeted therapies. Most targeted phototherapy devices (laser/nonlaser ones) emit radiation in the narrowband UVB range, but UVA emitting machines also exits.

Excimer laser

The device uses a mixture of a gas and a halogene, predominantly 308-nm xenon-chloride in dermatology. Besides psoriasis and vitiligo, effectivity was reported in oral lichen planus, alopecia areata, atopic dermatitis, morphea, prurigo nodularis, mycosis fungoides, and lymphomatoid papulosis. Bulky expensive machines and blistering reaction are disadvantages.

Monocromatic Excimer light (MEL)

Less bulky and cheaper machines with Xenon-Chloride lambs emitting monochromatic 304 or 308 nm are used. Relatively larger treatment areas are possible in comparison with excimer laser. Responsive dermatoses are similar.

Targeted NB-UVB/UVA

Devices with high-pressure burner and fibre-optic cable transmit energy directly to the lesion. They irradiate both UVA and NB-UVB. There are also handheld home therapy devices with the possibility of inproper administration.

Low level laser therapy (LLLT)

It is also known as photobiomodulation, cold laser and soft laser. Low doses of various light sources (inert gas lasers and semiconductor laser diodes) are insufficent for ablation, cutting and coagulating. LTTT serves to supress inflammation and to increase antioxydants. It is found to be beneficial in cutaneous conditions of acne, psoriasis, vitiligo, dermatitis, herpes, hair loss, keloids and skin aging.

Light emitted diode (LED)

LED is a safe, nonthermal, nontoxic and noninvasive technology. LEDs provide a peak energy output, a less harmful result and greater body application compared to lasers. They are used for inflammatory acne, wound healing, sunburn, hair loss, skin photoaging, scar preventation and postinflammatory hyperpigmentation. Since they reach the sebaceous glands, red and blue LEDS are alsoeffective for acne and rosacea. Visible-near IR (NIR) spectrum is found to be effective for atopic dermatitis and cellulitis. The antimicrobial effect of 405 nm LED had also been shown. In addition, LED technology enhances the activity of PDT.

Photodynamic therapy (PDT)

PDT uses photosensitizing agents to augmentate the effects of visible light or lasers. The absorbation of light by the target cells causes formation of reactive oxygen species, and thereafter apoptosis. PDT is effective in acne, seborrhea, psoriasis, morphea, verruca, molluscum, leischmaniasis and photodamage in addition to cutaneous malignities as actinic keratosis, Bowen's disease and superficial BCC. Fractional laser or microneedle assisted drug delivery of photosensitizers enhances the activity of PDT

Phototermal therapy (PTT)

PTT is the thermal ablation of tumours using photosensizers activated by pulsed laser irradiation at near-infrared (NIR). It has a limited penetration and less harmful to surrounding tissues. Unlike PDT, oxygen has not any role for the destruction of malign cells. It can also be combined with PDT for synergistic affects. Nanomaterials such as carbon nanotube, graphene, gold nanoparticles and quantum nanorods are used in PTT. Not only for cutaneous ones including melanoma, PTT is an advanced and adjuvant procedure in the treatment several malign tumours in general oncology. Except malignities, PTT is also reported to be beneficial in warts, wound healing, candidal granuloma etc.

These targeted therapies obtain quick delivery of energy providing less treatment time, less frequent clinic visits, ability to use in difficult areas as scalp, nails, oral mucosa, palmoplantar and intertriginous and genital regions, and minimizing side effects. But they are already expensive and appropriate for only small areas. Development of simple, smaller and cheaper devices in the light of nanotechnology will obtain less harmful and more effective therapies in dermatology.

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TYPE II INFLAMMATION AND ITS ROLE IN ATOPIC DERMATITIS AND BEYOND

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Type II inflammation underlies inflammatory diseases in a range of organs, including the skin. Type II inflammation is characterized by the action of type II cytokines such as interleukin (IL)-4, IL-13, but also alarmins such as IL-33 and TSLP. These cytokines contribute to the pathogenesis of atopic dermatitis and various other dermatological diseases, where they are key drivers of chronic itch and inflammation. In atopic dermatitis, IL-4 is held to sensitize sensory nerves in the skin and to contribute to itch directly. Type II inflammation is also a key feature of chronic spontaneous urticaria where type I and type II autoimmunity are underlying causes. Type I autoimmunity is IgE-mediated, and IgE-mediated inflammation is linked strongly to type II inflammation. IL-4 is increased in chronic spontaneous urticaria, drives IgE production and is pruritogenic. Ongoing studies in chronic spontaneous urticaria as well as cholinergic urticaria and cold urticaria with dupilumab, which inhibits IL-4 and IL-13, will characterize the benefit of this approach. TSLP (thymic stromal lymphopoietin) plays a pivotal role in allergy and inflammation and drives TH2-mediated immunity. It is produced by keratinocytes and activates mast cells and basophils. Mast cells express TSLP receptors and make TSLP, and TSLP increases mast cell proliferation and prolongs mast cell survival by interfering with apoptosis. TSLP is increased in the lesional and non-lesional skin of patients with chronic spontaneous urticaria. In addition to atopic dermatitis and chronic spontaneous urticaria several other inflammatory skin diseases show features of type II inflammation. These include chronic prurigo and bullous pemphigoid. In summary, type II inflammation plays a key role in the pathogenesis of several dermatological diseases. Type II cytokines, pruritus, a role for IgE and mast cells are all shared pathophysiological features of type II inflammatory skin diseases.

THE ROLE OF ALLERGENS IN ATOPIC DERMATITIS

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Atopic dermatitis (AD) is an important and chronic skin condition that has recently been the subject of enormous volumes of basic science, clinical, and epidemiologic research.

Clinical associations with AD have greatly expanded in recent years. Current concepts are well beyond thinking solely of the "atopic march":

• Eczema and food allergies as an infant • Asthma as a child • Hay fever as an adult

Well controlled studies suggest that allergens can impact the course of this disease.

Two important allergen group are: A) foods B) Aeroallergens

A) **Food allergens:**

Approximately 33% of infants and young children with AD will show clinically relevant reactivity to a food allergen. The most concerning reaction is an immediate immunoglobulin E (IgE)-mediated reaction leading to anaphylaxis. Some patients, instead have a delayed eczematous flare in response to food ingestion.

The NIAID recommendation states: Consideration of limited food allergy testing (ie, cow's milk, egg, wheat, soy, peanut) if a child < 5 years of age has moderate to severe AD and the following:

• Persistent disease in spite of optimized management and topical therapy

• A reliable history of an immediate allergic reaction after ingestion of a specific food

Identification of allergens involves taking a careful history and doing selective immediate-hypersensitivity skin tests or in vitro tests when appropriate. The gold standard for diagnosis of immunoglobulin E (IgE)-mediated food allergy remains the oral food challenge, with serum IgE testing and skin prick testing serving as acceptable alternatives.

Skin prick test: Negative skin tests with proper controls have a high predictive value for ruling out a suspected allergen. Positive skin tests have a lower correlation with clinical symptoms in suspected food allergen–induced AD and should be confirmed with double-blind placebo-controlled food challenge, unless the patient has a history of anaphylaxis to the suspected food. More importantly, avoidance of foods implicated in controlled challenges results in clinical improvement.

Specific IgE concentrations: In response to four food allergens measured by the Phadia ImmunoCAP assay—egg, 7 kUA/L (2 kUA/L age ≤2 years); milk, 15 kUA/L (5 kUA/L age ≤2 years); peanut, 14 kUA/L; and fish, 20 kUA/L—have been shown to be associated with a greater than 95% probability of clinical reaction . However, these levels do not identify the type or severity of reaction.

***The atopy patch test*:** It has revealed sensitization in some patients with AD but remains an investigational tool.

It is important that extensive elimination diets, which can be both burdensome and nutritionally unsound, are almost never warranted, because even patients with multiple positive allergy tests are rarely clinically sensitive to more than three foods on challenge.

B) Aeroallergens:

The evidence supporting a role for aeroallergens in AD includes the finding of both allergen-specific IgE antibodies and allergen-specific T cells. Contact reactions from aeroallergens have been associated in patients with eczema. Lesions tend to be on exposed areas of the body such as the neck and face. Dust mite has been the most implicated aeroallergen,

with positive patch tests in up to 40% of patients.

Environmental control measures aimed at reducing dust mite load may improve AD in patients who demonstrate specific IgE to dust mite allergen.

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INTEGRATIVE APPROACHES OF VITILIGO

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Introduction

Vitiligo is an acquired skin disease characterized by depigmented macules with the loss of functional melanocytes in the skin . The worldwide incidence varies between 0.1 and 2%. Although the average age of onset is around 20 years, it can occur at any age . The etiopathogenesis of the entity is clearly unknown but it has been reported to be associated with various factors including genetic factors, autoimmune factors, oxidative stress, neuro-humoral, and auto-cytotoxic mechanisms . Vitiligo can be subdivided according to the morphological presentation, the extent of the disease and the evolution of the disease.

- **Segmental Vitiligo (SV);** One or more vitiliginous patches, in a linear or flag-like pattern of mosaicism, with a unilateral dermatomal distribution.
- **Nonsegmental vitiligo (NSV);** Heterogeneous group of pigmentary disorders with different localization, usually in a symmetric pattern.
- **Unclassified or indeterminate**

According to the extent of involvement, severity and distribution of the depigmentation, vitiligo has been classified in different clinical classes. This classification is very useful to evaluate different therapeutics regimens.

Based on severity vitiligo can be divided into 4 stages ;

1. Limited (10%) involvement
2. Moderate (10–25%)
3. Moderately severe (26–50%)
4. Severe disease (50%) depigmentation

Prognosis and Clinical Course: The course of vitiligo cannot be predicted. Initial clinical sub-type of vitiligo does not predict future anatomical sites of involvement or activity of disease. Complete and stable repigmentation is rare. Spontaneous repigmentation - 10–20% of patients, most frequently in sun-exposed areas and in younger patients. Spontaneous repigmentation poliosis does not occur.

Treatment: Treatment of Vitiligo has two main objectives: the first is to stop the progression of the disease, the second is to induce repigmentation of the lesions and to achieve an acceptable cosmetic result. Essential is the psychological support for Vitiligo patients and the awareness of the social community that Vitiligo is not a contagious stigma.

Vitiligo treatment options are divided into 6 main branches: medical, physical, surgical, depigmentation, camouflage, and psychological support.

Medical treatments are divided into 3 as topical, systemic and phototherapy.

Complementary Treatments: Herbal products of different nature and effects have been used for the treatment of vitiligo since ancient times.

Polypodium leucotomos: P. leucotomos is a tropical fern native to Central and South America, which tends to have beneficial skin properties due to the presence of various compounds with antioxidant and photoprotective properties

within the extract. The P. leucotomos extract has been studied for treating various skin conditions like vitiligo, psoriasis, melasma. Oral intake of P. leucotomos has helped prevent photoaging effects of sunlight, such as hyperpigmentation and textural changes.

Green Tea: The antioxidant activity of green tea is due to catechins, secondary metabolites that are present in the tea. Epigallocatechin-3-gallate (EGCG) is the most abundant and biologically active compound in green tea. EGCG is a good scavenger of ROS/RNS and an anti-inflammatory, which has the potential to control the immune response.

Ginkgo biloba: Ginkgo biloba is a unique species of tree found in China, widely cultivated and used in traditional medicines. Although a specific mechanism of action is not known for ginkgo, it appears to have anti-inflammatory, immunomodulatory, and antioxidant properties all of which could potentially help in vitiligo which may have an oxidative stress component. In addition, GB can further inhibit the development of vitiligo via its anxiolytic properties as psychological stress has been shown to intensify vitiligo.

Curcumin : Curcumin, also called diferuloylmethane, is the main natural lipophilic polyphenol found in the rhizome of Curcuma longa (turmeric). Clinical trials demonstrated that curcumin has high antioxidant function, modulating directly and indirectly the antioxidant system and suppressing intracellular sources of ROS development.

Khellin: Khellin is an extract from the Mediterranean fruit Ammi visnaga. Since khellin is structurally similar to psoralens used in PUVA, interest has arisen in the use of khellin as a safer alternative to psoralens known to crosslink DNA and to be mutagenic. On the other hand, khellin does not produce DNA crosslinks when exposed to UVA in vitro or inside mammalian cells.

Punica granatum & Phyllanthus emblica L: Both Punica granatum L. and P. Emblica L. are polyphenolic compounds with high anti-oxidant activity. Studies have shown that anti-oxidant mixtures administered after phototherapy in vitligo patients increase the repigmentation rate.

Conclusions: While a number of studies have shown benefit associated with the use of these alternative treatments, larger, well-controlled trials are warranted to firmly establish the place of these agents in the therapeutic hierarchy. The use of these alternative treatments can be considered as a supplement to the treatment regimen of interested or treatment refractory patients as they appear to be relatively safe and may provide additional benefit in outcomes and patient satisfaction.

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INTEGRATIVE APROACHES OF MELASMA

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Melasma, is a common chronic, acquired hyperpigmentation of the skin that typically affects the sun-exposed areas of the face. Patients with melasma present with irregularly shaped, hyperpigmented macules on the face but can also rarely be seen on the neck, chest, and forearm. The color varies from light brown to dark brown or ash/blue, depending upon the site of melanin deposition in the skin. Melasma affects millions of people worldwide. It is commoner in women, especially in their reproductive years, but about 10% cases occur in men(1).

Melasma's complex pathology and recurring nature make it difficult to target therapeutically. Management of melasma is highly challenging, especially because it is prone to frequent relapse despite successful clearance. Melasma has a signifcant efect on quality of life due to its disfguring appearance, chronic course, and recalcitrance to treatment (2, 3). A better understanding of the pathological findings is key to developing novel and successful treatment options.

Several factors such as genetics, sunlight, cosmetics, pregnancy, hormonal treatments, thyroid dysfunction, and drugs have been implicated in the pathogenesis of melasma . Constitutive pigmentation reflects the genetically determined level of melanin and can be changed by several regulatory factors (4). Although earlier classified as epidermal and dermal, melasma is now thought to be a complex interaction between epidermal melanocytes, keratinocytes, dermal fibroblasts, mast cells, and vascular endothelial cells. It is known now that all melasma is "mixed" with the dermis often showing solar elastosis and increased vascularity as well. Factors influencing melasma may include inflammation, reactive oxygen species, ultraviolet radiation, genetic factors, and hormones (5, 6).

The pathology of melasma is complex although it was initially thought to involve only melanocytes. Evolving research points to a more heterogeneous pathogenesis involving an interplay of keratinocytes, mast cells, gene regulation abnormalities, increased vascularization, and basement membrane disruption (2). Although the melanocyte number is similar in lesional and perilesional skin, melanocytes in the affected skin are larger, contain more melanosomes, and show more and very prominent dendrites. In lesional skin, keratinocytes also show an increased number of melanosomes compared with healthy skin (7).

Most of the effects of UVB on melanogenesis are mediated by the keratinocytes through the secretion of several cytokines and hormones that stimulate not only the melanogenesis but also dendritogenesis, melanosome transfer and melanocyte proliferation). The main mechanism is mediated by UVB-induced DNA damage that activates the p53 protein. Then, p53 binds the Pro-Opiomelanocortin (POMC) promoter and induces the production of αMSH, which is the main pro-pigmenting hormone (8). The impact of ultraviolet (UV) radiation as a triggering factor of melasma has been known for decades. However, even when using potent UVB and UVA protection during the summer season , most patients have a worsening of their lesions. The shorter wavelengths of visible light (blue -violet light) have recently been shown to induce a hyperpigmentation through a specific sensor in melanocytes called opsin 3. (8, 9). Passeron's group detected higher levels of opsin3 (also called encephalopsin or panopsin) relative to other opsins in both primary melanocytes and skin prototypes III to VI, suggesting a role for opsin3 in skin pigmentation (9).

Solar elastosis refers to the accumulation of abnormal elastic tissue in the dermis resulting from chronic sun exposure or photoaging. Melasma patients have been found to have high levels of solar elastosis in affected skin. In addition, histological analysis shows that melasma skin tends to have thicker and more curled and fragmented elastic fibers when compared to normal skin. UVR also enhances reactive oxygen species (ROS) formation in keratinocytes and melanocytes, with consequent DNA damage (10).

Numbers of mast cells are higher in melasma skin than in unaffected skin (4). UV exposure triggers the release of histamine from these mast cells, leading to downstream effects. Histamine binding at the H2 receptor activates the tyrosinase pathway and induces melanogenesis. This finding may help elucidate the link between the inflammatory

process in UV radiation and the hyperpigmentation that follows. In addition, UV radiation also increases the production of mast cell tryptase, which activates matrix metalloproteinase (MMP) precursors. These active enzymes then go on to degrade type IV collagen and damage the basement membrane. Mast cells induce hypervascularization (2, 9). The number of blood vessels, vessel size and vessel density are greater in lesional melasma skin than in perilesional skin. Elevated levels of cytokines that could affect vascularization have been demonstrated in melasma skin, such as vascular endothelial growth factor (VEGF), stem cell factor (SCF) and inducible nitric oxide synthase (iNOs). Endothelin-1 (ET-1) released from endothelial cells stimulates the pigmentation through endothelin receptor B activation at the surface of melanocytes. Sebocytes have been hypothesized to contribute to the development of melasma (1).

Prolonged UV radiation causes dermal inflammation and activates fibroblasts. These cells then secrete SCF, which may diffuse into and induce melanogenesis in the overlying epidermis. Likewise, levels of stem cell growth factor receptor, also known as c-kit, are also upregulated in melasma lesions. When c-kit binds to SCF, it activates the tyrosine kinase pathway responsible for melanogenesis. Therefore, trauma induced by lasers or any therapies that further aggravate the basement membrane may worsen the disease. Similarly, restoration of the basement membrane may limit recurrence (2).

Current melasma therapies include topical agents, chemical peels, laser and light treatments, and systemic agents (2). Regardless of the treatment modality chosen, sun protection is crucial to prevent new lesions and avoid worsening existing melasma. The current recommendation is that patients use a broadspectrum UVA/UVB sunscreen with at least SPF30 daily, preferably with a physical blocking agent such as zinc oxide or titanium dioxide. Sunscreens that contain iron oxide, which blocks shorter wavelength of visible light and broad-spectrum UVA/ UVB filters, significantly lowered the relapse of melasma during summer when compared with broad-spectrum UVA/UVB protection alone Behavioral measures such as wearing wide-brimmed hats or avoiding peak sunlight hours may also help (2, 10).

Traditionally, melasma has been treated with topical agents, including hydroquinone (which inhibits tyrosinase), tretinoin, corticosteroids, and combination creams with varying formulations. Hydroquinone (HQ) has long been the conventional treatment, but the concern over its side effects have prompted the use of potentially safer alternatives. Safety issues for HQ have been raised, including exogenous ochronosis, permanent depigmentation andpotential carcinogenic risk (2) .4-n-butylresorcinol, niacinamide, ascorbic acid, resveratrol, azelaic acid, kojic acid and newer agents including arbutin, deoxyarbutin, aloesin, rucinol, topical flavonoids, ellagic acid, gentisic acid, topical linoleic acid are considered alternative topical agents that have been reported to exhibit depigmenting properties without severe adverse effects (10). However, topical depigmenting agents alone cannot restore photoaged skin condition in melasma. Thus, antiageing approaches should be combined with topical depigmenting agents because melasma frequently relapses without the correction of other photoaging-related conditions that affect melanogenesis. A triple combination cream (TCC) containing 4% HQ, 0.05% tretinoin and 0.01% flucinolone acetonide is the only HQ-containing drug approved by the United States Food and Drug Administration (FDA) to treat melasma. Tretinoin exhibits not only a hypopigmentary effect, but also an anti-ageing property. Steroids inhibit the secretion of ET-1 and granulocyte macrophage colony-stimulating factor (GM-CSF) that act against mild inflammation associated with photodamage and melanogenesis (10). The chemical peel is a well-known modality for treating melasma. It causes controlled epidermal dyscohesion and subsequent regeneration to remove epidermal melanin and suspend the transfer of melanosomes. However, the result is unsatisfactory, especially in Asian patients with Fitzpatrick skin types III-IV due to high risk of post-inflammatory hyperpigmentation (PIH) (10).

Systemic tranexamic acid (TXA), an antifibrinolytic agent, have been shown to inhibit UV-induced melanogenesis and neovascularization by hindering the plasminogen activator and plasmin activity. A histologic analysis revealed significant improvement not only in the level of epidermal pigmentation, but also in the number of mast cells and vessels. The expression of ET-1 was significantly decreased after TXA administration (10, 5)

Topical liquorice extract and oral and proanthocyanidin have significant antioxidant action and have been shown to be beneficial in melasma. Polypodium leucomatous extracts act by inhibition of UV induced ROS generation, including superoxide anions. AsA and alpha tocopherol are strong anti inflammatory agents with a marked antioxidant mechanism (5).

There are five major categories of light therapy and lasers used for the treatment of melasma: intense pulse light (IPL), Q switched lasers, ablative fractional resurfacing lasers, non-ablative fractional resurfacing lasers, and picosecond lasers. The major side effects of using lasers and light sources for the treatment of melasma include post-inflammatory hyperpigmentation (PIH) and recurrence. The thulium laser targets water instead of pigment molecules, and has less risk of PIH compared to traditional lasers. The 1927 nm wavelength delivers energy up to 200 µm into the papillary dermis. Therefore, it is generally used for epidermal lesions (11). Kurmuş and colleagues treated 100 melasma patients with a 1927 nm thulium fiber fractional laser. They reported that thulium laser is effective and safe in the treatment of melasma(11).

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INTEGRATIVE APPROACHES OF SKIN CANCERS

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Introduction

Modern medicine can take credit for tremendous achievements and advances in the understanding of human health and the prevention and treatment of disease. Antibiotics, vaccination, hygiene improvements, and modern pain control and anesthesia are just some examples of developments that have changed the world and, in some ways, have eclipsed the accomplishments of the first several thousand years of recorded medicine. But if modern medicine is so great, why are people so interested in alternatives? In reviewing studies and talking to many patients over the years, three major reasons seem to surface: when diseases are not curable, when our explanations are unsatisfying, and when our treatments are thought to be unsafe, questionable, and/or only "symptomatic." An unspoken reason also seems to be that the experience of seeing a modern doctor can often feel rushed, overly-focused, and impersonal, where many alternative practitioners pride themselves on having a slower pace, listening carefully to the patient, and generally being more "holistic" in considering the patient and his or her health issues. A provocative study approached this from a slightly oblique angle, but nicely demonstrates some of these principles in action.

Skin Cancer

Skin Cancer incidence is increasing at 3.1% per year [1]. Skin cancer spread over the body with the help of lymphatic and blood vessels. Thus, early detection of skin cancer is very important for proper diagnosis of the disease.Melanoma and Non-Melanoma are two major categories of skin cancers. Malignant melanoma is of several sub-types. Basal cell carcinoma and Squamous-cell carcinomas are two main types of non-melanoma skin cancers. Each type of skin cancers has different characteristics from other skin cancers.

Treatment of non-melanoma skin cancers has increased by 77% between 1992 and 2006 leading to continual reassessment of treatment. Morbidity has been minimized with techniques such as Mohs Micrographic surgery, and excellent cure rates have been reported. For malignant melanoma, by far the most dangerous of these three skin cancers, the outcomes are far less rosy, with good cure rates for thin tumors, but poor rates for thicker, invasive lesions. Importantly, options for metastatic melanoma are limited, with modest life prolongation at best. In fact, patients with visceral metastases have medial survival rates of only 4 months .Nonetheless, newer immunotherapies such as ipilimumab and PD1 inhibitors now offer hope to melanoma patients with advanced disease . Some skin cancer patients find the cost and/or resultant excision scar unsatisfactory, or fear surgery altogether. Perhaps surprisingly, complementary and alternative (CAM) therapy options are being increasingly sought out and utilized by skin cancer patients. In one survey, the prevalence of CAM use among adults reporting skin problems was nearly 50% As patients seek alternative options to conventional therapy for skin cancer, the use of 'natural products' cannot be assumed to mean 'safe'. Health providers need to be aware of several specific alternative therapies for skin cancer, some promising and others plainly dangerous. Some of these natural products have lead to major discoveries in skin cancer research (cyclopamine) or have proven efficacy (ingenol mebutate). However, randomized controlled trials (RCT) demonstrating efficacy and safety of alternative therapies are necessary before they can be considered viable options in the management of skin cancer. It is important to stress that invasive basal and squamous cell cancers, as well as all melanomas can metastasize and cause significant morbidity and even mortality. Failing to use proven techniques to properly diagnose (i.e., biopsy) and to surgically resect or debulk these tumors greatly increases the risk for poor outcomes, and may increase the medicolegal risk in such cases. Because of the inherent dangers of skin cancer, only adjuvants to conventional care should be considered until sufficient evidence displaces current standards of care.

Top Considerations

Treatment	How administered	Notes
Ingenol mebutate	Topically as 0.05% gel for the body (applied once daily for 2 days) and 0.015% for the face and scalp (once daily for 3 days)	FDA-approved and effective for AKs, easy to apply for short duration; local reactions common, but relatively mild
Solasodine glycosides (BEC)	Topically as 0.005% cream (BID × 7–60 days)	Limited data for AK, SCC, and BCC; no data for melanoma. Perhaps could be used in special circumstances as an adjunct to surgery or alternative trial for low- risk lesions under close supervision
Vitamin D	Daily or weekly supplementation Optimal dosing is unclear	Some studies suggest protective effect and survival advantage for melanoma; Safe and inexpensive
Coenzyme Q10	200 mg PO BID	May reduce risk of metastasis and potentiate efficacy of adjuvant therapies; data is very limited

Not Recommended

**The escharotics* (i.e., bloodroot, sanguinarine, and related compounds) should be avoided for known malignancies as they are unpredictable and have not reliably been shown to be a viable treatment without concomitant surgery.

**Gossypin* (an extract from cotton and hibiscus plants) has some promising data in mice and in vitro for melanoma, but is simply too experimental for clinical use at this time.

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PIEZOGENIC PEDAL PAPULES

Emine Müge Acar

Piezogenic pedal papules (PPP) are described as herniations of subcutaneous tissue of medial aspect of heels which is characterized by soft, round, skin colored papules measuring 0.2-1 cm. The term "Piezogenic" refers to the generation of the lesions by pressure. [1] Lesions can be seen in infancy and adulthood. Infantil variant occurs in nonweight bearing infants and lesions are seen as large nodules. [2]

Etiology.

A specific etiology has not been identified for piezogenic pedal papules and development of PPP can also be seen in an otherwise healthy individual. [3] Obesity may lead to large PPP which can present as nodules rather than plaques. Reports of cases in successive generations in the same family is also suggestive of a possible hereditary cause. [4] However hereditary transmission is not observed in the vast majority of the patients.

Piezogenic pedal papules appear during weight bearing in up to 60% of the population, 10% of the patients describe pain which may be possibly related to neurovascular anoxia. [1] The lesions can be triggered by jumping, running and standing long periods. Most of the cases occur spontaneously [5] No direct association has been observed between a specific connective tissue defect and piezogenic pedal papules. [6] Ehlers Danlors and Prader Willi syndrome have been anecdotally associated with PPP. [7,8]

Piezogenic pedal papules can also be one of the manifestations of GATA2 deficiency, which is a zinc finger transcription factor that plays a critical role in hematopoietic lineage commitment. [9] The development of PPP has been reported in patients with rheumatoid arthritis and rheumatic heart disease [10] A patient with mitral valve prolapse with PPP has also been reported in the literature suggesting a detailed systemic especially cardiologic examination is necessary in the patients with PPP. [11]

A high frequency ultrasonography can be used in the diagnosis. Biopsy can be considered in the presence of alternative diagnosis. Histopathological examination reveals dermal fibrosis and herniation of subcutaneous fat tissue from the papillary dermis.

Treatment

In asymptomatic lesions no treatment is necessary. Weight loss, avoidance of prolonged standing and reduced foot trauma are recommended in the presence of painful lesions. Compression stockings, heel cups and orthotics can be used.[1] In refractory cases invasive treatments can be considered. Intralesional betamethasone and bupivakaine injections have been reported to be benefical in patients with Ehler Danlors syndrome. [12] A good clinical response and pain control was obtained in a female case treated with a course of electroacupuncture. [13] Deoxycholic acid injection has been reported to be successful in one case. [5] Pulsed diod soft laser caused significant improvement in PPP lesions in another case. [14] Surgical excision can be performed in the case of severe pain.

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NOVEL MODALITIES IN KELOID AND HYPERTROPHIC SCARS

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Wound healing is a dynamic process which leads to regeneration or tissue repair. It consists of three main stages including inflammatory, proliferative and remodelling stages that happen consecutively. Dysregulation of these stages may lead to scar formation.

Keloids and hypertrophic scars are fibroproliferative disorders of the skin that result from abnormal healing of injured or irritated skin. Genetic predisposition, systemic and local factors may contribute to these disorders(1).

There are both clinical and pathological differences between keloid and hypertrophic scar. Hypertrophic scars usually occur after a definite injury within 4 to 8 weeks. These scars are firm and raised within the site of injury and do not extend beyond the borders. Although it takes years, there is a possibility of spontaneous regression for hypertrophic scars. Keloids may appear many years later and can develop from minute wounds such as a mosquito bite, vaccination or hair folliculitis. Unlike hypertrophic scars, keloids extend beyond the wound margins and spontaneous regression never occurs(2).

Pathologically in hypertrophic scar collagen is arranged in a wavy pattern parallel to the epidermis whereas in keloids collagen is seen haphazardly in a random pattern(2).

Although there are many differences between hypertrophic scars and keloid, increasing evidence support that hypertrophic scars and keloids are actually different stages of the same fibroproliferative disorder.

Various treatment modalities have been proposed for hypertrophic scars and keloid up to now. First line treatment modality is steroid either in steroid-impregnated tape form or as intralesional injection(3). Other treatment modalities include silicone gel or sheating, intralesional 5-Fluorouracil (5-FU) or intralesional combination of 5-FU and steroid, cryotherapy, Pulse dye laser (PDL), ablative lasers and surgical excision with adjuvant steroid, 5-FU, radiotherapy, bleomycin or mitomycin. However because no therapy has yet proven to be curative, novel approaches or combination therapies are being researched(3). Novel treatment modalities include botulinum toxin-A, hyaluronidase, hyaluronic acid, stem cell therapy, verapamil, and angiotensin converting enzyme (ACE) inhibitors(3, 4).

Botulinum toxin A (BoNT-A) is a widely used product for many medical conditions. In case of hypertrophic scars and keloid, intralesional BoNT-A is one of the promising methods. Mechanism of action on keloid and hypertrophic scar is not yet clearly understood. Alleviation of the scar tension, modulation of fibroblast cell cycle and collagen level and decreasing the level of TGF-β, are proposed mechanisms. Positive clinical effects of BoNT-A is shown by most of the studies. In addition to the clinical efficacy, the most favorable feature of BoNT-A is absence of side effects such as skin atrophy and telangiectasia which may occur with intralesional steroid injections(5).

Hyaluronidase is an enzyme which is used in dermatology mostly for the correction of complications related to hyaluronic acid fillers. There are various other dermatological conditions in which hyaluronidase is used. One of these conditions is keloid and hypertrophic scar. In these diseases hyaluronidase facilitates penetration of other treatment agents into tissue(6). Also combination of hyaluronidase with triamcinolone resulted in reduced side effect profile including atrophy together with increased efficacy(6). Hyaluronidase can also be used alone as an alternative treatment modality by modulating inflammatory response. It was suggested that the product of hyaluronidase degradation action, low molecular weight hyaluronans, stimulate angiogenesis and activates mesenchymal stem cells(7). However mechanism of its actions is poorly understood. Most side-effects of hyaluronidase are minor and transient and consist of post-enjection pruritus, bruising and swelling. The risk of anaphylaxis is reportedly increased in those with wasp allergies(6).

Mesenchymal stem cell therapy (MSCT) is one of the promising treatment modalities for hypertrophic scar and keloid. Mesenchymal stem cells (MSC) are involved in wound healing by increasing migration, angiogenesis and re-epithelisation. In addition to that MSCs secrete growth and differentiation factors that modulate inflammatory and

immune responses during wound healing. There isn't any human clinical trial that investigate the potential of MSCs in hypertrophic scars and keloid yet. However, it was shown that MSC have antifibrotic properties through paracrine signaling in vitro studies and and murine models(4, 8).

Verapamil is a calcium channel blocker which can alter fibroblast shape, induce TGF-beta apoptosis and reduce ECM production by inducing procollagenase secretion. According to the clinical studies, verapamil could improve keloid and hypertrophic scars either alone or as a part of combination therapies with fewer side effects. However there is still controversial results about this agent and further more qualified studies are needed to elucidate exact effect of verapamil(2, 4, 9).

Local renin-angiotensin system has been shown to involve in wound healing, collagen synthesis and fibrosis. There are some small clinical studies and a few case reports propose the beneficial effects of ACE inhibitors and Angiotensin receptor blockers on keloid and hypertrophic scars. It was shown that these modalities may involve in the treatment by decreasing collagen synthesis, fibroblast proliferation and reducing expression of TGF-beta(10).

There are various modalities which are currently available and new treatment modalities are being investigated for hypertrophic scar and keloid. None of these treatment modalities is accepted as gold standart. Each of the treatment modalities has its own benefits and side effect profile. Best treatment option can be decided by comprehensive clinical assessment and patients medical history. Further elucidation of the pathogenesis and finding new treatment modalities will lead to better patient outcomes and treatment options for these pathological scars.

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MOLLUSCUM CONTAGIOSUM: WHAT'S NEW?

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Molluscum contagiosum (MC) is a common, contagious viral skin disease that often affects children and adolescents. The virus is transmitted by close physical contact, autoinoculation, and fomites. Typically, molluscum contagiosum presents as usually asymptomatic, discrete, smooth, flesh-colored, dome-shaped papules with central umbilication.

Sometimes an inflammation may be seen in molluscum contagiosum which represents a host response that often precedes resolution of the viral disease, rather than secondary bacterial superinfection.This phenomenon has been termed as the "beginning of the end (BOTE) sign" and this does not require additional antibacterial treatment.

Although MC lesions usually resolve spontaneously in 6–12 months, many authors suggest active treatment of lesions for cosmetic reasons or concerns of transmission and autoinoculation. There is no consensus for the optimal treatment of MC. The choice of treatment method should depend on the physician's comfort level with the various treatment options, the patient's age, the number and severity of lesions, location of lesions, the preference of the patients/parents, and patient's immune status.

The diagnosis of MC is usually made on clinical grounds, but unclear cases may be confirmed by histopathological examination, polymerase chain reaction or electron microscopy.Molluscum bodies can also be identified by immunohistochemistry on paraffin-embedded, formalin-fixed material, and a cross-reactivity of molluscum bodies with Melan A, a melanocytic marker, has been recently reported.

Dermoscopy and in vivo confocal microscopy may be very useful to aid diagnosis. Dermoscopy may facilitate diagnosis by revealing a central polylobular white-yellow structureless area, surrounded by vessels in a crown pattern. Extraction dermoscopy was recently described as a new method for the diagnosis of MC.

Confocal microscopy shows a round, well-circumscribed lesion with central round cystic areas filled with brightly refractile material that correlates with the characteristic molluscum bodies seen on histopathological analysis.

Active treatments of MC may be mechanical (e.g. cryotherapy, curettage, pulsed dye laser therapy) chemical (e.g. cantharidin, potassium hydroxide, podophyllotoxin, benzoyl peroxide, tretinoin, trichloroacetic acid, lactic acid, glycolic acid, salicylic acid), immune-modulating (e.g. imiquimod, interferon-alpha, cimetidine) and anti-viral (e.g. cidofovir). Currently, intralesional immunotherapy (candida, combined measles, mumps, rubella vaccine, tuberculin purified protein derivative, vitamin D3, interferon α, and Streptococcal substrain OK-432) has been proposed as a beneficial treatment in MC infection. It creates a delayed-type hypersensitivity reaction that results in a virus-directed immune response by stimulating of the T helper (Th1) cytokine response, activating cytotoxic T cells to eradicate virally infected cells.

The other treatments which may be useful in patients with multiple resistant lesions are local hyperthermia, occlusion with adhesive tape, and the topical application of Polypodium leucotomos extract, immunoferon, zinc oxide,azelaic acid, and certain natural products such as essential oil of Australian lemon myrtle leaves, tea tree oil, sandalwood album oil and sinecatechins.

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INTEGRATIVE APPROACHES OF SUPERFICIAL FUNGAL INFECTIONS

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Superficial fungal infections are among the most common infections worldwide and limited to the stratum corneum, hair, nails and the surface of mucous membranes.

They are caused by yeasts (e.g., *Candida* species and *Malassezia* species), dermatophytes, and non–dermatophyte species of filamentous fungi (dermatomycoses). Although dermatophytosis, tinea versicolor and candidiasis are widely distributed over of the world, tinea nigra and piedra are rarely seen.

Mycosis is a public health problem, particularly in tropical and subtropical developing countries.

Topical antifungals are sufficient for many patients with tinea corporis, tinea cruris, and tinea pedis. Systemic antifungal therapy, although associated with both a higher incidence of side effects including potentially severe adverse reactions and the potential for drug–drug interactions, is typically required to cure tinea manuum, capitis, and onychomycosis (1).

In general, oral treatment is also needed for infections involving extensive areas of skin, in hairy areas other than the scalp (e.g. tinea barbae), or associated with excessive inflammatory reactions(1). Furthermore, in recent years, there are increasing antifungal drugs resistance. These infections are prone to recurrence. This drives the need to pursue for alternatives to conventional antimicrobial therapy.

Medicinal plants and chemical constituents isolated from herbs include essential oils, phenolic compounds, alkaloids and terpenoids and they display various levels of antifungal activity.

Traditional Chinese medicine (TCM) has been used in clinical practice for thousands of years in China and Eastern Asia (2). One of the most successful studies in this field was conducted by Bing Chen Jiang et al. They evaluated a total of 163 TCM herbs for antifungal activity against four strains of fungi and a hyphal growth inhibition effects against Candida albicans by using consistent methods and standards. Among these, active herbs were tested against six additional fungal strains. Their individual and synergistic antifungal activities in combination with fluconazole were evaluated against a fungicide-resistant Candida albicans strain (FLC-resistant C. Albicans). In this study, Rosa chinensis was found to be the most potent antifungal herb. The main antifungal constituents of Rosa chinensis were gallic acid and flavonoids. These compounds exhibited synergistic and additive antifungal effects. Rosa chinensis, Neopicrorhiza scrophulariiflora, Phellodendron chinense and Syzygium aromaticum displayed the strongest antifungal effects. The hyphal growth inhibition assay demonstrated that extracts from six herbs completely inhibited hyphal growth. However, only three of these (*Macleaya cordata, Anethum graveolens and Veratum nigrum*) showed antifungal activities (2).

Juanjuan Liu et al. demonstrated the anti-Candida effect and the cell wall remodeling induction potential of the five traditional herbal monomers (Sodium houttuyfonate, berberine, palmatine, iatrorrhizine, cinnamaldehyde) and their associated combinations (3).

In the literatüre, some studies examined the therapy potential of phenolic compounds in different plant extracts on fungal infections (4). Piper betle L., (Piperaceae) is a widely distributed plant in the tropical and subtropical regions of the world. The leaves of this plant have been used for a long time in many Asian countries to prepare traditional herbal remedies. Hydroxychavicol, the active component of P. Betle L., is a major phenolic component which has broad spectrum fungicidal effects against clinically significant cutaneous human pathogenic fungi (5).

Geraniol (C10H18O) is present in several types of flowers, and presents a characteristic odor and flavor. This natural organic acyclic compound is part of the constitution of various volatile oils. The antifungal activity of the terpene geraniol was also focused by many studies (6).

The essential oils of Mentha and Thymus albicans have been extensively studied for their antifungal activity against different species (7,8).

Bee products have been used in folk medicine since antiquity. Propolis is a resinous substance that bees collect from exudates of plants. Its chemical analysis has pointed to the presence of at least 300 compounds, mainly composed of resin, wax, essential oils, pollen, and other organic compounds such as phenolic compounds and flavonoids. Several in vitro studies have highlighted the antifungal activity of propolis and honey (9,10).

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BIOLOGICAL RHYTHMS IN THE SKIN

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In humans virtually all aspects of physiology is rhythmic. Most physiological oscillations occur in 24 hour periodicity but additionally periods of less than or greater than 24 hour also exist. Circadian rhythm refers to body's endogenous 24-hour physiologic, metabolic and behavioral rhythms to meet environmental stimuli associated with solar day and optimize cellular responses. It is an ancient evolutionary system to adapt to changes stemming from rotation of earth. Circadian rhythm is controlled by the master or central clock of the body which is suprachiasmatic nucleus (SCN) located in the anterior hypothalamus. Visible light enters the retina and then via retinohypothalamic tract it modulates suprachiasmatic nucleus. SCN initiates hormonal and neuronal signals that coordinate oscillations throughout the body. In the body, the core molecular clock system consist of an autoregulatory gene expression feedback loop. Clock and Bmal1 transcription factors form a heterodimer and stimulate genes termed clock controlled genes. At the same time Clock and Bmal1 induce expression of their own inhibitors, which are Period (Per) and Cryptochrome (Cry) leading to an approximately 24 hour oscillatory rhythm. Circadian rhythm of the skin is regulated both by the SCN and by the intrinsic regulators of the skin(1).

Skin is the largest organ in the body. Morphologically, skin contains various cell types and structures. There are evidences that there is a functional clock in the regulation of skin, if not all, of its cell types. Both the central clock, suprachiasmatic nucleus (SCN) and endogenous rhytmicity of the skin have impact on the activities of the skin. The peripheral clock in the skin is not a single entity rather it is composed of multiple independent clocks yet most likely work coordinated that function within distinct anatomical compartments of the skin. These clocks lead to formation of rhythmicity in the activities. Most known rhythmic activities of skin are epidermal turn over cycle and hair cycle(2).

In the skin circadian variations can be observed in keratinocyte proliferation, DNA synthesis and repair, sebum production, skin blood flow, transepidermal water loss, and skin temperature. Circadian variation of these functions, also any disruption of this rhythmicity may have impact on disease formation, cancer development or treatment strategies(3).

Circadian rhythm influences cutaneous blood flow and properties of skin barrier function, such as transepidermal water loss (TEWL). At night, blood flow to the skin and TEWL increase, sebum production and skin hydration decrease. In atopic dermatitis, high TEWL and low hydration at night contribute to nocturnal itching(4). Cortisol levels also fluctuate throughout the day which have a natural decrease during the evening. This could be also a contributing factor to increased pruritus at night seen in inflammatory dermatoses including atopic dermatitis and psoriasis. Increased inflammation and skin permability at night could be important clinically. Thus, to maximize effectiveness of the treatments, topical steroid and moisturizers might be used in the evening hours(3).

Circadian disruption may be more important for skin diseases than previously recognized. For example in a study increased psoriasis incidence was observed in shift workers. Also in a murine study it was shown that Clock transcription factor may modulate psoriasis like inflammation via Interleukin-23 pathway(1).

Relation of circadian dysrhythmia and skin carcinogenesis, is another topic which is under investigation. Disrupted melatonin synthesis, is one of the proposed reasons for this association(5). Melatonin has been associated with wound healing, antititumor and antioxidant effects and supression of ultraviolet damage in skin cells. It is mostly synthesized in pineal gland and also it can be synthesized in the skin. Melatonin levels fluctuate with the circadian rhythm and are typically high at night. Exposure to light leads to an acute drop in melatonin levels(6). Due to its antioxidant and antitumorogenic effect, any disruption in this rhytmicity of melatonin secretion may lead to cancer formation, however further studies are required for clarification of this association. It was shown that clock genes were down-regulated in melanoma as compared to normal adjacent tissue. Also reduced clock gene expression was associated with increased tumor thickness and mitotic level in melanoma(7).

Circadian rhythm of the skin has importance in many aspects of the skin functions including aging, regeneration of human skin and hair precursor cells as well as inflammatory disease occurence, cancer development and progression

and deciding effective treatment modalites. Future studies and further examination of these mechanisms would create new perspectives.

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HUMAN 3D SKIN MODELS

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Tissue engineering is used to fabricate 3-dimensional (3D) artificial scaffolds to create a microenvironment that mimics human tissue. Bioprinting uses biomaterials, cells, and/or bioink to fabricate prospective scaffolds to mirror the structural, compositional, and functional aspects of the skin (1). The relevance for *in vitro* three-dimensional (3D) tissue culture of skin has been present for almost a century. From using skin biopsies in organ culture, to vascularized organotypic full-thickness reconstructed human skin equivalents, *in vitro* tissue regeneration of 3D skin has reached a golden era (2) . The 3D Skin Model is a highly physiological, three-dimensional cellular system of keratinocytes, fibroblasts, and melanocytes for in vitro studies, suggesting an excellent tool to examine aspects of epithelial function and disease, particularly those related to skin biology and toxicology (3).

Threedimensional (3D) skin equivalents have been established as a valuable tool in dermatological research because they contain a fully differentiated epidermal barrier that reflects the morphological and molecular characteristics of normal human epidermis (4). Herein, we will summarize 3D skin bioprinting techniques, applications and approaches.

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ELISA IN DERMATOLOGY

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Anamnesis and clinical features of skin lesions are very important in the diagnosis of skin diseases. Dermatological examination findings may need to be supported by some laboratory tests and special examination methods. In some dermatological diseases, the demonstration of autoantibodies stored in the tissue and /or circulating in the serum is used in diagnosis and follow-up. One of the methods for this purpose is Enzyme Linked Immunosorbent Assay (ELISA). It is a test used to determine antigen or antibody in patient samples (serum, saliva, etc.). In dermatology practice this method is used especially in autoimmune bullous disorders, autoimmune connective tissue diseases, some viral and bacterial diseases.

A variety of highly sensitive and specific ELISA systems has become commercially available within the last two decades. These ELISAs identify autoantibodies against specific autoantigens, also make it possible to quantify serum autoantibody levels (1). In addition to clinical, histopathological and immunofluorescent methods, ELISA is used as a confirmation test in the diagnosis of autoimmune bullous disorders. Compared to other traditional diagnostic methods, it has advantages such as being faster, easier to apply, better standardized and that many samples can be studied simultaneously (2). ELISA is the most accurate diagnostic test for the diagnosis of pemphigus vulgaris and pemphigus foliaceus, separately measuring anti-Dsg3 and anti-Dsg1 (3). An ELISA for autoantibodies against envoplakin in paraneoplastic pemphigus has recently been developed. For pemphigoid diseases, ELISAs applying recombinant BP180 NC16A, BP230, and type VII collagen are available (1).

In autoimmune connective tissue disorders, autoantibodies occur secondary to autoimmunity. The presence of autoantibodies shown serologically in autoimmune connective tissue diseases can provide important information to the clinician in terms of disease diagnosis, activity and treatment follow-up. ELISA method is mostly used for anti-dsDNA measurement. dsDNA antibodies are associated with systemic lupus, but not subacute cutaneous lupus or discoid lupus; dsDNA antibodies increase in active disease and in the progression of lupus nephritis. dsDNA antibody assays can be negative after treatment, in clinical remission. Around 50–80% of patients with SLE have antihistone antibodies detectable by ELISA (4). Anti-neutrophil cytoplasmic antibodies are useful diagnostic markers for primary vasculitis, wegener granulomatosis, microscopic polyangiitis, and churg-strauss syndrome. Consensus has been developed regarding the administration of ELISA to detect autoantibodies against proteinase 3 and myeloperoxidase in indirect immunofluorescence positive sera (5).

An enzyme immunoassay (EIA, Captia Syphilis-G) for detecting IgG antibodies against *Treponema pallidum* was improved as a screening test for syphilis (6). Captia syphilis M test has been used for detection of congenital syphilis in the newborn. Infected infants can produce IgM in utero after 3 months of gestation. Ig M ELISA test is based on using anti-human IgM antibody to capture IgM in the patient's serum, followed by the addition of a purified *T.pallidum* antigen to detect those IgM antibodies in the patient's serum (7).

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FREE FATTY ACIDS IN DERMATOLOGY

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The skin is an effective barrier that protects the organism from harmful physical and chemical effects from the external environment and prevents the loss of water and other fluids from the body. The stratum corneum, the outermost layer of the epidermis, consists of corneocytes that emerge from the stratum basal, mature and rise, and then lose their nuclei.

Lipid matrix found between these cells; It consists of approximately equal molar proportions of ceramides (CERs), cholesterol, and free fatty acids (FFAs) (1). The SC structure is defined as similar to the bricks and mortar structure, the corneocyte being the bricks and the intercellular lipids the mortar. Intercellular lipids are assembled in two lamellar phases. Within the lamellae, most of the SC lipids prefer a dense orthorhombic lateral packing at skin temperature (30−32°C), while some of the lipids adopt the less dense hexagonal packing. The ordered lipid packing in SC is induced by the FFAs with predominantly saturated chains, carbon chain lengths ranging from 12 to 30 (mostly chain lengths of 22, 24 or 26 carbon atoms) and the CERs with a long hydrocarbon tail and small headgroups(1,2). The CERs may vary in headgroup structure and chain length. Currently, 18 subclasses of CERs have been defined in human SC.

Changes in SC lipid composition have been reported in one of the most common chronic inflammatory skin diseases called atopic dermatitis (AD). The etiology of AD is multifactorial and involves the interaction of immunological, genetic and environmental factors. Damaged skin barrier characterized by increased water loss through SC is characteristic of patients with AD. There are studies showing that impaired skin barrier is associated with changes in lipid composition.

In a study; a reduction FFA chain length, an increase in mono-unsaturated FFAs (MUFAs) and a decrease in hydroxy FFA have been shown in non-lesional and lesional SC of AD patients (3). FFA chain length reduction increased the formation of less densely packed hexagonal lipid organization, while the increased level of MUFA observed in SC of AD patients was also reported to increase a hexagonal lipid organization in in vitro studies. All changes were more pronounced in lesional SC than in non-lesional skin. Again, in this study, no relationship was observed between lipid changes and filaggrin mutations, which are an important predisposing factor for AD development (3).

In the skin of AD patients compared to healthy skin; a reduction in the levels of the CER NP, CER NH, CER EO classes, an increase in the levels of CER NS and AS (4-7), a decrease in the chain length of CERs have been reported. As these changes in lipid composition occur simultaneously, it has not yet been determined which of them is the underlying factor of the impaired skin barrier. In another study investigating the role of various anarmolytics in the composition of CERs and FFAs (palmitic acid (C16), stearic acid (C18), arachidic acid (C20), behenic acid (C22), in AD on model membrane systems, it was shown that the increased level of short-chain FFAs caused a greater reduction in barrier function than the compositional changes of CERs (8).

Another disease in which FFAs are investigated in pathogenesis is acne vulgaris. In the pathogenesis of acne vulgaris, it has been defined as abnormal ductal keratinization, increased sebum production resulting in seborrhea, excessive Propionibacterium increase. FFAs are formed from sebum triglycerides (TG) with lipase secreted by Propionibacterium acnes. FFAs are thought to be involved in abnormal ductal keratinization in acne. While there is much more sebum on the facial skin of a female patient with acne than that of a healthy woman, increased sebum levels do not directly cause acne development. In a pilot study involving 9 men, no significant difference was observed in the sebum FFA composition of the subjects in the two groups with and without acne. Free sature FFA composition has been reported to differ between acne and acne-free women. Furthermore, the diet with low glycemic load reduced the amount of sebum and these amounts changed the fat composition of TG in men with acne. In a study investigating the effect of fatty acid composition of sebum on acne vulgaris; the amounts of TGs and FFAs, fatty acid compositions and cutaneous superficial Propionibacterium acnes were examined.

Samples were taken from the foreheads of 18 female patients, 10 male patients, 10 healthy women and 10 healthy men by swab method. Significant differences were observed in the amounts of sebum, TG and cutaneous superficial P. acnes as well as the fatty acid composition of TG and FFA between acne and healthy female subjects. FFA compositions correlated

with the amount of TG in both groups. It has been reported that the fatty acid compositions of TG and FFA change with the amount of TG and that the fatty acid composition does not change with the presence or absence of acne (9).

A study has been carried out on the composition of free fatty acids from the skin surface and the barrier region of free fatty acids in normal and abnormal kertanization (psoriasis). The presence of substantial amounts of free fatty acids with chain lengths longer than C20 has been demonstrated, particularly in barrier zone lipids of healthy subjects and in both the surface and barrier zone of psoriatic individuals. Approximately one-third of the free fatty acids of lipids from the barrier region of normal healthy subjects have chain lengths longer than C18. Evidence is presented that long-chain acids from C18 are produced in the epidermis, at or near the barrier, and not by sebaceous glands. These acids are probably to be incorporated into the keratin or into the glycolipoprotein cementing substance during the normal keratinization process, so only small amounts are transported to the skin surface and are visible in the surface lipid film. In psoriasis, almost three-quarters of free fatty acids have longer chain lengths than C18 (10).

In psoriasis, there is probably both the overproduction of these acids and their failure to participate in keratin or glyco-lipoprotein. Therefore, these acids accumulate in the barrier area and are transported to the skin surface in extremely large amounts.

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TGF- BETA IN DERMATOLOGY

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Cytokines are signaling water-soluble non-immunoglobulin proteins and glycoproteins released by a wide variety of cells especially, immune cells. Cytokines play an important role in cellular communication and their function may be autocrine, paracrine or endocrine. In this lecture, we will talk about TGF- β in Dermatology.

Cytokines use several downstream pathways including JAK-STAT, NF-kβ, and serine/threonine kinase pathways. TGF-β mainly use the last pathway. There are three isoforms of TGFβ (TGFβ1, 2 and 3). The activation of these cytokins may lead to following factors:

• Cell proliferation

• Differantiation

• Immun response

• Angiogenesis

• Tissue repair

So far, TGF-β has been studied certain dermatological diseases such as hair loss (basically alopecia areata), psoriasis, wound healing, malignancies (squameous cell carcionoma, basal cell carcinoma), lipogenesis, hypertrophic scar, keloids, and vitiligo.

The activated TGF-β receptor I (RI) subsequently induces the signal intracellularly by phosphorylating SMAD2 and SMAD3. Upon phosphorylation, SMAD2 and SMAD3 make a complex with SMAD4, accumulate in the DNA and act as transcription factors. However, the actions of the TGF-β receptors are inhibted by Smad7. Smad7 interacts with the activated TGF-β RI to prevent activation of Smad2 and Smad3, hence interrupting TGF-β induced signaling. It has been shown that UVB exposure may induce rapid and transiet gene expression of Smad-7 which subsequently may inactivate TGF- β related pathways. These effect may be benefical for numerous TGF- β related dermatological diseases as it mentioned above. Furthermore, there are certain anti-TGF- β drugs such as kaempferol and galagin thath inhbitis fibroblast collagen synthesis and hypertrophic scar formation. These drug shed light on dermatological diseases in which TGF- β plays an important role.

To incrase knowledge of pathophysiological mechanism of TGF-β in certain dermatologic diseases such as alopecia areata, psoriasis, keloids, vitiligo etc. may lead to new treatment methods in the future.

CCR-5 IN DERMATOLOGY

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To date, we discovered over two hundreds cytokines including approximately 50 chemokines in our body.CCR-5 is a chemokine receptor that is mainly expressed on cytotoxic T cells and T helper 1 cells. Natural ligands for CCR5 consist of CCL-3, CCL-4, CCL-5 (RANTES), CCL-8, CCL-11 (eotaxin), CCL-14, and CCL-16.

CCR-5 is the among the most popular mediator in HIV patogenesis. CCR-5 acting as a co-receptor along with CXCR-4 for HIV entry into the CD-4 T cell. In recent years, CCR-5 has been started to be investigated in the field of dermatology.

Psoriasis, panniculitis, melanoma, mycosis fungoides, wound healing and alopcia area are the main diseases that has been studied on CCR-5. It has also been shown that CCR-5 has the effect on the edema and hemorrhage in the cutaneous reverse passive Arthus reaction.

The current studies on malignancy particularly mycosis fungoides revealed that the expression of chemokin receptors including CCR-5 contributes to the migration of tumour cells.

RANTES which is the one of the ligand of CCR-5 receptors has been found to have higher expression on lesional psoriatic skin. The increased mRNA expression of CCR-5 was also reported. These result provided to perform a new randomized placebo controlled study in order to see the effect of CCR5 antagonism on psoriasis. Interestingly, the study reported 50 mg twice daily CCR5 inhibitor does not have effect on the established study but rather may be a preventive effect.

In another study, genetic distrubition of CCR-5 has been found to associated with delayed skin wound healing and decreased neovascularization. However, it has no effect on macrophage recruitment in wound healing.

The previous studies on CCR-5 in dermatology imply that CCR-5 has considerable effect on the infammatory based dermatologic diseases. Therefore, CCR-5 antagonism may be adjuvant treatment in some dermatologic diseases. Further studies required in order to see the exact effect of CCR-5 antagonism in certain skin diseases.

WHAT'S NEW APPROACH FOR ANTIFUNGAL THERAPY?

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Cutaneous fungal infections are classified as superficial and deep mycoses. Most mycotic infections are superficial and are limited to stratum corneum, hair and nails. The main groups of fungi causing superficial fungal infections are; dermatophytes (tinea), nondermatophyte molds and yeasts (Candida including non albicans candida species, and dimorphic fungus as Malassezia).

Herein, new approaches in the management of superficial fungal infections and antifungal therapy will be mentioned shortly.

Dermatophytes (Trichophyton, Epidermophyton, *and* Microsporum genera) are one of the most common cause of superficial fungal infections. Despite the progress in medicine, the prevalence of dermatophyte infections is increasing from year to year. These infections lead to a variety of clinical manifestations, such as tinea pedis, tinea corporis, tinea cruris, Majocchi's granuloma, tinea capitis, and tinea unguium. For patients with limited tinea pedis, tinea corporis, or tinea cruris, treatment with a topical antifungal drug applied once or twice daily is recommended. Tinea capitis and onychomycosis require systemic antifungal treatment.

A variety of topical antifungal agents are available including azoles (clotrimazole, econazole, ketoconazole, miconazole, sulconazole), allylamines (terbinafine), butenafine, naftifine, and ciclopirox . The most important development in the treatment is the approval of new drugs. Some of the newer topical antifungal drugs are listed below.

1. Azoles: Sertaconazole, luliconazole and efinaconazole
2. Oxaborole: Tavabarole

Sertaconazole 2 % cream is FDA approved for treatment of tinea pedis in individuals 12 years of age and older and is approved in the EU for the treatment of tinea corporis/tinea cruris. It has broadspectrum antifungal activity against all three genera of dermatophytes, Candida and Cryptococcus. In addition, it is also effective against Grampositive cocci.

Luliconazole is approved by FDA for the treatment of tinea pedis, tinea cruris, and tinea corporis onca a day for a week. Luliconazole has a broad-spectrum activity against a variety of etiologic fungi in skin infections including dermatophytes, Candida, Malassezia subspecies, and Aspergillus.

Efinaconazole 10 % solution was approved for the treatment of onychomycosis. It has a greater nail bed penetration and efficacy than previous topical antifungal treatments. It is mainly indicated for the treatment of T.rubrum and T. mentagrophytes. However, it exhibits activity toward other dermatophytes and nondermatophytes including Microsporum, Epidermophyton, molds, Aspergillus, Cryptococcus, Trichosporon, and Candida genera fungi.

Tavaborole is an oxaborole antifungal drug approved for toenail onychomycosis. It has a broad-spectrum activity against a variety of fungi, including the dermatophytes T. rubrum, T. mentagrophytes, T. tonsurans, and E. floccosum.

In addition to new drugs, in order to enhance the dermal delivery and skin retention of the drug, the development of new formulated drugs such as water-soluble formulation of ciclopirox, ciclopirox8 % HPCH (P-3051) is another innovation.

Another issue apart from the development of new antifungal drugs is the increased awareness of drug resistance. Although generally considered easy to treat, recalcitrant infections, presenting as extensive and difficult dermatophyte infections are on the rise in some parts of the world especially in India.

Our frequent and prophylactic use of antifungal agents has led to the increased frequency of development of resistance to current antifungal drugs. Azole and terbinafine resistance have been recently emphasized. This high levels of resistance reveals warranting antifungal susceptibility testing in rcalcitrant cases.

The last issue to be mentioned is the approach to the treatment of onychomycosis. Systemic medications are widely used

because of their accessibility, low cost, and high efficacy. Oral terbinafine, itraconazole and fluconazole (fluconazole not approved by FDA) are approved for the treatment of onychomycosis. Because of higher cure rates with terbinafine and fewer drug interactions, terbinafine is usually preferred over itraconazole and fluconazole. Table 1 reveals the indications for oral and topical treatment of onychomycosis (Table 1).

Topical treatment with amorolfine, ciclopirox, tavaborole, or efinaconazole is appropriate for cases of mild to moderate toenail onychomycosis due to dermatophyte or mixed dermatophyte/Candida infection. In a study, in cases with the involvement of matrix; using amorolfine and systemic terbinafine has been found to be superior to using only systemic terbinafine.

Nail debridement may be preferred as an another treatment option. Avulsion with urea in combination with bifonazole is also a treatment option and is more attractive than undergoing surgical nail removal.

Photodynamic and plasma therapies have been explored, but larger randomized trials are needed to determine their efficacy in the clinical setting.

Laser treatment is approved by the FDA for onychomycosis. It is not recommended as a first line treatment since cure rates are lower than those for oral and topical antifungal treatment. Short, long pulsed, and Q-switched neodymium-doped yttrium aluminum garnet lasers, near infrared and dual wavelength diode lasers and fractional CO2 lasers have been used for the treatment of fungal nail infections with mixed results.

Table 1. Indications for oral and topical therapy in onychomycosis

Indications for oral therapy	Indications for both oral and topical therapy	Indications for topical therapy
Proximal subungual onychomycosis	Superficial onychomycosis	Contraindications to oral therapy
DLSO affecting >50% of the surface area of the nail plate with matrix involvement and nail plate thickness >2 mm	DLSO affecting <50% of the surface area of the nail plate without matrix involvement and nail plate thickness <2 mm	For prevention of recurrences or reinfection
>3 or 4 nails affected	Up to 3 or 4 nails affected	
Poor compliance and prognostic factors		

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IF SUPERBUGS ARE MONSTER, HOW CAN WE PREVENT THEM WHEN USING ANTIBIOTICS?

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The antibiotic use began with the discovery of penicillin by Sir Alexander Fleming in 1928.[1] Simple infections resulted in death or serious sequelae for centuries due to lack of antibiotics. While helping to extend average human life from 56.4 at 1920s to around 80 by the end of 20th century, it is impossible to consider antibiotics so innocent and life-saving.[2] Although the antibiotics saved the past and our generation from death, the antibiotic resistant bacteria, so called superbugs, will be one of the major causes of death in next generations.

Causes of the occurrence of superbugs

The infections caused by superbugs were listed among the top ten human life threading topics in 2019.[3] Superbugs are bacteria which are resistant to most antibiotics and other medications that are commonly used to cure the infections they cause. The main reason behind the existence of superbugs is the misuse of the antibiotics. The main headlines if this misuse are as follows.

Overuse of the antibiotics: 30% of the antibiotics are prescribed unnecessarily and the number of prescribed antibiotic units is increasing by millions in every year.[4] Over-prescribing of the antibiotics has led to the development of a number of protective mechanisms of the bacteria. The bacteria are clever microorganisms. They have the capacity to transfer their genes of antibiotic resistance mechanisms not only to their offspring, but also to other bacteria by gene transfer elements such as plasmids. In addition, antibiotic resistance may occur with various mutations.[4]

Inappropriate Prescribing: Sub-inhibitory and sub-therapeutic doses or unnecessary use of antibiotics may cause genetic changes such as mutations and gene expressions which may increase the virulence and also the increasing resistance in bacteria may help to spread.[1]

Extensive use in animals and plants: The antibiotics are added to animal feeds and the water of plants as preservatives in some countries. In addition, fruits are sprayed with water containing antibiotics in some regions. Thus, humans may inadvertently ingest antibiotics or antibiotic resistant bacteria with food.[1]

Lack of new antibiotics: The discovery of new antibiotics are very rare today. Drug industry developed 13 classes of antibiotics in thirty years till 1968, but only three since then. One reason for this is the main focus of the pharmaceutical companies shifted to the more profitable biological agents, drugs for neuromuscular diseases or cancer. Research on COVID-19, the major pandemic of the latest years, naturally proceeded all drug research. In addition, as with other drugs, years long phase studies are required for new antibiotics before marketing.

Over the counter use: The life saving properties of antibiotics have made them the most prescribed and used drug group in the world.[5] However, the only reason for the superbugs is not the prescribing habits of the physicians.[6] It is reported that one of the main causes of superbugs is the use of antibiotics without prescription in many countries.[7]

Measures should be taken to prevent antibiotic resistance[4,9,10]

- Both physicians and public should be trained on the conscious use of antibiotics.
- Over the counter antibiotic sales should be prevented.
- The antibiotics should not be prescribed for the viral or parasitic infections.
- Broad-spectrum antibiotics should not be used in infections that can be treated with narrow-spectrum antibiotics.
- Prescribing multiple antibiotics should be avoided while a single antibiotic is enough for therapy.
- Antibiotics should be used in appropriate doses and duration; neither long nor short time intervals.

- Auxiliary tests such as Gram staining and culture antibiogram should be carried out before prescribing antibiotics, if possible.
- These measures should be taken not only for humans but also for animals. Antibiotic use for prevention infections in animal feed or plant water should be avoided worldwide.
- More attention should be paid to discovery of new antibiotics and pharmaceutical companies should be encouraged in this respect and their work on this subject should be facilitated.
- Rapid diagnostic tests should be established to confirm bacterial infection, resulting in a few hours or even minutes.
- Superbugs can be transmitted by contact. Attention should be payed to the use of common item at home and healthcare professionals should wash their hands or apply disinfectant before and after each examination and use disposable gloves.
- In cases of possible non-antibiotic treatments such as acne vulgaris, other treatment options should be considered. The addition of topical benzoyl peroxide or retinoids to the antibiotics in acne vulgaris treatment should be done in case of prevent superbugs to form biofilms.

Conclusion

All life forms tend to adapt to changing environmental conditions in order to survive. This is the case for bacteria, too. Although superbugs are defined as monsters, it should kept in mind that human beings created these monsters by their own. The widespread and misuse of antibiotics has led bacteria to adapt to changing conditions. Necessary precautions must be taken against these monsters by humans. If we do not improve our antibiotic use habits, it seems that the next years will be tough for all humanity.

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POSTMODERN TREATMENTS IN DERMATOLOGY

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Postmodern medicine, in other words complementary and alternative medicine, has been the focus of attention worldwide in recent years. It has been defined as a group of health care practices and products, which is usually not considered part of traditional western medicine.

It is called "alternative medicine" when used instead of traditional medicine, and it is also called "complementary medicine" when used with traditional medicine.

Complementary and alternative medicine categories include,

- dietary supplements and herbals
- manipulations,
- body-based practices,
- mind-body interventions.

An increasing number of dermatology patients are using complementary and alternative medicine. During lifetime, the rate of using complementary and alternative medicine is estimated to be between 35-69% of adults in USA, and 42-70% in adults in Turkey.[1,2] It is claimed that approximately 84.5% of people who report skin problems use complementary and alternative medicine.

It has been reported that the demographic profile of patients using TCAM applications for skin diseases in the United States of America (USA) is mostly white women aged 26-50 with at least a high school diploma.[3]

In one study, the most common TCAM modalities used among adults with skin disease were found as supplements containing vitamins, minerals or herbs.[4] In a study was performed in Turkey, in which 1610 people attended; TCAM use, such as henna, cologne, moisturizing cream, prayer, and herbal therapy, was common among 43.7% of the participants.[5]

Complementary and alternative medicine is often chosen in chronic dermatologic conditions, such as atopic dermatitis (AD), psoriasis, rosacea, acne.[6]

Atopic dermatitis

The most common complementary and alternative treatment among patients with AD was dietary intervention (42%), homeopathy (34%), followed by herbalism and supplements (19% and 18%, respectively).[6] Patients with atopic dermatitis due to inconsistent evidence with respect to the guidelines for the treatment of atopic dermatitis, borage oil, evening primrose oil, fish oil, probiotics / prebiotics, multivitamin supplements, vitamin E, vitamin D, zinc, and vitamins B12 and B6 are not recommended.

Psoriasis

There are several randomized controlled studies on the efficacy and safety of complementary and alternative medicine for psoriasis.[6] Talbott and Duffy reported that there is a strong evidence in favor of climatotherapy and the use of Qing-Dai, also referred to as Indigo Naturalis, fish oil and herbs such as Mahonia aquifolium, in the treatment of psoriasis.[7] No evidence was found for herbs, vitamins, minerals such as vitamin D, zinc, or selenium. In a study, evidence of efficacy was found for inositol in the group of psoriatics taking lithium. One study demonstrated that the plants including neem and M aquifolium had a evidence of effect for psoriasis. There is a conflicting evidence for aloe vera, fish oil in the literature. In only one study found an evidence of effect on psoriasis treatment with Chinese medicine. Acupuncture had no efficacy on psoriasis treatment.

Rosacea

Evidence based on the efficacy and safety of complementary and alternative medicine for rosacea is composed of several methodologically non-strict clinical studies.[6] Some studies have noted that various herbal treatments can be promising for rosacea symptoms.[8] It has been showed that several phytochemicals and herbal extracts improved facial erythema and number of papule and pustule related to rosacea.

Acne

Recently, there is very restricted data on its efficacy and safety to recommend the use of herbal extracts and other complementary treatments for acne.[6] In a RCT, oral barberry extract showed better results in patients with moderate to severe acne.[9]

Conclusion

Despite the increasing popularity of complementary and alternative medicine in recent years, further studies are needed on its efficacy and especially its safety in dermatoses.

Keywords: complementary and alternative medicine, postmodern

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DOES METFORMIN REALLY WORKS IN DERMATOLOGY

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Metformin (dimethylbiguanide) has been used for years as a traditional herbal therapy in the treatment of type 2 diabetes. This hypoglycaemic drug was derivated from a herbal source from Galega officinalis (also known as galega, French lilac, goat's rue, Italian fitch) (1).

Drug shows its effect by increasing peripheral tissue sensitivity to insulin and peripheral glucose uptake. It inhibits gluconeogenesis, decreases hepatic glucose, and thus blood glucose decreases. Metformin also has a lipid lowering effect, such as reducing serum triglyceride and low-density lipoprotein (LDL) cholesterol levels, and increasing serum high-density lipoprotein (HDL) cholesterol levels (2).

Due to its wide effect mechanisms and properties, it is a suitable drug to be used in the treatment of many diseases other than diabetes mellitus. The spectrum of dermatological diseases is also quite wide such as psoriasis, hidradenitis suppurativa, acanthosis nigricans, polycystic ovary syndrome (PCOS) related acne, hirsutismus, skin cancer, and among others (2-4). It has been reported that metformin decreases the frequency or severity of flares in patients with HS (4). Again, adding to the treatment in patients with psoriasis leads to an improvement in the quality of life (5). Using metformin alone or as an adjuvant leads to acne recovery in patients with PCOS (6).

Adverse effects are not serious. It can be observed as cutaneous or noncutaneous (7). Metformin-induced lichen planus, leukocytoclastic vasculitis and bullous pemphigoid had been reported as a cutaneous adverse effect (8-10). Non-cutaneous adverse effects include indigestion, myalgia, nausea, vomiting, diarrhea, and flu-like symptoms (7).

Metformin is an agent that is thought to be effective in dermatological diseases, such as psoriasis, hidradenitis suppurativa, acanthosis nigricans, PCOS related acne, and hirsutismus (4). We can safely use this drug in our clinical practice and increase our experience.

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EGFR INHIBITORS AND SKIN

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Epidermal growth factor receptor inhibitors (EGFRIs) are anti-cancer agents targeting specific oncogenic pathways. They are approved for use in various malignancies including squamous cell carcinoma of the head and neck, colorectal carcinoma, non-small cell lung cancer, pancreatic cancer and breast cancer. The agents in the EGFRI group are as following; cetuximab, panitumumab, erlotinib, gefitinib and lapatinib. These treatments are often associated with similar cutaneous adverse effects (AE).(1, 2)

EGFRs are widely expressed in epidermis and skin appendages. As a result, cutaneous adverse effects are commonly observed among patients receiving EGFRIs.(3) In addition to EGFR blockade in skin, altering IL-1, TNF-alfa and IL-8 levels is another mechanism causing EGFRI-related cutaneous AEs.(1) Cutaneous toxicities occur in skin, mucosa and adnexal structures in the majority of the patients treated with EGFRIs. Therefore, it is essential for dermatologists to know the signs and management of EGFRI-related cutaneous AEs.(2) The most frequently seen reactions are; papulopustular rash, xerosis, pruritus, hair changes and paronychia.(1, 2, 4)

Papulopustular rash in a seborrheic distribution is the most common (>75%) and earliest cutaneous AE of EGFRIs. It occurs one or two weeks after initiation of treatment.(2) Pruritic follicular papules evolving into pustules is the main clinical sign. The severity of eruption and/or discomfort of patient determine the management. Topical antibiotics, topical corticosteroids, topical calcineurin inhibitors, oral tetracyclines and low-dose oral isotretinoin are the treatment options.

Xerosis and pruritus appear approximately in one third and half of the patients, respectively.(1, 4) Typically, xerosis is prominently seen in the extremities during the first months of the treatment.(1) Due to the xerosis; pruritus, fissuring, eczema and secondary skin infections can occur. Symptomatic treatment of xerosis with moisturizing agents is beneficial. (2) Oral antihistamines, pregabalin, gabapentin, doxepin and topical anti-inflammatory agents can be considered in case of severe and disturbing pruritus.(4, 5)

Paronychia is one of the most frequent AEs of EGFRIs occurring in the first to third month of the treatment.(4) The nail of the thumb or toe is commonly affected. Patients should be advised to avoid tight, uncomfortable shoes before treatment starts.(2) Antibacterial soaks, topical corticosteroids, warm compress and oral tetracyclines may be used to reduce inflammation.(1, 2, 4)

Hair changes include; slow growth of hair, finer, more brittle, curlier and kinky hair and mild alopecia. These changes occur in the second or third month of treatment. Trichomegaly of eye lashes or facial hypertrichosis may be observed. (2) Patient should be informed that the hair changes are reversible after the cessation of treatment.(1, 4)

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PERIORBITAL WRINKLES AND HYPERPIGMENTATION ETIOLOGY AND TREATMENT

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The periorbital region serves as a barometer of chronologic and environmental age and, as such, patients often seek its cosmetic rejuvenation(1). Maintaining a youthful appearance is a priority for many people. Global eye rejuvenation is sought more frequently and at a younger age than other treatments.

Periorbital Wrinkles and Hyperpigmentation Etiology

Main causes and mechanisms associated with the three major aging concerns of the periorbital area:

- Periorbital hyperpigmentation (dark circles and upper-eyelid discoloration),
- Puffiness,
- Lines and wrinkles(2).
- All these conditions are triggered by a variety of factors and therefore require a multi-factorial approach.

Skin aging, regardless of whether its origin is chronological or environmental, results in visible deterioration of the skin's condition and loss of its functionality. Periorbital wrinkles are formed with repetitive muscle contraction over time, and they contribute to the appearance of age. However, treatment of the periorbital area is difficult because of its delicate nature and important function(3).

Proper patient selection and assessment of aging severity are critical to determine the best therapeutic option(1).

Periorbital Wrinkles and Hyperpigmentation Treatment

Treatment modalities

- Ablative and Non-Ablative Lasers,
- Radiofrequency (RF) devices
- Chemical peels
- Platelet-Rich Plasma(PRP),
- Mesotherapy
- Botulinum Toxin
- Filler

Ablative and Non-Ablative Lasers; For patients seeking non-surgical options to improve the appearance of photoaged skin, several laser-based ablative resurfacing and non-ablative rejuvenation technologies have been employed. Although these systems have proven efficacy and good safety profiles, there are associated limitations. Certain ablative laser technologies, such as carbon dioxide and erbium:yttrium–aluminum–garnet lasers, are more effective but result in prolonged downtime and have greater potential for complications, including dyspigmentation, scarring, infection and prolonged healing. Non-ablative laser technologies are associated with shorter downtime, but the outcome often seems limited, and many treatment sessions are necessary.

Radiofrequency (RF) devices; Radiofrequency (RF) devices for skin rejuvenation have also been introduced. This technology produces volumetric heating via tissue impedance and subsequent heat diffusion, and it affects deeper tissue layers than laser-based methods.3 Recently, a novel minimally invasive bipolar RF device, the fractionated microneedle electrode system, has become available for clinical use(4). Collagen remodeling stimulated by this device may result from combined effects of dermal heating by RF and physical stimulation by microneedling. Radiofrequency is electrical current that can produce thermal effects via tissue resistance. These effects stimulate initial collagen contraction

and a wound healing response, which induces remodeling of dermal collagen and tightens skin tissues over a period of time(5). This neocollagenesis induces deep tissue tightening and thus improves periorbital wrinkles.

Chemical peels; The most commonly used alpha hydroxy acids (AHA) are glycolic 20% and lactic acid 15% which reduce periorbital pigmentation. Vavouli et al reported an improvement of up to 90% in dark circles following treatment with 3.75% trichloroacetic acid and 15% lactic acid(6).

Platelet-Rich Plasma(PRP); PRP can be used to treat aesthetic problems in the periorbital regions like wrinkles, pigmentation, erythema, xerosis, skin elasticity, and firmness. The best response was observed after three monthly injections and that is being recommended(7).

Mesotherapy; Mesotherapy, commonly known as "biorejuvenation" a technique used to rejuvenate the skin by means of a transdermal injection of a multivitamin solution and natural plant extracts that are thought to improve the signs of skin aging. The efficacy, treatment protocols, pharmacokinetics, and safety of mesotherapy are still of concern and under debate. Improvements in wrinkles, increased elasticity, and enhanced skin texture have been attributed to mesotherapy injection but have not been rigorously proven(8).

Botulinum Toxin; Neuromodulator, specifically botulinum toxin A (BoNT-A) is nonsurgical treatment that is frequently used to address signs of aging in the periocular area(9). Botulinum toxin can be injected in the lower eyelid in a dose of 2-4 units safely along with lateral orbital lines to give a synergistic response and eye widening(10).

Hyaluronic Acid Dermal Fillers; The use of hyaluronic acid fillers has become common nowadays. High patient satisfaction and low morbidity of these fillers have led to an increase in the acceptance to fillers(11). Fillers are used to restore age-related periocular volume loss, which is most pronounced in the lower eyelid as well as the superior sulcus. Injectables such as fillers and botulinum toxin can be combined with skin-tightening devices for a synergistic effect(9).

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ACOSUTIC WAVES IN AESTHETIC DERMATOLOGY

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Ultrasonography with frequency higher than 7 MHz allows the observation of the skin and its appendages, subcutaneous tissue and deep structures (muscles, tendons, bone margins and regional lymph nodes).

The era of ultrasounds in dermatology started in 1979, when pioneering use of 15 MHz by Alexander and Miller in measuring the skin thickness was introduced. Since then, some new applications of high-frequency ultrasonography (HF-USG) have emerged providing the clinicians with an extra hand in their everyday practice. The main advantages of HF-USG include the possibility of real-time imaging, measurements of morphological and physiological aspects of the skin, safety associated with the use of non-ionizing media as well as the lack of contraindications to its performance. Currently the main clinical use of HF-USG in dermatology regards preoperative assessment of the depth of invasion in melanomas and basal cell carcinomas.

High-intensity focused ultrasound is the result of the evolution of ultrasound from a simple diagnostic procedure to a therapeutic modality with broader potential. Ultrasound has long been an intriguing medical modality because of its noninvasive nature, low cost, and relatively low rate of complications.1 Sound is transmitted by mechanical vibrations; ultrasound technology utilizes vibrations that are outside of the range of human hearing. High-intensity focused ultrasound, in comparison to typical ultrasound, uses lower frequencies and higher energy levels by several orders of magnitude.1 As compared to normal ultrasound, where acoustic waves are resorbed and deflected through tissue, HIFU can target a specific volume (on the order of millimeters) within the body cavity without harming surrounding tissues.2 A major advantage is that the energy is nonionizing and can theoretically be repeated an unlimited number of times.

High-intensity focused ultrasound (HIFU) safely and effectively improves skin elasticity and clinical contouring of the face and body.

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LOW-LEVEL LASER TREATMENT IN DERMATOLOGY

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It has long been known that red or near-infrared laser light promotes tissue repair and regeneration and low-intensity light called low-level laser therapy (LLLT) stimulates cellular activity [1]. The most commonly used devices have wavelengths in the range 500–1,100 nm and they deliver fluences of 1–10 J/cm2 with a power density of 3–90 mW/cm2. LLLT has shown beneficial effects for a variety of medical conditions such as wound healing, nerve regeneration, joint pain relief, stroke recovery, and the prevention and treatment of mucositis

Low-level laser (light) therapy (LLLT) is a fast-growing technology used to treat a multitude of conditions that require stimulation of healing, relief of pain and inflammation, and restoration of function. Although the skin is the organ that is naturally exposed to light more than any other organ, it still responds well to red and near-infrared wavelengths. In dermatology, LLLT has beneficial effects on wrinkles, acne scars, hypertrophic scars, and healing of burns. LLLT can reduce UV damage both as a treatment and as a prophylaxis. In pigmentary disorders such as vitiligo, LLLT can increase pigmentation by stimulating melanocyte proliferation and reduce depigmentation by inhibiting autoimmunity. Inflammatory diseases such as psoriasis and acne can also benefit. The non-invasive nature and almost complete absence of side-effects encourages further testing in dermatology.

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CRYOLIPOLYSIS: WHAT IS NEW?

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Cryolipolysis is a non-surgical body sculpting method that uses controlled cooling for localised nonsurgical fat reduction. Cryolipolysisis is a popular noninvasive treatment method because of its efficacy, convenience, and safety profile; multiple sessions may have equal efficacy to liposuction.

Cryolipolysis involves placing an applicator over an area containing unwanted excess subcutaneous fat. The applicator varies in temperatures from +7C to -15C for 25 to 60 minutes. Adipocytes are susceptible to these low temperatures, whereas the surrounding soft tissues remain unaffected.6 At these temperatures, a combination of fat apoptosis and necrosis takes place. Apoptosis of fat cells begins after 2 to 3 days, peaks at 2 weeks, and is completed approximately 3 months post-treatment with replacement of adipose tissue by fibrotic tissue.

As this procedure becomes more popular, the wide range of adverse events (AEs) will be well understood.

Concerns of treatment-induced hyperlipidemia following cryolipolysis were initially warranted, however, there is no evidence of this occurring in practice. A study showed that lipid levels and liver function tests were virtually unchanged following this procedure.

Most AEs were reported to be mild and transient. The most commonly reported AE was erythema and this was followed by numbness/paresthesia, bruising, and edema or swelling. There are no reports of permanent loss of sensation following the procedure. One clinical trial reported that 96% of participants experienced mild procedure-related pain. Severe, delayed, or persistent pain, and excessive treatment related discomfort were infrequent.

Paradoxical adipose hyperplasia (PAH) is a rare but serious complication of this procedure, presenting as a well-demarcated hyperplasia of subcutaneous fat, developing months post-treatment. Paradoxical adipose hyperplasia is a benign growth of adipocytes, however it does not resolve

spontaneously and worries patients who underwent treatment to decrease the adipose tissue. The exact mechanism of PAH remains unknown, however hypotheses include subapoptotic injury to adipocytes due to inadequate contact with the cooling applicator, which then stimulates growth of these cells. There are no cases of spontaneous resolution of PAH, and liposuction is the current mainstay of treatment.

The results of one study revealed incidence rates of PAH between 0.05% and 0.39%, which are slightly higher than the manufacturer's quoted rate of 0.025% (1 per 4000 cycles). However, incidence rates at all sites were dramatically reduced by over 75% with the implementation of newer models of CS units. Of patients who developed PAH, 55% were male and 77.8% were of European ethnic origin in this study. The majority of PAH cases (76.9%) were associated with older models of CS units. Thus development of PAH may be related to a combination of factors, including older models of CS units and applicators, as well as individual characteristics that predispose certain patients to this complication.

Treatment of the submental region can result in injury to throat structures causing swelling and hoarseness and mandibular nerve palsy may occur after submental treatment. Radial nerve palsy may occur following upper arm treatment. Reported nerve injuries took place within a range of 1 hour to 6 months after the procedure.

There are some noteworthy contraindications of this procedure. People with conditions exacerbated by cold temperature, such as paroxysmal cold hemoglobinuria, cryoglobulinemia, and cold urticaria, should not receive this treatment. Moreover, people with diabetic neuropathy, bleeding disorders (or those using blood thinners), hernias, and active pacemakers may not be fit for the cryolipolysis procedure.

Severe frostbite complication after cryolipolysis was reported. This case report presents a full-thickness frostbite complication following cryolipolysis for subcutaneous fat reduction performed in a non-medical esthetic clinic. The deep and large abdominal wound (15 × 12 cm) required hospitalization and surgical treatment.

Clinical research on cryolipolysis has been growing and new evidence is available. The latest systematic review showed that reduction of the adipose layer can approach 30% per treated region. There are a few clinical trials disclosing that the reduction of the fat layer can reach 17.4%-20.4% after 2 months and 21.5%-25.5% after 6 months of treatment. In addition, an epidemiological study showed that two sessions per treatment area were required to obtain some satisfactory result, with the exception of the abdomen that acquired satisfactory results with only 1 session in 21% of the cases.

Large number of clinical trials rely on tape measures or cutometers to quantify fat loss following treatment; High-resolution ultrasound and magnetic resonance imaging can also be used to characterize changes in adipose tissue. However, given the long period over which cryolipolysis results take place and limitations of current quantitative measurements, it is difficult to monitor treatment response over time. Diffuse optical spectroscopic imaging (DOSI) is a novel, noninvasive imaging technology that can be used to assess functional and metabolic changes in treated adipose tissue.

Twenty-seven/28 patients (54 body areas) were considered as treatment 'responders' in a clinical trial. In these patients, mean skinfold thickness decreased from 35.4 ± 9.9 mm pre-treatment to 22.2 ± 7.6 mm at 12 weeks (mean change: -40%; $p<0.001$). Mean change in skinfold thickness was greater with ≥ 3 cycles versus 1-2 cycles of CoolSculpting ($p=0.01$). Patient satisfaction with treatment was high (n=51/58; 88%). No adverse effects were recorded. This study shows that multiple cycles/sessions of CoolSculpting can safely improve overall treatment benefit in body contouring, with greater decreases in skinfold thickness.

In a single-arm intervention study thirty-six subjects underwent one session of cryolipolysis in each area (22 subjects treated the arms, 20 the submental region and 9 the breast). A mean reduction of 19.1% was observed. So cryolipolysis is a useful noninvasive tool in reduction of visible localized fat in arms and submental region and of pseudogynecomastia. Obese subjects are not benefited by this treatment.

Three-dimensional cryolipolysis for submental and lateral neck fat reduction was performed in one study. Posttreatment, 82.05% of patients marked the results of fat reduction as exceptional or very improved,12.82% as improved, 5.13% as no result, and 0% as worse.

One study investigated cryolipolysis-induced abdominal fat change. Single unilateral cryolipolysis tended to decrease the cross-sectional areas of visceral adipose tissue, by 8.4 cm2 (9.9%), the waist circumferences, and the percent body fat, by 2.8 cm2 (0.6%), overall. The cross-sectional area of visceral adipose tissues on the treated side significantly reduced, by 6.8 cm2 (15.6%; $P = 0.003$), and that of the untreated side tended to decrease by 1.2 cm2 (3.6%). Split-body trials have shown that a single unilateral session of noninvasive selective cryolipolysis can be considered as a safe and effective treatment for reduction of visceral adipose tissue over a period of 12 weeks, which should also result in metabolic improvement.

Effects of cryolipolysis on lower abdomen fat thickness of healthy women and patient satisfaction were studied in a randomized controlled trial. The study showed that a single application of the utilized protocol of cryolipolysis does not produce any significant effect on fat thickness of the lower abdomen of healthy women.

Investigation of systemic effects of cryolipolysis in central obese women was performed in a randomized controlled trial. In this study there were statistically significant improvements of waist-to-hip ratio, body mass index, total cholesterol, triglycerides, low-and high-density lipoprotein, as well as liver enzymes in favor of the study group ($P < 0.001$).

The effect of ultrasound cavitation in combination with cryolipolysis as a non-invasive selective procedure for abdominal fat reduction was studied. Apart from fat-free mass, the combination therapy significantly reduced body fat mass, weight, BMI, and abdomen circumference compared to the control group ($P < 0.01$).

Feasibility Study of Electromagnetic Muscle Stimulation and Cryolipolysis for Abdominal Contouring - with 3 cohorts: EMMS alone, Cryolipolysis alone, and Cryolipolysis + EMMS in combination was performed. Mean circumferential reduction measurements were greatest for Cryolipolysis + EMMS cohort group followed by Cryolipolysis only, and then EMMS only cohort. So a multimodal approach using cryolipolysis and EMMS was safe and demonstrated enhanced body contouring efficacy for this feasibility study.

A randomized double-blind trial evaluating the efficacy and tolerability of topical body treatment with TriHex

Technology® combined with abdomen cryolipolysis or radiofrequency was performed. Nonsurgical fat reduction procedures using cryolipolysis and radiofrequency are among the most popular noninvasive aesthetic procedures. In this clinical study, TransFORM Body Treatment (TFB) with TriHex Technology® (ALASTIN® Skincare) improved the contour and reduced skin laxity following cryolipolysis of the arms. This product is formulated by using a combination of peptides and other active ingredients designed to stimulate the autophagic breakdown of lipid droplets and expedite the apoptotic process after fat reduction procedures. In another study, topical application of TFB significantly increased adipose volume loss and improved clinical outcomes of nonsurgical fat reduction procedures.

To claim that CLL is a noninvasive technique that could be a good alternative to liposuction in patients with moderate excess fat as claimed by some is not justified after review of literature on this subject. Certainly further research should be performed to prove positive effects of this treatment modality and to determine categories of patients in whom most favorable outcomes might be expected.

SMOKING AND SKIN AGING

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Cigarette smoke is a highly complex aerosol composed of thousands of chemical substances, including carbon monoxide, reactive oxygen species, and reactive nitrogen species.

Smoking affects several aspects of health and skin. Smoking leads to disruption of the mitochondrial respiratory chain and induction of reactive oxygen compounds, leading to apoptosis and cellular damage.

Aging in general has been linked to telomere-associated cellular senescence. Oxidative stress contributes to telomere shortening, and because smoking increases oxidative stress or secondary oxidative events and inhibition of antioxidant mechanisms it is therefore involved in exogenous aging of the skin. Chemical substances from cigarette smoke increase transepidermal water loss, degeneration of connective tissue in the skin and upregulation of matrix metalloproteinases-1 and 3 which degrade collagen and elastic fibers.

Tobacco smoking is an independent risk factor for facial wrinkles as a sign of aging, and extrinsic aging by ultraviolet irradiation is aggravated also by smoking. Smoking is also a risk factor for eyelid sagging. Smoking causes premature aging with a characteristic pattern of wrinkling and orange-purple skin discoloration. Premature facial skin aging in smokers was defined as smoker's face. Smoker's face typically has lines or wrinkles radiating at the right angles from the corners of the eyes or upper and lower lips, numerous shallow lines on the cheeks and lower jaw, or deep lines on the cheeks. Smoking was found to be associated with an increased severity of forehead, crow's feet, and glabellar lines; under-eye puffiness; tear-trough hollowing; nasolabial folds; oral commissures; perioral lines; and reduced lip fullness but not midface volume loss or visible blood vessels in a study performed in women. The skin is slightly pigmented gray with orange, purple and red complexion, and the bony contours become prominent. It has been observed that wrinkling in a 40-year-old heavy smoker resembles that of a 70-year-old nonsmoker. Sometimes, large open and closed comedones with furrows (smoker's comedones) are seen in the periorbital area. There is yellow discoloration of nails, yellowish discoloration of the hair and beard (e.g. smoker's moustache), premature graying and loss of hair, gingival pigmentation (smoker's melanosis), leukoplakia of the tongue (smoker's tongue), oral leukoplakia and a gray-white keratinized palate with multiple red umbilicated papules (smoker's palate/nicotine stomatitis). Smoking contributes to premature hair graying in men. Smoking is the third most important factor for premature graying after a positive family history and obesity, but is not related to severity of graying.

Various mechanisms have been postulated for premature aging caused by cigarette smoke.

Particularly owing to nicotine, smoking negatively affects the dermal microvasculature and the healing process. It also has a toxic effect on keratinocytes and fibroblasts by increasing the expression of metalloproteins and tropoelastin. Furthermore, smoking increases the expression of small proteoglycans and reduces the synthesis of procollagen. In mice models, second-hand smoke, also known as passive smoke caused premature aging by increased cytoplasmic translocation of high-mobility group box 1 protein, and hence, the loss of collagen.Transcription of p16INK4a has been associated with aging, and p16INK4a is a known gerontogen. In murine models, both cigarette smoke and ultraviolet light have augmented the transcription of p16INK4a. Cigarette smoke extract caused senescence of fibroblasts, possibly by oxidative stress injury and inhibition of antioxidant defense activity in in vitro studies. Cigarette smoke-induced early growth response-1 induces the expression of cysteine-rich 61 in human skin dermal fibroblasts. DNA mutations also result from oxidative effects or direct toxic damage. Smoking can accelerate advanced glycation end-products formation and increases their deposition in various tissues, including the skin, similarly to UV radiation. Smoking is an important independent factor in skin aging, observed in an identical twin study, which concluded that 5-year difference in smoking history is associated with skin changes.

ENDERMOLOGIE IN AESTHETIC DERMATOLOGY

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LPG endermologie is a well-tolerated and effective alternative treatment modality for slimming and body contouring. It is also an alternative treatment of cellulite.

Cellulite is a common phenomenon that gives the skin an orange-peel appearance which is particularly observed on the thighs and buttocks of post-adolescent women. It is present even in most of the fit women. There are debates on its treatment methods which, most of the time, lack scientific evidence of efficacy such as liposuction, mesotherapy, subcision, topical creams, and carboxytherapy.

LPG endermologie is a FDA – approved, non-invasive mechanical massage technique for the treatment of cellulite. LPG endermologie system consists of a deep tissue mobilization provided by a medical device composed of a treatment chamber with an aspiration system and two independent motorized rollers that roll and unroll skin folds. The positive pressure from the rollers combined with the negative pressure from aspiration is believed to cause sublethal damage to the subcutaneous fat cells. As these damaged fat cells heal, they rebuild with an improved contour of the skin and a better distribution of subcutaneous fat as a result. Although the fat layer is altered, this mechanical force does not affect the overlying skin, bones, or muscles.

The scientific evidence of LPG in the literature is inconclusive and has only level-II evidence strength (at least one controlled study without randomization). Thus, comparing other treatment modalities such as mesotherapy, carboxytherapy, radiofrequency, and ultrasound should enhance the knowledge of clinicians on the efficiency of LPG treatment on cellulite.

However, LPG endermologie seems to be an effective, well-tolerated and satisfying non-

invasive technique for reducing cellulite grade, BFP, and body circumference measurements.

A study with a porcine model demonstrates that Endermologie treatment does not cause fatty tissues to be broken down, mobilized, and excreted. A standard regime of Endermologie sessions does not produce an inflammatory or classical wound healing response. Increased cell proliferation, neovascularity, or injury to the dermis and epidermis do not occur. However, changes in subdermal tissue architecture result from Endermologie treatment, and these changes are proportional to the number of Endermologie treatments performed. Although adipocyte injury occurs, there is no net decrease in thickness of subcutaneous tissue. However, significant accumulation of collagen fibers occurs mainly in the deep subdermal layer, primarily in the form of dense longitudinal collagen bands. These bands may be largely responsible for the smoothing effect to the skin that has been reported following Endermologie treatments. The question of whether these changes are temporary or permanent must be addressed by future long-term experimental studies.

Endermologie (LPG Systems, Miami, FL), or mechanically-assisted deep soft tissue massage, remains a controversial adjunct to lipoplasty and other forms of body contour surgery.

Endermologie remains an interesting and potentially valuable adjunct to body contouring surgical procedures. However, the fact that it is so operator dependent may explain some of the variable clinical results that have been reported so far.

Recent laboratory studies have shown that various maneuvers in Endermologie treatment, such as smoothing, kneading, and bouncing, create unique waveforms. The amount of pressure generated with each maneuver depends more on the operator's technique than on the suction setting or the force of the spring-loaded rollers. This observation might explain the variable clinical results for Endermologie that have been reported.

Endermologie has been used during liposuction surgery, and in some patients after lipoplasty surgery (i.e., Endermologie-assisted lipoplasty [EAL]).

The technique involves applying Endermologie to a body region just suctioned while another area is being infused. So the operating time is not prolonged. A palpable difference in the subcutaneous fat can be appreciated because it becomes more even and pliable after the application of Endermologie ® to the suctioned area. Endermologie applied in this manner also helps with the even dispersion of the wetting solution during lipoplasty procedure.

Ecchymosis and swelling dissipated quite rapidly in EAL patients and as early as the first dressing change (2 to 4 days after surgery).

During the long-term follow-up of the patients, it seems that postlipoplasty surface irregularities have been lessened.

ALPHA AND BETA HYDROXY ACIDS IN DERMATOLOGY

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Hydroxy acids (HAs) represent a class of compounds which have been widely used in a number of cosmetic and therapeutic formulations in order to achieve a variety of beneficial effects for the skin (1). Alpha-Has (AHAs) are carboxylic acids with one hydroxyl group attached to the α-position of the carboxyl group. The simplest representative of αHA is glycolic acid (chemical name, hydroxyacetic acid), which was the first of this class of compounds to be introduced into skin care products. Lactic acid, with optimal biologic activity in its L-form, is also used in various topical formulations to exfoliate the skin and also to provide antiaging properties (1,2). The cosmetic and dermatologic use of AHAs, i. e. the indication for the treatment with the acids and their salts, depends mainly on concentration, pH, formulation and application time. The higher the concentration and the lower the pH of the product, the greater is the exfoliative, toxic, and corrosive action (1,3). Lower concentrations with 5 % up to 20 % of AHAs are formulated in creams or gels for use prior to peelings and for long-term application in acne as well as in hyperkeratotic or aged skin (4). Solutions containing free AHAs at concentrations of 20 % up to 70 %, partially neutralized AHA-solutions (30 % to 70 %) as well as gels at 70 % are used for peelings carried out profession- ally by a dermatologist (2).

β-Hydroxy acids (βHAs) are carboxylic acids having one hydroxyl group attached to the β-position of the carboxyl group. The most common βHA is β-hydroxybutanoic acid. A lipid soluble βHA is tropic acid (2-phenyl-3-hydroxypropanoic acid). Some βHAs are also considered αHAs as they contain a hydroxyl group in the α-position to one carboxyl group and in the β-position to the other carboxyl group. Malic acid and citric acid are prominent representa- tives in this category. Citric acid is widely used in topical formulations as an antioxidant, and its antiaging benefits are well established (1).

In the cosmetic and dermatologic literature, salicylic acid SA is often described as a βHA, but that classification is incorrect. In SA, both the hydroxyl and the carboxyl groups are directly attached to an aromatic benzene ring and both exhibit acidic properties. In contrast, the hydroxy groups in αHAs, and βHAs are neutral under the conditions used in clinical and cosmetic settings. On the basis of knowledge to date, SA does not function physiologically or therapeutically as a βHA. SA is used in cosmetic formulations for a variety of applications, more specifically, it is fat soluble, which makes it useful in subjects with oily skin (1).

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FRACTIONAL PHOTOTHERMOLYSIS IN AESTHETIC DERMATOLOGY

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Fractional Photothermolysis (FP) a novel treatment concept that utilizes focused laser beams to create a 3-dimensional pattern of microscopically small lesions within the skin.1

Ablative lasers (CO2 and Er:YAG) provide the greatest improvement in photoaging, but significant adverse effects limit their use. Nonablative lasers have reduced adverse effects, but limited efficacy. Fractional photothermolysis produces arrays of microscopic thermal wounds called microscopic treatment zones (MTZs) at specific depths in the skin without injuring surrounding tissue. Wounding is not apparent because the stratum corneum remains intact during treatment and acts as a natural bandage.2 Tissue in the MTZs is typically either thermally damaged in non-ablative FP (nFP), or physically removed (vaporized) in ablative FP (aFP). Due to the small size of the MTZs—generally in the sub-millimeter range—and the availability of surrounding unharmed tissue, such lesions can regenerate very quickly with relatively few side effects as compared to macroscopic lesions extending to similar depth.1 In contrast to ablative lasers, fractional lasers coagulate only 20 percent of the treated skin, sparing islands of viable epidermis and untreated dermis that maintain the skin's barrier function while speeding re-epithelialization. The fractional approach may achieve comparable results to fullsurface ablative lasers without the associated side effects.3 Downtime is minimal and erythema is mild, permitting patients to apply cosmetics immediately after treatment. As with other nonablative laser modalities, multiple treatments are required.2

FP represents an alternative for treatment of dermatologic conditions without the adverse effects of ablative laser devices and can be used on all parts of the body. FP can be used for the treatment of facial rhytides, acne scars, surgical scars, melasma, and photodamaged skin.2 A multitude of FP devices employing different wavelengths and exposure parameters have been developed and are currently used clinically.

The fractional approach of laser delivery offers significant benefits in terms of rapid tissue healing and enables its use in all skin types and nonfacial areas which greatly expands the treatment capacity for laser resurfacing. The development of the newer ablative fractional devices may further increase clinical efficacy while minimizing the number of treatment sessions required to achieve optimal results.

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HYALURONON AND SKIN

Filiz Canpolat

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Skin aging is a combination of multifactorial mechanisms that are not fully understood. It is the result of two biologically independent processes. Intrinsic and extrinsic factors modulate skin aging, activating distinctive processes that share similar molecular pathways. The first is intrinsic or innate aging, an unpreventable process, which affects the skin in the same pattern as it affects all internal organs. The second is extrinsic aging, which is the result of exposure to external factors, mainly ultraviolet (UV) irradiation, that is also referred to as photoaging. Intrinsic skin aging is influenced by hormonal changes that occur with age, such as the gradual decreased production of sex hormones from the mid-twenties and the diminution of estrogens and progesterone associated with menopause. It is well established that the deficiency in estrogens and androgens results in collagen degradation, dryness, loss of elasticity, epidermal atrophy and wrinkling of the skin. [1]

Skin aging is also associated with loss of skin moisture. One of the main characteristics of youthful skin is its large capacity to retain water, and this decreases significantly as we age. The key molecule involved in skin moisture is hyaluronan or hyaluronic acid (HA), a glycosaminoglycan (GAG) with a unique capacity to bind and retain water molecules. HA belongs to the extracellular matrix (ECM) molecules. Hyaluronan (HA) is a key component of the extracellular matrix and is involved in several mechanisms of the wound healing process. It is highly hygroscopic and is involved in the visco-elasticity of the skin.[2, 3] It has been proven to modulate via specific HA receptors, inflammation, cellular migration, and angiogenesis, which are the main phases of wound healing. Degradation of HA by specific hyaluronidase enzymes produces HA fragments that can help to regulate inflammatory processes. HA is also the most popular and commonly employed dermal filler.[4]

Functions of HA include the following: hydration, lubrication of joints, a space filling capacity, and the framework through which cells migrate. The synthesis of HA increases during tissue injury and wound healing and HA regulates several aspects of tissue repair, including activation of inflammatory cells to enhance immune response and the response to injury of fibroblasts and epithelial cells. HA also provides the framework for blood vessel formation and fibroblast migration, that may be involved in tumor progression. The correlation of HA levels on the cell surface of cancer cells with the aggressiveness of tumors has also been reported.[1]

In this presentation, I summarize the role of HA polymers of different molecular weight in tissue regeneration and provide a short overview of main cellular receptors involved in HA signaling. In addition, the role of HA in 2 major steps of wound healing is examined: inflammation and the angiogenesis process. Finally, the antioxidative and antiaging properties of HA are discussed and its possible clinical implication presented.

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INTEGRATIVE APPROACHES OF PRURITUS

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Pruritus (synonymous with "itch") can be defined as "an unpleasant sensation that provokes the desire to scratch" It is a common feature of many inflammatory skin diseases such as atopic dermatitis, irritant and allergic dermatitis, scabies, and lichen planus, but may also be seen in a large number of systemic conditions, including cholestasis, thyroid disorders, and kidney failure. Pruritus is a common symptome,which has a negative effect on quality of life. Current treatments do not fully control the pruritus, these drugs can provide temporary relief but can also cause side-effects and do not help modulate overactive immune responses or address other underlying factors that cause pruritus.

Thus effective, safe treatments for pruritus are still needed. For many years, integrative medicines have found to be very active in the treatment of pruritus (1).

Integrative treatments: Possible underlying factors involved in the development of chronic and acute pruritus, toward which holistic treatments may be targeted, include:

• Intestinal dysbiosis and "leaky gut" related to food allergies

• Chronic inflammation

• Oxidative stress

• Latent infection.

Dietary changes and immune-modulation therapies—Numerous published studies suggest that pruritus can be related to food allergies.

A gluten-free diet and other antiallergenic diets have successfully reduced inflammation and immune responses in pruritus as well as in autoimmune conditions.

The foods considered allergenic include fish, shellfish, beef, lamb, egg and spicy foods. Patients choose to eliminate these possible allergic foods from their diet without further diagnostic procedures (2).

Botanical and herbal therapies— In East Asian regions, by virtue of safety and fewer adverse reaction, a variety of herbal medicines are used in the treatment of pruritus and they are likely to be a good substitute for Western medicines. Some herbs or herbal formulae have been shown to be effective when applied alone or combined with antihistamines, even when antihistamine did not work alone, with low or high evidence.Botanicals that reduce inflammation, combat oxidative stress, and treat underlying infections, particularly in the intestines, Curcumin (active constituent of Turmuric), Gingerol (active constituent of Ginger), Aaragawdha, Shirish and few other plants have actively been used for pruritus since ages (3).There is evidence about sunflower seed oil especially relevant to pruritus. The itch-scratch cycle with its associated barrier damage and secondary inflammation can occur even in the absence of primary skin disease. Sunflower (Helianthus annus) seed oil is rich in linoleic acid, and has been used topically in the treatment of essential fatty-acid deficiency, rapidly reversing the disease (4). These essential fatty acids can also help maintain the skin barrier and decrease transepidermal water loss, both important features in thinking about the barrier problem in atopic dermatitis and, presumably, in other situa- tions where the barrier has been damaged. Several studies have also suggested that there are anti- inflammatory properties of sunflower seed oil, perhaps via the PPAR pathway, which may also be helpful given that the mechanical act of scratching can contribute to inflammation in the skin (5). Safe and inexpensive, sunflower oil could play a role in managing itch, regardless of the etiology. Aromatherapy refers to the use of essential oils extracted from botanical sources to treat diseases . It is commonly administered by massaging into the skin, although can be vaporized and inhaled, taken orally, or even used in the bath. Aromatherapy often implies a mixture of oils, rather than a single oil. Because of the wide range of botanicals, their variable concentrations, and the multiple routes of administration, it is difficult to postulate a single mechanism of action. Clinically, however, several studies sug- gest that aromatherapy can cause a reduction in anxiety and improves mental status, which could play a role in the perception of itch (6).

Acupuncture /Acupressure— Acupuncture has a long history and been widely used in clinical practice for treating pruritus in China and other countries. Many clinical studies have reported that acupuncture is effective for the treatment of pruritus (2).

Acupuncture is based on the idea that energy meridians in the body can become unbalanced and that by stimulating certain points (acupoints) with needles, pressure, magnets, or even lasers, the flow can be restored and rebalanced. From a conventional standpoint, there are studies that show clear changes in specific brain areas with acupuncture, and evidence that there is endorphin production with acupuncture, suggesting a neurocutaneous connection (7). While formal acupuncture would require a specially-trained practitioner, more limited ver- sions (including the single point study discussed below) could be performed by nearly anyone, including patients themselves.

Mind–body therapies, Hypnotherapy Biofeedback, and Cognitive Behavioral Therapy:

Allergies can be ameliorated with mind–body exercises, such as mindfulness meditation. Mind–body practices help to calm an overactive immune system, while supporting greater adaptation and tolerance to one's environment on all levels: physical; mental; and psychospiritual. Stress is known to be a significant trigger for atopic dermati- tis, and the itch-scratch cycle may become a deeply ingrained behavioral response that is elicited more during times of anxiety, regardless of the cause (6). It follows, then, that techniques to reduce stress could be helpful in the management of itch. Safe and somewhat holistic, hypnosis and cognitive behavioral techniques do seem to be helpful in both adults and children, and appear to have a durable response.

Cupping therapy

Cupping therapy is a complementary and alternative medical technique with a long history in China. There are two main types of cupping therapy: dry cupping and wet cupping . In dry cupping, a vacuum created in the cup exerts tension on the skin and draws it into the cup. In wet cupping, a small incision is first made on the skin and then the negative pressure applied to the cup draws out a small volume of blood . In recent years, cupping therapy has been widely used in the treatment of skin diseases , including pruritus (7).

Probiotics—A preliminary study was conducted to examine the effect of ENDOLAC (Lactobacillus acidophilus, Lactobacillus delbrueckii, and Streptococcus thermophilus) on CD34+ cells in patients with clinical symptoms of asthma and/or conjunctivitis, rhinitis, urticaria, atopic dermatitis, food allergy, and irritable bowel syndrome. After the treatment, circulating CD34+ cell values were significantly reduced (8).

Ozone Therapy, autologous whole blood therapy: Ozone, a classic oxidant and sterilizer, has been widely applied in clinic, which involves in mechanisms of antimicrobial effect, antioxidant defenses, immunoregulation, epigenetic modification, biosynthesis, analgesics and vasodilation. Ozonated water and oil have been widely used in treatment of inflammatory and infectious skin conditions because it can quickly relieve symptoms such as pruritus and edema thus mitigating disease severity. Topical ozone therapy is highly effective for treatment for AD. It can change the proportional ratio of Staphylococcus and Acinetobacter, thereby restoring the microbiological diversity in AD lesions (9).

Treatment with autohemotherapy has been proposed as a strategy to induce tolerance to circulating histamine-releasing factors.

Psychiatric medications and psychotherapy

Anxiety, depression and somatoform disorders have been reported as the most prevalent mental disorders in patients with pruritus. Patients with pruritus had a higher prevalence of psychiatric disorders and psychiatric medication use than control groups in the general population. Mental health evaluations and management are important elements in pruritus management (10).

Patients turn to complementary and alternative medicine (CAM) when they are faced with pruritus, particularly when they experience the ineffectiveness and side-effects of Western medicines used to treat the condition or if their symptoms are not resolved.

An integrative Eastern and Western medicine approach can be very effective for managing pruritus and the root condition that causes pruritus.

Correct and appropriate applications can be used by trained people in every field of medicine, as treating pruritus.

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INTEGRATIVE APPROACHES OF URTICARIA AND DRUG ALLERGY

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Drug hypersensitivity reactions are a prevalent phenomenon and affect more than 7% of the population. Skin is the most frequently involved organ. Drug hypersensitivity reactions can be immunologically and non-immunologically mediated. Urticaria is one of the main clinical manifestations in immediate reactions and are usually mediated by specific IgE binding to the FcεRI receptor on mast cells and basophils leads to degranulation and release of preformed mediators that cause the clinical symptoms. Urticaria can also be mediated by a pharmacological mechanism with non-steroidal anti-inflammatory drugs being the most frequent culprits. Up to 35% of patients with chronic spontaneous urticaria (CSU) experience exacerbation of skin symptoms when exposed to NSAIDs. Analogous to AERD, the designation AECD (NERD) has been recently proposed for this condition. Acute urticaria also may develop in some patients who do not have CSU on exposure to NSAIDs. Serum-specific IgE antibodies specific for the drug have been detected in tghis condition. Skin test (ST) is the best-validated method in IgE-mediated reactions. It is challenging for the clinicians to perform skin tests to patient diagnosed with CSU since most patients are unable to withdraw their ongoing treatments or have comorbid dermographism. Drug provocation test is the gold standard in drug allergy diagnosis and in non-immunologically mediated reactions, DPT is the only available tool. There is still a gap in the standardization of procedures of DPT and interpretation of test results. In another perspective, it was shown that prevalence of reported drug allergy in chronic ut-rticaria patients is dramatically higher in comparison to that of the general population showing a significant proportion of patients labeled with multiple drug allergies have an underlying, undiagnosed chronic or recurrent urticaria ultimately leading to overdiagnosis of drug hypersensitivity.Current diagnostic tools to detect drug allergy in patients diagnosed with chronic urticaria will be discussed in this section.

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INTEGRATIVE APPROACH TO ATOPY

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Atopy is a predisposition to respond immunologically to diverse antigens/allergens, leading to CD4+ Th2 differentiation and overproduction of immunoglobulin E (IgE). The clinical consequence of this is the propensity to develop hypersensitivity reactions to allergens. Complex genetic, environmental, and site-specific factors contribute to development of allergies. Prevalance of atopic diseases including asthma, allergic rhinitis and atopic dermatitis are considered to be rising in world.

The evaluation of immediate hypersensitivity includes both in-vivo (e.g. skin prick test, intradermal test, provocation tests) and in-vitro (e.g. eosinophil count, spesific IgE, basophil activation test) objective testing. Here, we will discuss an integrative approach to atopy an allergic diseases.

SKIN BIOPSY TECHNIQUES

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The skin biopsy is a simple but vital clinical skill of the dermatologist. Skin biopsy for diagnostic and therapeutic purposes is a central component in the management of skin diseases. When performed properly, it can be quick and comfortable for the patient, and yield a very high level of diagnostic information. However when performed incorrectly, it can lead to delays in diagnosis and treatment for the patient. While the technical aspects of performing biopsies are familiar to most clinicians, a number of other aspects of the skin biopsy pathway are equally important such as optimal selection of the most characteristic lesion at the most appropriate anatomic location, correct biopsy technique, proper handling of specimens, and providing detailed clinical information for the dermatopathologist.[1-5]

The most important skin biopsy techniques are shave (horizontal) biopsy, punch biopsy, incisional and excisional biopsy. Punch, incisional, or excisional biopsy is suitable for dermal and/or subcutaneous lesions, where as shave biopsy is preferred for more superficial lesions and haemostasis may be achieved with pressure, 25 % aluminium chloride solution or electrocautery. Punch biopsy is quick and easy technique performed using a circular blade. Punch blade sizes range from 2 to 8 mm in diameter, however 3–4 mm punches are often used which usually provides adequate tissue for pathologic evaluation. Incisional and excisional biopsies are performed with a scalpel. A representative portion of the lesion can be excised and the defect should be closed with sutures. The shape of the incision should be fusiform, with angles of 30 degrees at the wound tips. Skin biopsy can be performed with a clean (modified sterile) technique. For smaller biopsies cleaning the area with alcohol for 10 seconds is the fastest and practical option. Alcohol instantly denatures the proteins but it has no residual activity. For long lasting operations povidone iodine should be preferred. When povidone iodine is applied to the skin the dermatologist should wait 2 minutes for the optimum antimicrobial activity. Skin biopsy will usually be performed using local anesthesia, which usually relates to anesthesia of a small area of the body. Preferring a dermal injection technique results in quick and long lasting anesthesia but it is more painful compared to subcutaneous injection technique. When operating on skin, care must be taken not to distort anatomic structures and it is important to be familiar with Langer's lines, also known as relaxed skin tension lines when deciding how to locate an incision to optimize healing and minimize scarring.[1-8]

The objective of this presentation is to provide basic information about the skin biopsy techniques and to offer practical advice on the approach to some common skin lesions.

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ADVANCED SURGICAL SUTURE TECHNIQUES IN DERMATOLOGICAL SURGERY

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Surgical treatment is the mainstay of cutaneous tumors and some otherwise intractable skin conditions. The remaining scar is the visible track left behind by the dermatological surgeon. An unsightly scar will soon let the patient forget what he/she had before and may ruin his/her future life. Sutures are the most common way to close an incisional wound and a skin defect. This requires sutures in most cases as non-suture wound closures are only available for some special situations like incisions without tension.

The number of different skin sutures available for closure is vast. The easiest is the simple percutaneous stitch with the knot outside of the skin. It can be used for virtually all wounds, but its disadvantage is sutures marks after stitch removal. In order to overcome this adverse result, intradermal sutures of various kinds can be used. The most commonly used stitch technique is the intradermal suture. The needle is inserted at the undersurface of the dermis and exits just under the epidermis at the level of border between the papillary and the reticular dermis. This gives good support as it can be tied firmly because no stitch marks will appear. However, it is crucial not to take subcutaneous fat as this will be resorbed within a short period of time and the suture will be loose inviting wound dehiscence.

Many textbooks claim that sutures must not be done under tension. This is nonsense as virtually all skin defects will result in some degree of skin tension. However, there are techniques facilitating suturing under tension by using two or even three loops for one knot, this kind of pulley suture may be transepidermal or intradermal the latter not leaving stitch marks. For an intradermal parallel pulley suture, the needle is inserted at the undersurface of the dermis, exits under the epidermis, is re-inserted at the same level at the oppositie wound margin , exits at the dermis underside and a second loop like the first is performed 3 – 5 mm lateral from the first throw. The ends of the thread are then pulled towards each other to close the wound and tied. This suture has double strength while distributing the tension at two suture points, it is easy to knot as it usually does not slip and therefore does not require help of an assistant. A particular variant of the parallel pulley suture may be used for the pole of a small defect with a relatively large angle (> 35°) combining the pulley action with skin sparing. The first throw is performed as described, the second is performed obliquely so that upon tying the knot the end of the fusiform excision is pulled down preventing the formation of a dog-ear or standing cone. If there is even more tension, the parallel double stitch can be extended to a triple suture: The first throw is performed as usual, the second as in the parallel double stitch, the third is parallel to the first and second but on the other side of the first bite. This triple suture is very versatile for wounds after excision of naevi of the back. The preferred suture material is polyglactin which remains stable for several months.

Commonly, 3/8 curvature needles are used. They are practical for percutaneous stitches but may not be easy to use for intradermal stitches as they do not allow the needle to be inserted and exited in the dermis. A half-circle needle is more practical for intradermal sutures. However, it must be taken with care with the needle holder in order to avoid bending it. If you can still not exit the needle within the dermis you may exit the needle through the skin approximately 5 mm from the wound margin and re-enter it through the same exit point to come out at the wound margin at the border between the papillary and reticular dermis. In a mirror fashion, it may be repeated on the other side of the wound. The knot is tied at the undersurface of the dermis. A tiny dimple is seen for 24 hours where the exit and re-insertion point was. This suture can also be performed as a parallel buried pulley suture.

Running intracuticular sutures are usually performed parallel to the skin surface. They give nice results, however, they cannot hold tension. In contrast, a running intradermal spiral suture is extremely supporting and holds a lot of tension as it is pulled tight with each new loop.

In summary, there are many useful alternatives to common suture techniques giving excellent aesthetic results.

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BASICS OF FLAPS AND GRAFTS IN DERMATOLOGICAL SURGERY

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A flap is a form of adjacent tissue rearrangement where a unit of the tissue is transferred from one site (donor site) to another (recipient site) while maintaining its own blood supply. They have different shapes and forms, and are categorized according to their location, blood supply and the primary tissue movement… How does a flap differ from a graft?

A graft (autogenous) is a skin transplanted from one location to another on the same individual, they are usually classified either as full-thickness, split-thickness or composite grafts.

In this presentation, and for the purpose of aiding communication with peers, I will review a simplified "vocabulary for tissue movements" for the common flaps, and survey the principles and stages of some grafts used in dermatologic surgery.

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CRYOSURGERY AND ELECTROSURGERY: WIDEN YOUR HORIZON

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Is medicine an art or a craft? In the historical process, medicine is evolving from being an art to being a craft. Guidelines that must be followed closely are prepared for almost every disease. And physicians are forced to comply with these guidelines. However, in guidelines, the financial condition of the patient, the mood he is in, the knowledge and skill of the physician, and the facilities of that country or region are not mentioned. This makes it difficult for physicians to act according to the situation.

Electrosurgery and cryosurgery are increasingly being pushed out of the guideline. However, it is obvious that very good results will be obtained if used in the hands of an experienced physician.

Here are a few examples of patients successfully treated with electrotherapy and cryotherapy.

PREDATORY PUBLISHING AND CONGRESS IN DERMATOLOGY

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With the increasing use of Internet and electronic facilities together with the globalization of all areas of life including medicine and science, also medical journals are affected by an increasing 'flood' of clinical and scientific material to be published (1). In particular, young researchers are placed under constant pressure to publish their work to increase their rating and receive funding (2). So; The past few years have witnessed an emergence of predatory publishers. However, as the majority of these journals do not conduct proper peer review processes or offer customer service, these journals have been named 'predatory journals' by Jeffrey Beall – a librarian at the University of Colorado.

In 2010, the number of papers published in predatory journals reached 53,000, however, by 2014, 420.000 were estimated to have been published. By the end of 2016, the number of predatory journals listed on the Beall's list had reached approximateyl 10,000, approaching in number the journals found on the Journal Citation Reports and Directory of Open Access Journals (3).

In 2016, researchers Stefan Eriksson and Gert Helgesson identified 25 signs of predatory publishing (4);

- The publisher is not a member of any recognized professional organisation committed to best publishing practices (like COPE or EASE)
- The journal is not indexed in well-established electronic databases (like MEDLINE or Web of Science)
- The publisher claims to be a "leading publisher" even though it just got started
- The journal and the publisher are unfamiliar to you and all your colleagues
- The papers of the journal are of poor research quality, and may not be academic at all (for instance allowing for obvious pseudo-science)
- There are fundamental errors in the titles and abstracts, or frequent and repeated typographical or factual errors throughout the published papers
- The journal website is not professional
- The journal website does not present an editorial board or gives insufficient detail on names and affiliations
- The journal website does not reveal the journal's editorial office location or uses an incorrect address
- The publishing schedule is not clearly stated
- The journal title claims a national affiliation that does not match its location (such as "American Journal of ..." while being located on another continent) or includes "International" in its title while having a single-country editorial board
- The journal mimics another journal title or the website of said journal
- The journal provides an impact factor in spite of the fact that the journal is new (which means that the impact cannot yet be calculated)
- The journal claims an unrealistically high impact based on spurious alternative impact factors (such as 7 for a bioethics journal, which is far beyond the top notation)
- The journal website posts non-related or non-academic advertisements
- The publisher of the journal has released an overwhelmingly large suite of new journals at one occasion or during a very short period of time
- The editor in chief of the journal is editor in chief also for other journals with widely different focus

- The journal includes articles (very far) outside its stated scope
- The journal sends you an unsolicited invitation to submit an article for publication, while making it blatantly clear that the editor has absolutely no idea about your field of expertise
- Emails from the journal editor are written in poor language, include exaggerated flattering (everyone is a leading profile in the field), and make contradictory claims (such as "You have to respond within 48 h" while later on saying "You may submit your manuscript whenever you find convenient")
- The journal charges a submission or handling fee, instead of a publication fee (which means that you have to pay even if the paper is not accepted for publication)
- The types of submission/publication fees and what they amount to are not clearly stated on the journal's website
- The journal gives unrealistic promises regarding the speed of the peer review process (hinting that the journal›s peer review process is minimal or non-existent)—or boasts an equally unrealistic track-record
- The journal does not describe copyright agreements clearly or demands the copyright of the paper while claiming to be an open access journal
- The journal displays no strategies for how to handle misconduct, conflicts of interest, or secure the archiving of articles when no longer in operation

What about predatory journals in Dermatology?

1058 publishers as of July 2016, 76 journals were identified in dermatology, cutaneous surgery and venereology. Due to the poor quality of the majority of the publishing websites, several were unsearchable, no longer existed, or were not in the English language. For these reasons, this is not a complete and comprehensive list of predatory journals in dermatology and it is probable that there are more (5) (Table 1. List of predatory journals in Dermatology).

What about predatory conferences in Dermatology?

The big challenge is how to identify a predatory conference. A few points are worth considering: the organizer holds low-quality academic meetings with the primary aim of making money and not supporting scholarships; there is no effective peer review, allowing anyone to purchase a speaking slot; and the organizer employs deceit, the most common forms being false claims of peer review, hiding the true location of the company headquarters, and concealing the for-profit nature of the company (6).

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MYTHS AND FACTS IN DERMATOLOGY

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In the clinical practice of dermatology, we hear similar questions from our patients and observe that they have similar beliefs about some diseases. Are there any truth to these beliefs according to the literature?

(**Q**: Question, **A**: Answer)

Q1: Are acne related to nutrition?

A1: Nutrition was believed to cause or worsen acne. But it has become a dermatological doctrine that there is no direct association between diet and acne. > 3 portions of milk consumption per week, excessive intake of dairy products and hyperglycaemic food were found to be associated with acne. Dairy products are increasing plasma insulin-like growth factor (IGF)-1 levels. Cow's milk is available at different fat levels: skimmed milk was associated with higher plasma IGF-1 levels. IGF-1 stimulates the synthesis of androgens in both ovarian and testicular tissues and inhibits hepatic synthesis of sex hormone-binding globulin resulting in increased bioavailability of androgens. Skimmed milk also contains less oestrogen, which is known to reduce acne. Chronic and acute hyperinsulinemia activates a hormonal cascade that favours unregulated tissue growth by simultaneously elevating the free (IGF-1) level and reducing levels of insulin-like growth factor binding protein 3 (IGFBP-3). A low-glycaemic-load diet improved acne severity and insulin sensitivity. IGF-1 have been shown activating the PI3K and Akt pathway which plays a key role in the sebaceous lipogenesis. Although there are studies showing that alcohol, tea, coffee and salty foods also increase acne, the level of evidence is low or there are conflicting results.

Patients should be questioned during their first visit about their daily food habits, lifestyle or eating disorders. Should nutrition be an issue, then patients may be advised to change their food habits or, if necessary, seek the help of a nutritionist in addition to a pharmacological treatment of their acne, according to the severity of the condition and current treatment guidelines.

Q2: Is it necessary to pay attention to food for urticaria?

A2: In acute urticaria, a relationship with food can be detected in children. Frequently, a relationship is found with milk, egg, soy, tree nuts, soy and wheat. Although the nutritional relationship is lower in adults, a relationship can be detected with fish, shellfish, tree nuts and peanuts. Food is a very rare etiology in chronic urticaria. In one study, a response to pseudoallergenic diet was observed in 28% of chronic urticaria patients. Pseudo-allergen diet is not recommended routinely, but can be recommended if the person has a very strong relationship with food.

Q3: Patients with chronic pruritus, urticaria want to have an allergy test?

A3: Prick test and patch test are allergy tests in dermatology and their indications are limited. Atopic dermatitis, total IgE height, acute urticaria, contact urticaria are indications for prick testing. Atopic dermatitis, mainly allergic contact dermatitis, and some drug eruptions may be indications for patch testing. Although prick test positivity can be detected with food in patients with atopy in patients with chronic urticaria, the relationship between food and urticaria induction cannot be established frequently.

Q4: Does laser hair removal cause skin cancer?

A4: Laser is a technology that uses non-ionizing radiation as a concentrated light source, and the UV wavelengths used are different from sunlight. Although there are no long-term risk studies yet, changes have been observed in melanocytic nevi; however, malignant transformation has not yet been reported.

Q5: If a razor is used in epilation, will darker and black hairs grow?

A5: In epilation, it removes unwanted hair at the level of the skin surface, the trapezoid edge of the cut hair is felt harder on the skin surface. Hair base is thicker than distal. As the bristles grow, their colors lighten with sunlight, chemical exposure, and may appear darker when first starting to grow.

Q6: Does performing biopsy from skin cancer increase the risk of metastasis?

A6: In lesions with suspicious melanoma, an excisional biopsy that extends to subdermal adipose tissue with 1-2 mm margin should be performed, if possible; However, punch biopsy may be recommended in large lesions and in cases where the diagnosis is doubtful. Tumor seeding phenomenon: shown in breast, gastrointestinal, thyroid, hepatic, urological cancers. However, it has not been detected in skin malignancies.

Q7: Isn't Lidocaine + epinephrine used in the anesthesia of the end regions?

A7: There are cases reported in the literature about hypoxia and necrosis in the distal regions due to the vasoconstrictor effect of epinephrine; however, there are no reported cases of necrosis in standard dosage and technique. Although careful use is recommended in patients with vascular insufficiency, elderly, cardiac disease and using b-blockers, standard lidechoin + epinephrine is safe in infiltrative and block anesthesia, provides better pain control, less pain and tourniquet use and less total anesthesia need.

Q8: Does systemic isotretionine cause infertility?

A8: In terms of female patients, although there are studies showing that the results have a significant negative effect on the contradictory ovarian reserve, there are also studies that do not see a significant effect. However, it has been shown that female hormone levels may be low. In terms of male patients, although there was no significant change in the hormonal profile, positive changes were found in the spermiogram after treatment.

Q9: Should we wait 6 months for systemic isotretinoin ablative procedures?

A9: It has been reported that systemic isotretinoin suppresses collagenase and triggers keloid formation with increased angiogenesis. There is not enough scientific data to support that systemic retinoids impair wound healing or cause atypical scar formation. A safe time margin is set due to medicolegal problems.

Q10: Is there no cure for psoriasis?

A10: With the understanding of the etiopathogenesis of psoriasis at the molecular level, it is now much easier to reach PASI90 levels with the use of new biological agents. Patients now think that it is a treatable disease and they apply to our clinics with this desire. However, a cure without treatment seems not possible yet.

Q11: Does regular sunscreen use cause vitamin D deficiency?

A11: 90% of the daily vitamin D requirement is produced on the skin through UVB. In experimental studies, severe low vitamin D was found with the proper and continuous use of sunscreen; however, it should be keep in mind that patients do not use it"ideal and optimized" in daily practice. There is no scientifically proven safe dose and duration of UVB to synthesize vitamin D without increasing the risk of skin cancer. It makes sense to avoid the sun and to supplement your vitamin D orally. It is important to recommend simultaneously routine vitamin D supplements in patients with diseases such as skin malignancy, lupus, rosasea, for which we recommend absolute and continuous sun protection.

Q12: Does verruca vulgaris heal with pray?

A12: Verruca vulgaris regress spontaneously, especially in children. Therefore, it is difficult to understand what is the main reason for success in treatment. Destructive methods are frequently used in treatment. The immune system plays an important role in the treatment of the disease. Suggestion, prayer, etc. methods can also affect the immune system with the effect of psychotherapy. in a placebo-controlled study, there were no significant differences between the plasebo group and the group which be prayed in terms of healing.

Q13: Can pruritus be caused by liver pathologies?

A13: Pruritus originates from the liver only in the case of cholestasis. Cholestatic pruritus, which occurs due to the impaired secretion of bile, is a common symptom in certain forms of liver disease. It is typically generalized and often begins on palmoplantar regions that are uncommon sites for pruritus in other systemic diseases. Intrahepatic cholestasis of pregnancy, sclerosing cholangitis, viral hepatitis, drug-induced cholestasis, as well as cases of obstructive jaundice are cholestatic diseases. Patients with cholestatic pruritus have elevated plasma opioid levels, which may contribute to itch.

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PIONEERS IN DERMATOLOGY

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Because skin is visible with eyes and skin diseases are very common, the history of Dermatology lies beyond on deep history. Even, it is very hard to consider initial cornerstones through ancient scripts.[1] In one way or another, according to reliable documents, the very first known written sources of Dermatology belongs to Egypt, The Ebers and Smith Papyri. Is it surprising? Little bit because roots of European and modern medicine mostly depend on ancient Greek and Roman sources. However, in the field of Dermatology, Egyptians initially described many conditions and treatments according to these scripts such as inflammatory reactions, tumors, epidermal cysts and its treatment, ulcers, burns, several rashes, hair disorders, topical treatments, wound repairing and dressing, cauterization and anti-sepsis. Also, cosmetics, anti-aging applications and daily skin care was existed in Ebers Papirus. These scripts also demonstrated patient evaluation depending on history and examination and prediction of prognosis. All of these and of course many more inventions and definitions were upgraded by Greek physicians.[2]

Hinduism had also too many inflictions on Dermatology, and for some, they were the most successful in medicine in antique era. They invented many treatments several of which are still being used such as treatment of pediculosis with mixture of sulfur and mercury. Also, they were the first who described elephantiasis and acne.[3]

Like in many fields of medicine Greeks, and of course Hippocrates, had many contributions to Dermatology. Hippocrates, the father of medicine, was the first who split the human health from religious and philosophic dogmas. He defined many skin conditions which are under use even today. For example, herpes, ecthyma, erysipelas were just several of these. Furthermore, although defined as different names; psoriasis, filiform warts, chilblains, carbuncles were first described by him. Term of “pityriasis”, “sycosis”, “psora”, “erythema” and “exanthema” were also first used by him.[3]

In Roman era, maybe the most important physician, at least whom works remained until today, Celsus described many Dermatologic conditions. He treated erysipelas and defined carbuncle and furunculus. He defined impetigo and maybe firstly reported lichen planus. Another important Roman physician Paulus Aeginata who lived seven centuries after Celsus reviewed and invented many Dermatologic treatments and firstly reported alopecia areata patients.[3]

One of the most important steps in Dermatology was getting in order of these scattered knowledge from antique and medieval era, and of course criticization of these. Robert Willan (1757-1812), an English physician, reviewed and ordered all of these knowledges in such a clear way. He designed taxonomy and reviewed different terms that had been used for skin disease including impetigo, lupus, psoriasis, scleroderma, ichtiyosis, sycosis and pemphigus.[3] He classified diseases according to physical signs such as papules, scales, exanthems and bullae.[1] Many regarded him as founder of Dermatology as a specialty. He also described erythema infectiosum and he is the first physician to use word of “lupus” to describe skin lesions of tuberculosis.[3] He also reviewed sources from Arabic medicine and assembled with Greek and Romans. Even not the first, his textbook was the most important one which impressed many physicians in that era. Even Hebra, one of the most important pioneers of Dermatology, appreciated his publishments 50 years later.[3] Thomas Bateman was another British Dermatologist who clearly defined Molloscum contagiosum, Purpura Senilis, Alopecia Areata and Herpes Iris with their exact names.[3]

At the same time with Willan, Jean-Louis-Marc Alibert of France (1766-1837) independently founded school of Dermatology at the St. Louis hospital in Paris. He categorized skin disorders through macroscopic view initially and subsequently in more detailed manner which he called “the tree of dermatoses”. Also, he was the first who defined Keloids, Mycosis Fungoides patients and gave the disease its name. Laurent-Theodore Biett (1781-1840), who studied with Willan, Alibert and Bateman, expanded works of Willan and Alibert. Although mostly regarded as the real establisher of St. Louis school and most of his career was hold there, he preferred classification of Willan rather than Alibert. He defined the term “Lupus Erythematoides”.[3] Another French pioneer Pierre François Rayer (1793-1867) distinguished true eczema, clearly described exfoliative cheilitis, firstly reported the case with adenoma sebaceum and studied about glanders.[3,4] Marie-Guillaume-Alphonse Devergie (1798-1879), founder of the most famous Dermatology museum in

St. Louis hospital, described eczema marginatum and pityriasis rubra pilaris. Antoine Pierre Ernst Bazin (1807-1878), best known for describing of erythema induratum, studied about ringworm, defined acne varioliformis, acne keloid and hydroa vacciniforme.[3]

Sir Erasmus Wilson (1809-1884) was the one most important pioneer of Dermatology. According to several resources daily bath became common habit after him. Also, he tried to establish Turkish bath in Britain. He described lichen planus, exfoliative dermatitis, erythema nodosum, trichorexis nodosa under the name of trichodasis and punctate bleeding of psoriasis lesions after scraping the surface which was going to be named Auspitz sign later.[3]

Joseph Jacob Plenck (1738-1807) described treatment of syphilis with mercury. He categorized 150 types of skin diseases into 14 groups according to the physical properties of lesions, causes and involvement area.[5] Ferdinand Ritter von Hebra (1816-1880) founder of Vienna School of Dermatology and author of one of the most important atlas of skin disease. He made classification based on pathological anatomy but, however it was criticized at that era. He defined erythema multiforme, impetigo herpetiformis, rhinoscleroma, lichen scrofulosorum. He founded the cause of scabies and was the first who invented skin resurfacing with chemical peel.[3] Mortiz Kaposi (1807-1902) was a student of Hebra. He continued Hebra's teachings and defined eczema herpeticum, pigmented sarcoma, diabetic dermatitis and lymphoderma pernisciosa.[1,3]

Tilbury Fox (1836-1879) wrote the best textbook of its time. He described kerion, lymphangioma and first case of epidermolysis bullosa.[3]

Otto Schrön (1837-1917), such a highly talented a histologist and drawer in scientific manner, firstly discovered desmosomes, tonofilament system and observed cell to cell connections. He also took very important part in studies under his mentor, Carl Thiersch, to discover epithelial origin of cancer and demonstrate, although under different names, squamous cell carcinoma and basal cell carcinoma.[6]

Paul Gerson Unna (1850-1929) had many contributions in Dermatology literature other than Unna boot and Thost-Unna palmoplantar keratoderma. He reviewed the knowledge about anatomy and physiology of epidermis. He was the first who correctly demonstrated structure and functions of epidermal layers in his book. He also defined plasma, foam and balloon cells.[6,7]

Josef Jadassohn (1863-1936) was the one of the important pioneers of Dermatopathology. He re-classified skin diseases according to etiology. He was the inventor patch test which is still being used today. He defined many diseases correctly such as nevus sebaceous, pityriasis lichenoides chronica, granulosis rubra nasi, incontinentia pigmenti, blue nevi, pachyonychia congenita. He also described borst-jadassohn phenomenon.[8]

Helen Ollendorff Curth (1899-1982) was the one of the rare women physicians in her era. She was the one of the leading authors in genodermatoses. With Macklin she described ichtiyosis hystrix which is called ichtiyosis Curth-Macklin today. She also described dermatofibrosis lenticularis disseminata with Buschke. Today patients with multiple connective tissue nevi, osteopoikilosis and sclerotic bone disorder in addition to that lesions is called Buschke-Ollendorff syndrome. She also very clearly demonstrated the association of acanthosis nigricans with malignancies.[9]

Stephen Rothman (1894-1963), Hungarian pioneer of investigative Dermatology. He influenced new and molecular sights in Dermatology. He published the "Physiology and Biochemistry of the Skin" in 1954, the first textbook which reviewed biochemistry and physiology of the skin. The book impressed and inspired many physicians in that times. With Julius M. Coon, they discovered cholinergic innervations of vessels and eccrine sweat glands. They also identified pilomotor response and neurophysiology of flushing. He firstly demonstrated molecular effects of UVR on melanogenesis, suggested para-amino benzoic acid as sunscreen, observed tendency of melanin to bind metal ions, recognized trans-epidermal water loss and association of its with altered cornification, observed cross reaction between substances that cause allergic contact dermatitis, skin hardening treatment with UV radiation in solar urticaria. He also investigated skin surface lipids with Konrad Bloch. The disappearance of tinea capitis that caused by *Microsporodium Audouinii* after puberty by increasing levels of free fatty acids in scalp sebum was recognized and explained by him. His works about skin surface lipids leaded to great insights in skin barrier, antimicrobial defense, regulation of innate immunity. He also demonstrated that testosterone could induce sebaceous gland hyperplasia. He was also a great teacher. Many

of students also became one the pioneers of Dermatology too. He was widely considered as the father of investigative Dermatology.[10]

Of course, many more important Dermatologists and pioneers existed in history of Dermatology. Even several of them are still active physicians, academicians and scientists.

In conclusion, one can foresee that history of Dermatology passed through three main paths. First the ancient era including mostly Egyptians, then Greeks, Romans and Arabs and finally, mostly by efforts of Sir Willan, the modern era.[3] In all that path, too many pioneers have passed and of course, many new leading physicians, authors and scientists will come. Today our knowledge totally depends on their analyzed, written and published masterful observations, efforts in clarification of problems in nomenclature and treatments and of course, reviews and classifications that were created through their visions.

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FINANCIAL TOXICITY IN DERMATOLOGY

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The term "financial toxicity" describes problems a patient experiences related to the cost of medical care. This challenge, which was first defined for cancer patients, is mainly a result of out-of-pocket costs and indirect costs for diagnosis and treatment, as well as the intangible costs. The financial distress of medical care can significantly affect quality of life and treatment compliance.

Exposure to financial toxicity for which there are quite limited studies regarding dermatological diseases, varies widely depending on the country and health system, the type and severity of the disease. For instance, out-of-pocket expenses for eczema include all healthcare costs, even moisturizers and topical steroids for uninsured patients from the US, in Europe extra costs of everyday products such as clothing, washing etc. are included for patients with a healthcare insurance. In skin cancers, as more expensive drugs and more intensive treatment processes are involved, the financial burden becomes greater. Most dermatological diseases have a chronic course and long-term treatments, often comprise of several procedures, produce lifelong and higher costs. New techniques such as laser therapy, which can now be used for previously untreatable conditions, and expensive but highly effective 'biologics' have been used for many dermatological diseases in recent years. Increase in drug prices, use of new techniques and new drugs expand the amount of payment by patients for many diseases. On the other hand, while objective financial distress varies by country, subjective financial distress may be equally high for all patients.

Skin diseases are extremely common and with studies investigating the actual size of financial toxicity in dermatology in Turkey and worldwide, to which extent the prescribed treatments can be reached by the patients and the sustainability of these treatments will come to light.

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DERMOSCOPY IN NON-MELANOMA SKIN CANCERS: WHAT'S NEW?

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Nonmelanoma skin cancer (NMSC) is the most common skin cancer affecting both sexes. It includes mostly basal cell carcinoma (BCC), actinic keratosis (AK), keratoacanthoma (KA), Bowen's disease (BD) and squamous cell carcinoma (SCC). And also vascular malignancies such as Kaposi Sarcoma (KS) and angiosarcoma are included in NMSCs. In most NMSC tumors, diagnosis is easy with morphologic appearance; however, it is sometimes difficult to differentiate the pigmented-nonpigmented skin lesions. With naked eye, only half-of-pigmented lesions are correctly diagnosed; dermoscopy increases the diagnostic sensitivity to 95%.

BCC is the most common of all cutaneous malignancy. It is locally invasive and often grows slowly. Up-to date, dermoscopy has been shown to increase BCC diagnosis by enhancing the differentiation from other skin tumors and inflammatory skin diseases. Classical dermoscopy algorithm for the diagnosis of BCC, especially for the pigmented variant, includes the absence of pigmented network and the presence of at least one of the following criteria: multiple blue/gray ovoid nests, spoke-wheel structures, arborizing vessels and ulceration. However, BCC may reveal a large variety of dermoscopic features. These non-classical features include some additional criteria more frequently seen in superficial BCC or Fibroepithelioma of Pinkus such as short-fine superficial telangiectasia, concentric structures, multiple small erosions, multiple in focus blue/gray dots, shiny white-red structureless areas.

AK has been characterized as"precancerous" or "premalignant" because the atypical keratinocytes within these lesions are confined to the epidermis. Dermoscopically, facial AKs commonly reveal a red pseudonetwork pattern and white keratotic hair follicle openings, the "strawberry pattern", white/yellow surface scales, linear or wavy vessels surrounding the hair follicles, and yellowish keratotic plugs. The strawberry pattern consists of an erythema forming a marked pink to-red "pseudonetwork" around the hair follicles. Some special AK subtypes may reveal different patterns. For example, Bowenoid AK is typified by glomerular vessels, which are regularly distributed and not arranged in clusters, as seen in classic BD. Hyperkeratotic AK frequently shows surface scale and erythema. Pigmented AK is often characterized by lack of associated erythema and has a hyperpigmented or reticulated appearance.

BD is a malignant intraepithelial tumor that affects older adults, especially women. Typically, it presents as a slowly enlarging, flat, pink, scaly patch or plaque on lower extremities, face, and intertriginous areas. Dermoscopy of BD shows a peculiar pattern characterized by glomerular vessels and a scaly surface. In addition to these clues, pigmented BD may exhibit irregular pigment globules in a patchy distribution, gray-brown homogeneous pigmentation, and pseudonetwork.

SCC presents with various clinical appearances. Clinical lesions of SCC in situ range from ill-defined, rough, pink patches similar to AK, to sharply demarcated verrucous papules or plaques. The typical SCC is a skin-colored papule-nodule-plaque localized on sun-damaged skin. It may be hyperkeratotic with central necrosis or bleeding. The biologic behavior differs by location, size, depth, and grade of histologic differentiation. There are significant differences in the dermoscopic patterns of AK, intraepidermal carcinoma, and invasive SCC and these differences may assist in their clinical diagnosis and subsequent management. Progression of AK into intraepidermal carcinoma and invasive SCC can be observed on dermatoscopic examination. Initially, AK shows a red pseudonetwork: ''strawberry pattern.'' The first step of progressing toward intraepidermal carcinoma ischaracterized by progressive development of redstarburst pattern and yellow-white opaque scales.Initially, scales are discrete; however, with further progression to intraepidermal carcinoma, they become thicker and coalesce to be located in a predominantly central position. Also, increased neovascularization, the development of clustered dotted/glomerular vessels, can be seen. Further steps toward invasive SCC are characterized by progressive development of elongated vessels, keratinization, and ulceration.

Dermoscopic features of KS are homogenous with the color ranging from reddish to bluish, pinkish, whitish, or violaceous. Rainbow-like pattern that characterized by the presence of multicolored areas, compared with the rainbow spectrum, is the most striking dermoscopic feature of KS. It can be seen with polarized dermoscopy, and can be also seen in other skin tumors. The other findings in KS are scaly surface, small brown globules, white colarette, rosette sign, and

vascular structures such as coiled, dotted and curved vessels.

In this presentation, a summary of the dermoscopic features of NMSCs and also the value of dermoscopy for diagnosis and management of NMSCs will be discussed.

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BLACK, RED AND GREEN: SIASCOPY

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SIAscopy (Spectrophotometric Intracutaneous Analysis Scope) is one of the Multispectral digital dermoscopic examination methods that, used for analytical examination of skin lesions. It is a newly developed modern diagnostic tool that is non-invasive just like dermoscopy and other multispectral procedures. In a multispectral examination, lights of different colors and wavelengths are applied to the skin surface. Then, the parts of these lights emitted and reflected on the skin are processed and recorded on a computer base by an analytical software [1,2]. Three different devices capable of multispectral examination have been approved recently. Of these, Melafind, SolarScan provides computer-aided fully automatic diagnostics. The images obtained with the SIAscope require the interpretation of the physicians according to various algorithms in order to increase the diagnostic accuracy as well as the computer-aided analysis. (Figure 1).

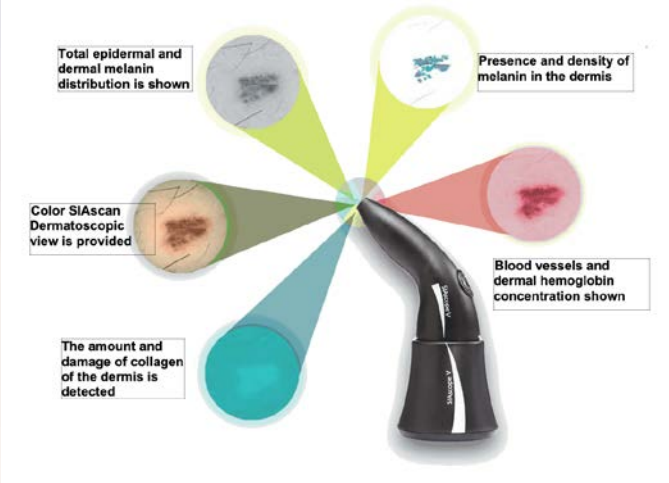

Figure 1: Five different siascans of SIAscopy

Figure 2. Contact SIAskop V

In a Siascopic examination, light from 5 different spectra between 400 and 1000 nm is shined into the skin lesions. These are white, blue, green, red and infrared glows. Siascan images are obtained by analyzing the part of the light reflected or scattered from the epidermal and dermal region spectroscopically. Hence, the Siascope is composed of a combination of contact remittance spectrophotometer with a dermatoscope and hyperspectral imaging [5] (Figure 2). As a result, four different images are taken in addition to a dermoscopic view with SIAscopic examinations. These images contain some valuable data on structural chromophores from the skin surface (papillary dermis) to a depth of 2-2.5 mm.

These data include the concentration of melanin, hemoglobin, dermal collagen, and hemoglobin of blood vessels belonging to epidermal and dermal structures. Thus, qualitative and quantitative digital data on the distribution and placement of these pigments are obtained. These data are processed with a digital colorimetric analysis technique and transformed into images used in the diagnosis of pigmented skin lesions [2,3]. The five images obtained consist of a color dermoscopic image, as well as total melanin, dermal melanin, blood and collagen images [4].

Dermatoscopes, which are widely used in the diagnosis of skin lesions, can be useful when used by physicians with long-term training and experience in this field. Therefore, it can only be used by dermatologists. The SIAscope device is also primarily designed for use in primary health care for patients with pigmented skin lesions. Naturally, it has primarily been used in melanoma screening in primary health care to increase diagnostic accuracy, reduce unnecessary patient referrals and invasive diagnostic procedures. A computerized scoring algorithm "PCSA", which is integrated with the scanner, has been developed to increase diagnostic accuracy. In addition, optional 7-point and 3-point scoring software has been added to the structure to be used for the same purpose.

It is much easier to learn the characteristics determined for skin lesions in siascopy and to use the device in siascopic examination. Long-term experience and various agorithms are not required. Two hours is enough for its training. The color image taken with the SIAscope is evaluated just like the dermotoscopic image. Histological maps and suggestions provided with the red, blue, green and infrared light spectrum are always more useful.

Some symptoms such as dermal melanin, erythematous appearance, prominence of blood vessels and the presence of collagen holes are very characteristic in a siascopic examination to be used in the diagnosis of pigmented lesions, especially melanoma.

In studies performed, its sensitivity in the diagnosis of melanoma has been reported to vary between 79-94% and specificity ranging from 80.1-84% [6,7] (Table I).

Table I: Melanoma Research via Siascope.

Author	Year	Lesion	Melanoma	Sensitivity	Spesivity	Journal / meeting
Moncrieff	2001	348	52	80.1	82.7	Br J Dermatol 2002, 146(3):448-457
Tomatis	2004	1391	184	80.4	75.6	Physics Med Biol 2005, 50(8):1675-1687
Carrara	2006	1966	287	88.0	80.0	Physics Med Biol 2007, 52(9):2599-2613
Hunter	2006	679	40	**94-100**	69.0	Br J Dermatol 2007, 156(6):1350-1352
Govindan	2007	886	54	94.4	64.0	J Plast Recon Aest Surg 2007, 60(6):639-45
Haniffa	2007	881	31	87.0	**91.0**	Br J Dermatol 2007, 156(6):1350-1352
Glud	2009	83	12	**100.0**	59.0	Melanoma Res 2009, 19(3):176-179
Terstappen	2013	60	42	24.0	84.0	J Biomed Optics 2013, 18(6):061223
Total	**-**	**6294**	**702**	**85**	**81**	-

Moreover, it has been found useful in the diagnosis of non-melanoma skin cancers [8] (Table II). However, there are studies that find siascopy less sensitive and specific than dermoscopic examinations. However, all of these were carried out in advanced research institutions where physicians who have mastered dermoscopy work and where histopathological examination facilities can also be made.

Table II: Non-melanoma cancer research via siascopy.

Author	Year	Patients	Lesion	Sensitivity	Specivity	Research Department	Journal or Meeting
Tehrani	2013	250	250	-	-	PRC	Annals of Plastic Surgery 2013
Tehrani	2006	302	363	98.0	95.7	PRC	Br J Dermatol 2006,
Tehrani	2007	-	323	97.5	86.7	PRC	Ann Plast Surg 2007
Emiroğlu	2018	72	33	93.9	53.8	Dermatology	AAD Annual Meeting, 2018
Hacioglu	2013	76	80	55- 93	88-53	Dermatology	Clin Exp Dermatol 2013

On the other hand, siascopy is used in various skin diseases and cosmetic problems as well as pigmentation disorder and malignancy, although it is rare. These; issues such as photoaging, psoriasis, keloid, wound healing, burns, rosacea, planer warts [9,10]

Considering the present value and condition of the siascopy; "Although it provides a color image equivalent to dermoscopy, it has remained in the shadow of dermoscopy" and it is possible to say that it has not yet found its rightful place in dermatological practice. This is probably because the technique is new, the technology is different, the devices are expensive, the optical principles are complex, and it is difficult for the dermatologist to understand.

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DERMOSCOPY: WIDEN YOUR HORIZON!

M. Cüneyt Soyal

In recent years, Artificial intelligence (AI) has been widely used in various fields of medicine, as well as in Dermatology. Most of the clinical studies on AI use in Dermatology are particularly focused on the diagnosis of skin cancers. Recent reports have also pointed out that AI has surpassed dermatologists in skin cancer detection. This presentation aims to present an overview of AI basics and results of AI applications in classification and diagnosis of skin cancers, especially melanoma.

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DERMOSCOPY IN INFECTIOUS SKIN DISEASES

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Dermoscopy born to be an instrument for early diagnosis of skin cancer, however today, it can be routinely used to support diagnosis in general dermatology such as cutaneous inflammatory and infectious diseases. In this paper, dermoscopic features of cutaneous infectious diseases will be told.

The first description of dermoscopic findings among cutaneous infectious diseases has been scabies.[1] Then, many dermoscopic findings of various cutaneous infectious diseases have been published. Before dermoscopy, diagnosis of scabies is made by direct observation of mite, feces and eggs after skin scraping. But the sensitivity of the the test is low and depends on the personal experience. Delta-wing jet with contrail sign has been defined for scabies. It indicates the irregular burrow excavated by the mite. The mite's anterior part of body is visible at dermoscopy as a small black arrowhead area at the end of the whitish wavy line. This finding is considered pathognomonic for scabies.[1] Currently a novel dermoscopic sign namely the noodle sign was described in crusted scabies. The sign represents an accumulation of hundreds of burrows in the same dermoscopic field.[2] Human papillomavirus infections are very common in human. It has very different clinical variants and dermoscopic findings. The most important feature is dotted vessels and/or hemorrhagic points. It can often found in different kinds of warts. Common warts are the most common type of warts. It's dermoscopy demonsrate grouped papillae with dotted or loop vessels and/or hemorrhagic points and lines often surrounded by a whitish halo, it is likened to a ''frogspawn appearance''.[3,4] Dermoscopy of filiform warts demonstrate the same features as cpmmon warts with more prevalent papillae. Small dotted vessels on a yellowish background may be seen in dermoscopy of flat warts. Plantar warts show at dermoscopy as small dotted hemorrhagic structures corresponding to thrombosed vessels, visible in the context of whitish or yellowish paillae which interrupt cutaneous dermatoglyphics. Genital warts show at dermoscopy grouped dotted or glomerular vessels at center surrounded by a whitish network. The finding is the so-called mosaic pattern. Dermoscopy of pigmented genital warts demontrate a cerebriform or seborrheic keratosis-like appearance.[3,4] Molloscum contagiosum is a very frequent infection in human. It shows usually at dermoscopy as the presence of a central pore on a white-yellowish amorphous area, often surrounded by thin crown vessels.[4] Only central amorphous area may be observed without central pore and vessels may have different patterns radial or dotted except crown. On the other hand, vessels sometimes may be not visible.[5] Dermoscopy has an important role of diagnosis of dermatophytosis especially tinea capitis. Tinea capitis is a frequent dermatophytosis of the scalp of especially children. The exact diagnosis is made by potassium hydroxide examination and microbiological culture but dermoscopy plays an important role in differential diagnosis with causes of hair loss such as alopecia areata and tricchotillomania.[3] Tinea capitis may show at dermoscopy comma hair, zig-zag hair, corkscrew hair, Morse code-like or barcode hairs, black dots, dystrophic hairs and hair casts.[6-8] The most common dermoscopic finding is comma hair. It is a shortened, curved hair resulting from the fungal inasion of the shaft.[6] Pediculosis capitis is a common infestation in world. It's diagnosis is usually easy. The detection of lice is diffucult in dermoscopic examination. But nits are easily seen through dermatoscope as ovoid structures anchored to the hair shaft. Pthirus pubis is predominantly a sexually transmitted disease among adults. Dermoscopy confirms diagnosis of pthirus pubis by direct detection of the Pthirus. Pthirus adherent to pubic hairs and blood feding. Nits can be detected to.[3,4] Cutaneous leishmaniasis is a protozoan infection, affects people by the vectors sandflies. Dermoscopic examination often shows that generalized erythema and yellowish White round-to-oval structures. The latter is named as yellow tears. Moreover hyperkeratosis, central erosion, ulceration, white starburst-like pattern and various vascular structures may be observed.[9,10] Dermoscopy has been suggested in diagnosis of pseudomonas onychopaty, trichomycosis axillaris and common form of folliculitis too.[3]

Dermoscopy is not a definitive diagnostic method of most cutaneous infectious diseases such as potassium hydroxide examination, culture and histology. However it is low cost, practical and easy diagnostic method. Consequently, it should be commonly used in differential diagnosis of cutaneous infectious diseases by dermatologists.

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SYNDROMES ASSOCIATED WITH HAIR AND NAIL PROBLEMS

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Hair loss can represent a broad differential diagnosis. Especially hair loss in children and hair shaft disorders can further be a therapeutic challenge as it might be an isolated phenomenon or a sign of genetic multisystemic syndromes. Similar to hair disorders, nail diseases and abnormalities are often with systemic diseases and syndromes.

Thus, physicians should carefully evaluate personal and family history, and examine the hair on the scalp and on all body areas, also all nails and other ectodermal structures to establish the correct diagnosis. In this oral presentation the main syndromes associated with hair and nail problems are summarized. I will further discuss the most common clinical features of hair and nail abnormalities and known associated genetic abnormalities with these abnormalities.

Hair shaft disorders with increased fragility	**Hair shaft disorders without increased fragility**
Acquired	**Acquired**
Bubbled hair Acquired Trichorrhexis nodosa	Acquired progressive uncombable hair
Congenital	**Congenital**
Trichorrhexis nodosa Monilethrix Trichorrhexis invaginata Pili torti Trichoschisis	Pilli annulati Pseudopili annulati Woolly hair Uncombable hair syndrome (Pili annulati et canalikuli) Loose anagen hair syndrome Pili bifurcati Pili multigemini

Hair shaft disorders and associated syndromes	
Monilethrix	Ectodermal dysplasia syndrome
Trichorrhexis nodosa	Argininosuccinicaciduria Citrullinemia
Trichoschisis	Trichothiodystrophy
Trichorrhexis invaginata	Netherton syndrome
Pili torti	Bjornstad syndrome Crandall syndrome Menkes syndrome Ectodermal dysplasia syndromes *Other syndromes;* Familial acne conglobata Rapp-Hodgkin syndrome/ankyloblepharon-ectodermal dysplasia-clefting syndrome Salti-Salem syndrome Monilethrix Pseudomonilethrix Woolly hair Mitochondrial disorders Netherton syndrome Bazex syndrome Beare syndrome Condradi-Hünermann syndrome Longitudinal grooves Trichorrhexis nodosa Trichorrhexis invaginata Citrullinemia Laron syndrome
Woolly hair	Hereditary dominant woolly hair Familial recessive woolly hair Woolly hair syndromes with cardiac abnormalities; Naxos disease Carvajal syndrome Naxos-like disease Woolly hair syndromes without cardiac abnormalities; Woolly hair and skin fragility syndrome Diffuse partial woolly hair Woolly hair nevus
Curly hair	Tricho-dento-osseous (TDO) syndrome CHAND syndrome Costello syndrome Noonan syndrome Lipoatrophic diabetes
Miscellaneous	Marie Unna hypotrichosis Uncombable hair syndrome Loose anagen syndrome Pili annulati Mitochondrial disorders

Nail disorders and associated syndromes	
Hereditary Disorders with Secondary Nail Changes	Darier–White disease Lesh–Nyhan syndrome Neurofibromatosis type 1 (Recklinghausen) Pityriasis rubra pilaris Tuberous sclerosis
Dystrophic nails	Ectodermal dysplasia/skin fragility syndrome Hidrotic ED, Clouston syndrome Hypohidrotic ectodermal dysplasia (Christ–Siemens– Touraine syndrome) Focal dermal hypoplasia/Goltz–Gorlin syndrome Epidermolysis Bullosa Incontinentia Pigmenti Pachyonychia congenita Naegeli–Franceschetti–Jadassohn syndrome Dyskeratosis congenita Naxos disease CHANDS syndrome Conradi–Hünermann–Happle Schopf–Schulz–Passarge syndrome KID syndrome Meleda syndrome Thost–Unna syndrome PIBIDS/IBIDS/ Trichothiodystrophy Olmsted syndrome Papillon–Lefevre syndrome Haim–Munk syndrome Costello syndrome Vohwinkel syndrome Rapp–Hodgkin syndrome Bart–Pumphrey syndrome Ankyloblepharon– ectodermal–cleft (AEC) syndrome
Anonychia	Zimmerman–Laband syndrome DOOR syndrome Glossopalatine ankylosis syndrome Otoonychoperoneal syndrome Klein syndrome/ popliteal pterygium syndrome Nail–patella syndrome/ hereditary osteoonychodysplasia Dyscephalic–mandibulooculofacial syndrome

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TOPIC OF THE LECTURE: TOPICAL "JUMP START" THERAPIES IN DERMATOLOGY

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Topical treatments provide an alternative modality, bypassing the systemic effects of oral drugs and minimizing drug-drug interactions. Rapid onset and long duration of action are the most two important factors that increase patient compliance with treatment. Undoubtedly, patients with dermatological diseases have a higher demand for treatments with rapid onset of action, because the lesions are easily noticeable by both themselves and other people. For this reason, many physicians prioritize many topical treatments that provide a 'jump start' effect in their clinical practice. Topical steroids are the best-known example of 'jump start' therapies in dermatology with rapid effect in a wide range of diseases. Topical steroids are used in the relief of many skin eczemas such as psoriasis, atopic dermatitis, burns, bullous autoimmune diseases, or suppression of inflammation before antimycotic treatment in diaper dermatitis, etc. They are the first agents that come to mind with rapid activity in many cases. Magistral prescriptions are another example of topical 'jumps start' therapies, for examle eau-borique solution that is very effective in rapidly drying an irrigated area. However, many other topical treatments can be considered as 'jump start' therapies, including topical antibiotics, moisturizers and many other topicals can show 'jump start' efficacy with several physical manipulations such as occlusion and laser assisted drug delivery.

This lecture primarily aims to discuss 3 main topics that demonstrate successful outcomes of topical 'jump-start' therapies: wound healing, superficial peelings, and in the last part, physical manipulations such as occlusion or laser assisted drug delivery that accelerate the onset of action will be focused on.

A wound is a disruption of the normal structure and function of the epidermis and associated underlying tissues. The healing process proceeds in four phases: hemostasis, inflammation, proliferation, and remodeling. Wound healing appears to be the most popular dermatology topic in the literature where the role of topical 'jump start' treatments has been objectively observed. Hyperbaric oxygen, topical supplemental oxygen (1), surgical and mechanic debridements (2), vacuum-assisted closure devices, topical growth factors, enzymatic debridement dressings and wound care dressings, platelet-rich plasma (3), platelet-rich fibrin (4) stand out as fast-acting topical therapies that accelerate wound healing.

Chemical peelings are commonly used cosmetic procedures but they also provide an additional therapeutic benefit to medical management of acne, acne scars, melasma, hyperpigmentation disorders, and photorejuvenation (5,6). In dermatology, peels are generally used either alone or in combination treatment with other treatments to provide a rapid onset of action. They are classified based on their depth of skin penetration into superficial, medium, and deep peels. Due to limited damage to the epidermis, superficial peelings are more preferred for 'jump start' therapeutic effect with significant improvement especially on active acne, acne scars, melasma, and photorejuvenation.

When a topical agent does not have sufficient potency and rapid onset of action, some physical manipulation can be performed to increase these two drug-related parameters. These methods include conventional methods such as administration of the drug under occlusion or the more popular one, laser-assisted drug delivery. Laser-assisted drug delivery (LADD) is an evolving new therapy with many possible applications as a highly targeted customizable method for the distribution of drugs within the skin. LADD offers the advantages of accessibility and rapid onset of topical treatment (7).

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ARE THEY IMMORTALITY FORMULAS: RESVERATROL AND RAPAMYCIN

Şule Güngör

Resveratrol is a polyphenol that has three hydroxyl groups which are involved in free radical scavenging and metal chelation. Food sources of resveratrol include wine, grape, berries, and peanuts. It has antiglycation, antioxidant, anti-inflammatory, neuroprotection , anticancer activity. It can prevent age-related diseases like diabetes, hypertension, atherosclerosis, renal disease, metabolic syndrome, nörodejenerative diseases. So it can be considered as an antiaging medicine.

Rapamycin (sirolimus) is a macrolide targeting the "mechanistic target of rapamycin" (mTOR) complex. It is used FDA-approved as an immunsupressant following organ transplantation and to reduce proliferation of fibrous, vascular, muscular tissues in tuberosclerosis. Topical rapamycin is used for the treatment of angiofibroms. Rapamycine acts its benefical effects by inhibiting mTOR pathway. The mTOR pathway regulates the proliferation, growth, metabolism and aging. The activation of mTOR pathway leads aging, the inhibiton of mTOR pathway prevents aging. As rapamycine inhibits mTOR pathway it can be considered as an antiaging medicine. In 2009 it was shown that rapamycin increased lifespan in mice by lowering the activity of the mTOR pathway. Since then, numerous studies showed that rapamycin prevents cancer and age-related diseases. It was told that rapamycin will be most effective when administered at the pre-disease stages of age-related diseases, in other words it is most effective before organ damage and loss of function. The limitations of using rapamycin as an anti-aging drug is its side effects. It can cause stomatitis, hyperglycemia, hyperlipidemi, anemia, trombopenia, leukopenia and infections. These side effects are seen in continuous taking of rapamycin for medical purpose. For anti-aging purpose rapamycin can be used in intermittent administration but there is not a standard intermittent dose schedule. It was shown that the side effects of rapamycin is due to mTORC2. So, in the future, new "rapamycin-like" agents should be discovered, similar to rapamycin inhibits mTORC1 leading to anti-aging effect, but not inhibiting mTORC2.

HYPERICIN- THE FACTS ABOUT A CONTRAVERSIAL AGENT

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Hypericin is a naturally occurring substance found in the plant St. Johns Wort (*Hypericum* species) and can also be synthesized from the anthraquinone derivative emodin. (1) Hypericin and its derivatives are accumulated in special morphological structures, so called dark nodules, occurring in the aerial parts of hypericin-producing *Hypericum* species. It is also found in some basidiomycetes (*Dermocybe* spp.) or endophytic fungi (*Thielavia subthermophila*). (2) It historically has been used for medicinal application. Today, it is still of remarkable interest and is a main topic of discussion. Antidepressive, antiviral, antiretroviral, antineoplastic, antitumor, photodynamic and photodiagnostic activities of hypericin are currently under investigation.(3) On the other hand, several light-independent actions of hypericin have also been described, eventhough its effects in the dark have not been studied as intensively as those of photoactivated hypericin. On the contrary, hypericin can induce the expression of some ABC transporters, which are often associated with the multidrug resistance of cancer cells and the hypericin-mediated attenuation of the cytotoxicity of some chemotherapeutics was revealed.(4-5) Thus, the chronic usage of St. John's wort extracts as an antidepressant by oncological patients undergoing anticancer treatment should be avoided. (2)

Topical application of St. Johns Wort such as oils or tinctures is also very common in some skin diseases in folk medicine such as minor burns and wounds, sunburn, abrasions, bruises, contusions, decubitus ulcers, keloid scars and many others. The plant contains a broad spectrum of pharmacologically active substances, but mostly two chemical classes; the phloroglucinols (hyperforins) and the naphthodianthrones (hypericins) were found to be effective for dermatological applications. Hypericins show antimicrobial, anti-inflammatory, and anticancer activities, especially when irradiated with visible light, and their photo-induced cytotoxicity can be used for photodynamic treatment of non-melanoma skin cancer and also for diagnostic purposes.

Modern clinical research on the role of SJW in dermatology has been scarce compared to the numerous trials with oral forms in depression and other psychiatric indications. The official 2009 HMPC monograph of the European Medicines Agency regards none of these topical applications as scientifically well established but accepts the use of topical SJW preparations for "symptomatic treatment of minor inflammations of the skin (such as sunburn) and as an aid in the healing of minor wounds" in the context of traditional medicine (6).

Recently, sporadic trials have been conducted in wound healing, atopic dermatitis, psoriasis, and herpes simplex infections, partly with purified single constituents and modern dermatological formulations. Potential adverse effects of dermal application may be irritation/ sensitization and unwanted photosensitization, although clinical data available suggests that the risk is relatively low. (7)

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TOPIKAL BRIMONIDINE IN DERMATOLOGY

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Brimonidine is a alpha-2 selective adrenergic receptor agonist and it has strong vasoconstrictive effects on a2-ARs of vessels and—to a lesser extent—on a1-ARs.It has anti-inflammatory properties and reduces vasodilation and edema. It is a medication using to treat open-angle glaucoma for about 20 years. In 2013, FDA approved brimonidine 0.33% gel for the treatment of persistent facial erythema of rosacea. It can also used for hemostasis in Mohs micrographic surgery. Brimonidine can reduce the post-treatment erythema of daylight-activated photodynamic therapy. It can be used in camouflaging redness of immature scars. Brimonidine prevents laser treatment therapy-related erythema and hyperpigmentation. It can reduce Ipl-induced erythema. And also in the literature it is reported that brimonidine can be used in treating telangiectasia of dermatomyositis.

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VINEGAR IN DERMATOLOGY

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Introduction

Vinegar may be defined as a condiment made from various sugary and starchy materials by alcoholic and subsequent acetic fermentation. The concentration of acetic acid ranges from 4% to 8%. Vinegar was first made from wine, as its name indicates. It has been produced and sold for thousands of years, dating back to before the 6th century (1).

Use in pediculosis

Several studies have been conducted on the use of vinegar in the treatment of pediculosis. Abdolhosseini et al. evaluated to efficiency of squill vinegar in 10 patients with head pediculosis. Squill vinegar locally applied to head for one week after using permethrin shampoo twice. Examinations were done on 2nd, 7th and 14th days. Infestation was not observed in 4 patients in 7th and 14th days examinations. In two cases, infestation was significantly reduced (75%) in 7th and 14th days. In all cases, the itchiness was gone.

This report stresses the effectiveness of Squill vinegar in the treatment of head Pediculosis resistant to treatment and recommends its implementation in school health units (2).

In another study, compared to efficiency of 1% permethrin shampoo, 4% dimethicone lotion and (1:1) vinegar wet combing for the treatment of head pediculosis. At the primary endpoint of day 7 post-treatment, the cure rate were 86% in dimethicone group, 64.2% in permethrin group and %60.8 in vinegar group (3).

Because none of the pediculicides are 100% ovicidal, manual removal of nits with a fine-toothed nit comb after treatment with any product is recommended. Some products are available that claim to loosen the “glue” that attaches nits to the hair shaft, making the process easier. Vinegar or vinegar-based products (Clear Lice Egg Remover Gel) are intended to be applied to the hair for 3 minutes before combing out the nits (3).

Use in pruritus

In interesting article about Scabies and Pruritus, the authors said Cosimo Bonomo discovered that prolonged antiseptic baths can eliminate pruritus and vinegar compresses or baths may have also have been used to treat “the itch” (4).

Nakhaee et al. compared the effects Avena sativa, diluted vinegar and hydroxyzine on the reduction of uremic pruritus. In this crossover randomized clinical trial, 23 hemodialysis patients with uremic pruritus were randomly divided into 3 groups. The first group was treated with Avena sativa lotion, twice a day, for as long as 2 weeks; the second group received diluted vinegar; and the third group took hydroxyzine tablets for the same time span. The data were collected by a pruritus scale and a visual analogue scale, which were completed before and after the interventions. Vinegar solution (30-mL synthetic white vinegar 5% in 500 ml of water) was used on pruritic areas with a vinegar sponge by the patient twice daily for 2 weeks. Vinegar significantly decreased all of the scores. According to this study, diluted vinegar reduced all pruritus dimensions and vinegar was more effective than Avena sativa (5).

Use in fungal infection

The use of vinegar (5% acetic acid) to treat fungal infection has also been studied. A randomized controlled trial was designed to efficacy of apple cider vinegar as an adjunct to 2% ketokonazole shampoo in the treatment of tinea versicolor. Twenty patients with tinea versicolor were randomly assigned to receive 2% ketoconazole shampoo and apple cider vinegar or 2% ketoconazole shampoo alone over a 5-day intervention. Efficacy was assessed in terms of clinical signs and symptoms (pruritus/itchiness, scaling and erythema), and laboratory parameters (Wood’s lamp examination and 10% KOH Test). A comparison of the measures of effectiveness between the two groups did not yield significant differences. However, the percentage of treatment success favored the apple cider vinegar-ketoconazole group where

the clinical signs and symptoms and laboratory parameters were negative in all the subjects compared to the control group. In conclusion the authors suggested Apple cider vinegar may be considered as a safe and potential adjunct to 2% ketoconazole shampoo in the treatment of tinea versicolor (6).

Use in bacterial infection

An another indication is Gram- Negative Bacterial Toe Web Infection (GNBTWI) often accompanied by fungal infection. The first description of acetic acid as treatment for purulent wounds was made by Taylor at 1916 (Taylor, 1916). Later on, Aste et al. described systemic treatment of GNBTWI with oral antibiotics such as ciprofloxacin along topical amikacin treatment and hot compresses of 2–5% acetic acid solution. They reported relatively high rate of success and only 7% relapse rate, and therefore concluded that acetic acid is effective for treating GNBTWI (7).

Use in leg ulcer and non-healing wounds

As the development of bacterial resistance to antibiotics continues, the need for new antimicrobial agents has led to reemergence of therapies that have been used for centuries.

Vinegar debridement therapy was used in many hospitals around the world for treating bone and soft-tissue infections due to its antimicrobial properties, meanwhile, it has been used as an antibiotic for the dressing of wounds as well as other uses, so that the vinegar has been suggested as a cure or ingredient in a cure for most human and many animal ailments.

Chronic non-healing wounds have an elevated alkaline environment. Healing occurs more readily in an acid environment. As a 0.25% to 0.5% solution, white distilled vinegar has bactericidal action against many Gram-positive and Gram-negative organisms, and is effective in reducing bacterial burden. Vinegar has been used as an adjunctive short-term treatment for superficial wound infection (8).

A study conducted from Iran to assess the efficacy of vinegar therapy on bacterial growth in the process of treating diabetic foot ulcers. Total of 30 patients with non-healing ulcers were divided into 3 groups; 10 wounds were treated with conventional therapy, 10 with vinegar therapy, and 10 with hypertonic saline. After 3 weeks of therapy, conventionally treated wounds were still covered with necrotic tissue over 41% of their surface and still growth of different pathogens , whereas after only 3 weeks of therapy vinegar-treated wounds were completely debrided (P = 0.001) and 70% of cultures were negative. Vinegar therapy was also associated with hastened growth of granulation tissue and grater wound healing rates.

The author said that vinegar therapy was more effective and efficient in debriding non healing foot and leg ulcers in diabetic patients than was continued conventional care and associated with lower bacterial growth rates (8).

Use in atopic dermatitis

The acidic pH of the stratum corneum (SC) is important for epidermal permeability barrier homeostasis. Acidification of the skin surface has been suggested as a therapeutic strategy for skin disorders such as atopic dermatitis (AD).

Lee et al. conducted an animal study to evaluate the usefulness of acidification of SC for inhibition of AD lesions. Five groups of six oxazolone-treated (Ox)-AD mice were treated for three weeks with creams of different acidity: vehicle cream alone (pH 5.5), neutralized vinegar cream (pH 7.4), pH 5.0 vinegar cream, pH 3.5 vinegar cream, and pH 3.5 hydrogen chloride (HCl) cream. Ox-AD mice treated with acidic creams exhibited fewer AD-like lesions, had significantly lower eczema scores, decreased basal by transepidermal water loss (TEWL), and increased SC hydration compared to the groups given only vehicle and neutral cream. There was no significant difference between the acidic vinegar and HCl groups. Between the groups treated with vehicle and pH 5.5 vinegar cream, there was no difference in eczema score, basal TEWL and SC hydration. Application of topical acids, regardless of their source materials, inhibits the development of AD lesions by maintenance of skin surface pH and skin barrier function in murine model. Collectively, maintenance of acidic skin surface pH by topical application of acidic cream could be an effective therapeutic modality for AD by improvement of skin barrier function (9).

There are also studies that find the opposite of these results. In another study, A total 22 patients with atopic dermatitis soaked both their forearms for 14 days, with one arm dilute apple cider vinegar (0.5% acetic acid) and other in water 10

minutes daily. Transepidermal water loss and pH were measured pre- and post-treatment. In both groups, transepidermal water loss increased and pH decreased at 0 minutes post-ACV treatment, but these effects were not sustained at 60 minutes. Therefore, although epidermal acidification would theoretically be beneficial in treating AD, results showed that acidification by way of topical bathing in a 0.5% ACV solution as performed in this study was not useful in AD treatment (10).

Use in diagnostic procedures

The use of 3% to 5% acetic acid (vinegar) can help in detecting anogenital warts and differentiating warts from other lesions in genital area.

The lesion or lesions can be soaked in acetic acid, and, if a change occurs in color to a white appearance, the lesions are most likely HPV lesions. This color change may be seen with the naked eye; magnification may be needed to detect subtle changes (1).

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5-FU IN DERMATOLOGY

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Topical 5-Fluorouracil (5-FU) is an antimetabolite drug and has been widely used for the treatment of various dermatological conditions. As a structural analogue of thymidine, it hinders thymidylate synthase and interferes with DNA and RNA synthesis in neoplastic cells, resulting in decreased cell proliferation and apoptosis. Because 5-FU interferes with DNA replication, rapidly proliferating cells are most sensitive to its cytotoxic effect (1, 2).

5-FU is currently available in topical formulations ranging from 0.5% to 5% concentrations in solutions or creams. Generally, topical formulations of 5-FU are indicated for twice daily application, while a controlled-release 0.5% microsphere formulation is indicated for once daily application. During the treatment phase, inflammation and erosion of the lesions increase and subclinical abnormal lesions become visible (1, 3).

Topical 5-FU is approved by the Food and Drug Administration for the treatment of actinic keratoses and superficial basal cell carcinomas, however its efficacy is demonstrated in other dermatological diseases such as kerathoacanthoma, Bowen's disease, malignant melanoma, psoriatic nail dystrophies, vitiligo, verruca vulgaris, Darier's disease and photoaging. Topical 5-FU offers an alternative to ablative and surgical treatments, which may cause scarring or require reconstructive procedures. Of the mucocutaneous diseases, topical 5-FU is also effective in the treatment of actinic cheilitis, condyloma acuminata, anogenital Bowen's disease and extramammary Paget's disease. The most common side effects of topical 5-FU treatment include erythema, pain, pruritus, irritation, erosion, and eczematous reaction. Several combination treatments, such as cryotherapy, salicylic acid, and photodynamic therapy, may increase the efficacy and tolerability of 5-FU. Topical 5-FU should not be used in women who are or may become pregnant, since it is teratogenic and classified as pregnancy category X (1-3,4).

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TOPICAL TIMOLOL AND NIFEDIPINE IN DERMATOLOGY

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Topical Timolol

Timolol maleate is a non-selective β-blocker originally used for the treatment of open-angle glaucoma. It is available in formulations of 0.5% eyedrop and 0.5% ophthalmic gel. TM is also an off-label option for various dermatological conditions, such as infantile hemangioma (IH), pyogenic granuloma, Kaposi's sarcoma, or chronic wounds. Herein the dermatological use of topical timolol is summarized.

Oral propranolol, a non-selective β-blocker, is the first line therapy for IH. Possible mechanisms of action of propranolol -and also timolol- are: vasoconstriction, supression of genes encoding vascular endothelial growth factor and basic fibroblast growth factor, and capillary endothelial cell apoptosis. Because of the side effects of propranolol such as bronchospasm, hypotension, and hypoglycemia, a topical β-blocker, timolol, serves an alternative with a good safety profile.

In a prospective study conducted on 124 patients with superficial infantile hemangiomas (IHs), "controlled growth" in 35.6% and "promoted regression" in 56.4% of 101 patients treated by timolol drops (3 times daily, 4 months), were demonstrated. In another study, 278 patients with superficial IH were divided into three groups: topical ultrapotent corticosteroid, TM 0.5% solution, and TM 0.5% gel. TM groups were significantly superior to corticosteroid in terms of size reduction of IHs2. A retrospective study of 731 patients with IH supports that the best responders of topical TM are those who have IHs <1 mm thickness.

Timolol is also a good adjunct therapy to propranolol. Using topical timolol subsequent to oral propranolol shortens the duration of propranolol treatment by 2.2 months (9.7 months vs 7.5 months; p=0.006), provides a 1.7 months younger completion of propranolol treatment (14.0 months vs 12.3 months; p=0.007), and removes the need for propranolol reinitiation (p=0.036)3. In a meta-analysis including 8 randomized controlled trials with 759 cases, topical timolol had a similar response rate to oral proplanolol (risk ratio [RR]=0.97; p=0.63), and the combination of timolol and propranolol was superior to oral propranolol (RR=1.14; p=0.03) or topical timolol (RR=1.36; p=0.01) monotherapies4.

Pyogenic granuloma (PG) is another dermatological condition that can be treated with TM. In a series of 10 patients with PG who applied TM 0.5% ophthalmic solution 4 times a day, complete response in 4 patients (duration: 3-24 days) and partial response in 3 patients were demonstrated5. Timolol is a therapeutic option for PG, especially where surgical procedures are not favorable such as pediatric population, debilitated cases, or critical localizations (face, nail, gum).

Timolol can be used for Kaposi's sarcoma. There are approximately ten cases in the literature, regarding the use of 0.1%-0.5% topical timolol in the treatment of radiotherapy-refractory iatrogenic Kaposi's sarcoma, classic Kaposi sarcoma, or HIV associated Kaposi's sarcoma. The remission was achieved in 5 to 24 weeks6. Timolol can act via inhibition of angiogenesis. Besides, oral propranolol has been shown to suppress Kaposi's sarcoma-associated herpesvirus infection and this property may be another mechanism of action of timolol. Topical timolol may be an alternative when surgery, radiotherapy, or chemotherapy are inappropriate.

Timolol induces keratinocyte migration via β2 blockade and thus supports re-epithelialization in chronic wounds, so it can be used for the treatment of recalcitrant ulcers. In a retrospective study, of the 55 chronic wounds of varying etiologies (median duration of wound before treatment: 118 days) treated with timolol, 34 wounds had healed, 15 had improved, and two had worsened. The median treatment duration of healed group was 89.5 days7.

Topical timolol have also been used for the treatment of EGFR-inhibitor induced paronychia and pseudopyogenic granuloma, hypergranulation, fissures and erosions of hand eczema, fissures of heels, post-acne erythema, junctional epidermolysis bullosa, angiofibroma, pyoderma gangrenosum, red scrotum, and scars. Randomized controlled trials are needed to confirm the efficacy of topical timolol in these conditions.

Although timolol is a safer alternative of oral propranolol, it may also cause adverse effects such as bradycardia, AV block, or local irritation. In infants with IH treated with topical timolol and adults who applied TM 0.5 % gel to their wounds, serum/plasma levels of timolol were similar to levels seen with adult ophtalmic timolol use. The scarcity of adverse effects of topical TM in various clinical studies may be due to lack of proper monitoring8.

Topical Nifedipine

Nifedipine is a dihydropyridinic calcium channel antagonist that inhibits the contraction of smooth muscles. It is originally used to provide internal anal sphincter relaxation in the treatment of anal fissure and acute thrombosed hemorrhoids. It is available as 0.5% cream form.

In dermatology practice, topical nifedipine cream has been used for facial wrinkles. It is thought to act via inhibiting the contraction of mimic muscle fibers, and may be an alternative to Botulinum toxin A injections. In a single-arm study of 64 women with periocular wrinkles, topical 0.5% nifedipine cream (once daily, 90 days) was shown to reduce the depth of wrinkles. In a randomized controlled trial, 20 women with moderate-moderately severe facial wrinkles were treated with 0.5% nifedipine based topical formulation or moisturizer twice daily for 90 days. Nifedipine group was demonstrated a significant decrease in wrinkle severity rating scale (3.85 to 1.84 vs. 3.78 to 3.36) and a significant increase in skin hydration and lightening, compared to placebo9. Nifedipine has been shown to improve transepidermal water loss and later this finding has been confirmed by an experimental study.

Topical nifedipine is also used for the treatment of pressure ulcers. Nitric oxide (NO) plays an important role in wound healing, and is an NO donor. Vasodilatation, collagenation, and antioxidant effects are other potential mechanism of action of nifedipine in the treatment of ulcers. In a randomized placebo controlled trial of 200 patients with stage I or II pressure ulcers, patients who treated with topical nifedipine 3% ointment for 2 weeks (n=83) have demonstrated a significantly higher mean decrease in the stage of ulcers and in the surface area of ulcers10.

The dermatological use of topical nifedipine appears to be safe, and it has no side effects other than local irritation seen in some patients.

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INGROWN NAIL: NON-SURGICAL APPROACH

Gülru Erdoğan

Ingrown nail is the erythema, edema and pain of the nail folds, usually lateral nail folds.

It is usually the result of an acute irritation on nail fold.

While ingrown nail starts with edema, penetration of nail into the nail fold is not a must. Edema of the toe by securing the feet closed for long hours especially in hyperhydrotic patients lead to prominent edema together with moist and sweat accumulation may cause irritation of nail fold and hence pain.

Sometimes erythema, edema and pain on nail fold can be misdiagnosed as bacterial paronychia. This may be the reason why sometimes local or systemic antibiotics may not help for nail fold pain and edema. Therefore focus on edema, remove edema so you remove pain.

Usually patients try to cut deep their nails just at this stage which makes the picture worse.

Objectives;

Cease the pain.

Relieve pain ASAP

There are various conservative methods for treating ingrown nails; eg bands, wiring, braces, cotton, dental floss, lotions,etc. Choosing the correct method is as important as early diagnosis (1,2,3,4,5,6).

Methods usually followed can be classified in three main groups;

1.Put a mechanical barrier between nail and nail bed; most commonly used however nail has to be long enough:nail braces, nail wiring, etc

2. Soften the nail; just one product. Nail is better long, not in hyperhidrotic feet as nail is already soft in hyperhidrotic feet.

3. Remove edema; Nail may be very short, asymmetrical, all shapesrespond as nail is not treated but rather the nail fold is.

Here we may propose an algorythm to choose the correct method by using three important variables; hyperhydrosis, overcurvature and nail length.

1.Decide whether there is hyperhidrosis or lateral nail fold hypertrophy; this leads the nail to be soft, therefore wiring or bracing can break the nail. Choose band, cotton or lotion.

2.Decide whether there is an overcurvature of the nail on the sides; then wiring, bracing or softening the nail can be appropriate if there is no hyperhidrosis. Lotion may also help remove the edema and pain.

3.Decide whether nail is too short to put on a brace, wire or not; then you can use cotton or lotion or softening gel and wait till nail side elongates. After then you put on wire or brace if there is overcurvature.

Granulation tissue formation;

Granulation tissue is not infectious. It is a kind of reactive vascular tissue as in the case of foreign body reaction. Therefore, it bleeds easily and leaves a crust.

Once you see crust on nail fold, it is the sign for a granulation tissue. It is not infection.

Once you see the crust, most probably there is a subungual granulation tissue as well as on the nail fold. Therefore by applying cream on nail fold, most probably you will not reach the subungual portion and hence be successfull.

This is why we apply an undernail cushion for such cases; to reach subungual granulation tissue. You may pour antibiotic lotions through it or hyperosmolar, astringent lotons as we prefer.

Take home lessons;

1.Recognize ingrown nail ASAP. Erythema, edema on one nail side, not usually covering all sides.

2.Recognize crust ASAP. It is the sign for a granulation tissue, usually with a subungual extension.

3.Edema is the main reason of pain. Remove the edema, you cease the pain.

4.Pay attention to hyperhidrotic feet, cream formulations usually increase mositure and edema!!! It may be better to dry up.

PS: Please prefer conservative methods first, as conservative methods lead to recurrence in previously operated cases (7).

Early diagnosis and commencement of correct conservative treatment increases the success rate and decreases the need for operations. Please remember conservative means are patient friendly, pain free and cost effective.

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SURGICAL PRINCIPLES IN NAIL UNIT TUMORS

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Surgery is the gold standard of nail tumor treatment although there are a few options of conservative therapies; however, they are not safe with regard to treatment control.

Before considering nail surgery the diagnosis should be made or at least a suspect diagnosis. Then the nature of the tumor – benign or malignant – has to be assessed. A thorough discussion of the type of surgery with the patient, its alternatives, possible risks inclusive those of doing nothing follow. After informed consent the surgical technique has to be explained so as to let the patient know what he/she will have to face in terms of anesthesia, postoperative pain, healing time, risk of infection, disability to work, etc. Further, the patient must know how to get home after surgery, to bring wide shoes for toenail surgery, organize transport and pain relief.

The most common nail tumors are viral warts – and they are virtually the only ones that are not treated surgically but rather by aggressive keratolysis.

Ungual fibrokeratomas may have their origin in the depth of the nail pocket and emerge on the nail from under the proximal nail fold. An incision is carried around their base, which is the released with pointed curved iris scissors from the bone. Fibrokeratomas of the mid-matrix grow in the nail plate. The overlying portion of the plate is gently carved away and the lesion the removed like the epiungual one. Fibrokeratomas of the nail bed cause a rim and their tip is usually visible under the nail. The overlying nail is separated allowing access to the tumor, which is again cut down to bone and removed.

Glomus tumors are characteristic for the nail and best known for their typical symptomatology although they are relatively rare. Inspection, probing and magnetic resonance imaging allow their exact localization. If the tumor is located in the lateral third, a lateral subungual approach is used whereas central localization requires a transungual technique. For this, the overlying nail portion is lifted allowing the matrix and nailbed to be observed. The glomus tumor is seen as a violaceous spot, mostly in the distal matrix and proximal nail bed. A slightly arched shallow transverse incision is made in the matrix and the tumor usually pops out as a greyish glassy round lesion surrounded by a thin connective tissue capsule. It is cautiously dissected out and the wound sutured with 6-0 fast resorbing stitches. A nailbed glomus tumor is dissected after a longitudinal incision has been made.

Subungual exostosis is a characteristic lesion of children and young adults. It is visible as a stone-hard circumscribed swelling raising the overlying nail plate margin. The exostosis characteristically has an epidermal margin like a collarette whereas the overlying epidermis is smooth and shiny. An incision is made along the border down to phalanx bone, the surrounding soft tissue is dissected, and the exostosis finally clipped of the bone. The skin is sutured to close the defect; however, this is often not completely possible and wound margin adaptation with transungual stitches are recommended.

Longitudinal brown streaks in the nail present a major diagnostic and therapeutic challenge in adults as they may be the sign of a subungual melanoma. The rule is that an acquired brown streak in the nail of an adult is rather malignant than benign until otherwise proven. This requires a biopsy for histopathological examination. Several different biopsy techniques are available, from a small punch to excisional tangential biopsy. A punch is technically easy but may not contain enough tissue for a reliable diagnosis. Therefore, we have developed a tangential matrix and nailbed biopsy that allows the whole melanocyte lesion to be remove with sufficient depth but virtually without the risk of postbiopsy nail dystrophy. Proximal nail fold is incised on both sides, freed from the underlying nail and reclined. The proximal third of the nail plate is incised transversally and opened so as to allow the melanocyte focus to be seen. A shallow incision is

carried around the pigmented lesion with an adequate safety margin, the width of which depends on the clinical suspect diagnosis, and the lesion is then tangentially removed. The tissue slice should be 0.8 mm thick. This will leave enough matrix dermis behind so that re-epithelialization will yield matrix epithelium again. The specimen is stretched out on filter paper, on which a nail schema has been drawn and immersed into the fixative. This technique permits to take virtually the entire matrix epithelium for diagnosis. The nail plate is then laid back and the proximal nail fold stitched in place again. Healing is commonly uneventful without nail dystrophy.

Bowen disease and squamous cell carcinoma of the nail are probably the most frequent ungual malignancies. Up to 80% of the Bowen cases are associated with high-risk human papillomaviruses, particularly HPV 16 and 18, but also many other high-risk types. Bowen disease may be very extensive and require large excisions. Mohs micrographic surgery is the treatment of choice. Defect closure depends on the size and particular localization of the defect. Local flaps are technically demanding but very rewarding. Large defects are gest grafter after guided granulation of the wound.

Nail melanoma is the most serious nail disease. It is not uncommon with approximately 1.5 to 2% of all melanomas in light-skinned Caucasians, >20% in Blacks and up to 40% in East Asians; however, race is no risk factor as the absolute number of nail melanomas does not differ. The peak age is between 45 and 60 years, but ungual melanoma has also been observed in children. The prognosis of nail melanomas is said to be poor as they are often diagnosed and treated very late. The treatment of choice of early melanoma – in situ and under Breslow 1 mm – is wide local excision with preservation of the digit. This treatment was described by us 43 years ago and is now adopted world-wide. Large studies comparing conservative or functional surgery with amputation have demonstrated comparable cure rates and a much better quality of life for functional surgery. The surgery comprised total extirpation of the whole nail unit with a 6 mm safety margin around the anatomical borders of the nail apparatus. As so-called field cells may extend for up to 9 mm around in situ melanoma, we extend the safety margin in case of Hutchinson sign to 10 mm. The defect is usually left for granulation and may then be grafted with full-thickness skin.

Nail tumor surgery is critical as it has to ensure that the neoplasm has been completely removed but no uninvolved tissue has been sacrificed. Atraumatic surgery has to be combined with aesthetic and tumor surgery principles.

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PSORIASIS AND ALOPECIA

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Abstract

Psoriasis is a chronic, multi-factorial, immune-mediated skin disease that presents a variety of clinical manifestations. Scalp involvement in patients with psoriasis is one of the most common manifestations throughout the course of the disease. Between 50% and 80% of patients have scalp involvement alone or with lesions in other parts of the body.[1] Alopecia may accompany patients with scalp involvement more often than thought. It can be a cause of secondary cicatricial alopecia.

Alopecia and other hair abnormalities that occur in patients with psoriasis were described for the first time in 1972.2 Three types of scalp alopecia have been defined by Shuster: (i) alopecia confined to lesional skin, (ii) generalized telogen effluvium, and rarely (iii) scarring alopecia.[2,3] It may be directly related to psoriasis itself, to the topical therapies or systemic treatments such as methotrexate, retinoids, and biological agents used to treat it, or to associated autoimmune conditions. It can affect both the scalp and other psoriatic plaques on the trunk and limbs. Histopathological findings are similar to those seen in the interfollicular epithelium of psoriasis, which also includes perifollicular lymphocytic inflammation, atrophy or loss of sebaceous glands, and a marked increase in telogen hairs. [4,5]

In most cases, there is regrowth of hair, scarring alopecia is rarely seen. The exact incidence of this complication is not known. In the largest case series reported, 12% of patients with psoriatic alopecia resulted in permanent scarring alopecia.[6] Psoriatic scarring alopecia was most frequently associated with long duration and higher severity of scalp psoriasis. Scratching and secondary infections especially staphylococcal infections were thought to be the main drivers of the cicatricial process. Proper control of psoriasis inflammation is important to avoid progression to scarring alopecia. Familial cases have also been reported, suggesting that some genetic variants of psoriasis may trigger scarring alopecia. [4]

More recent reports describe a wide variety of cutaneous reactions as an adverse effect or paradoxical reaction with biological agents. One of the rare side effects of treatment with anti-TNF agents is the development of alopecia, often associated with psoriasiform lesions on the scalp or elsewhere in patients without previous psoriasis. These lesions may be clinically similar to primary psoriatic alopecia or alopecia areata.[7] There are also a few cases of alopecia associated with IL-17 use in the literature. They were defined as an unexpected ‘’paradoxical reaction’’, as IL-17 inhibitors could also be used in the treatment of alopecia. It has been reported that the use of IL-17 inhibitors can lead to alopecia by converting the Th17 / Th1 axis into a Th1 dominant immune state.[8] The presence of psoriatic alopecia may affect the choice of systemic treatment for psoriasis.

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NAIL LACQUERS IN DERMATOLOGY

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Anatomy of the Nail

*Nail matrix *Nail bed *Cuticle *Nail plate *Nail folds *Lunula

Unlike the skin,

- nails have a low lipid content (around 1%), mainly composed of cholesterol,

-and the water content is higher than in the stratum corneum at around 10–30% (as a protein solvate) in a normal state

Factors Affecting The Nail

Environmental factors (e.g., low relative humidity, winter, etc.) could reduce the water content, leading to nail brittleness.* Constant use of nail cosmetic products (nail polish) based on a high amount of organic solvents (e.g., butyl acetate, ethyl acetate) could extract nail water and lipids, leading to progressive dehydration. *Nutritional deficiencies (biotin deficiencies) *Diseases;microbial infections, psoriasis, lichen planus, alopecia areata, Darier's disease, could affect the nail structure

Nail Psoriasis

Psoriasis is a chronic immune disease affecting the skin. Keratinocyte hyperproliferation and inflammation are observed in patients and the involvement of the nail apparatus happens in around 50% of cases.Nail alterations in psoriasis usually involve-the nail matrix (pitting, leukonychia or white spots, and crumbling) and the nail bed (onycholysis, hyperkeratosis, and discoloration).

Topical drug delivery systems

Transungual delivery is an effective approach in the treatment of onchomycosis where the drug penetration is influenced by compact structure of nail. Nail lacquers based on novel formulation approaches are being focused upon to improve the delivery of active ingredients in a more economical way.The transungual delivery seems to be an attractive approach in the treatment of nail infections however, the delivery system faces difficulties to reach all the required sites of deep-seated infections due to their limited penetration into the nail unit. The success of transungual delivery for the effective treatment of nail fungal infection directly depends on the thickness and compact structure of nail.Transungual drug diffusion across the nail plate depends on a number of factors like degree of hydration of nail, nature and pH of vehicle, molecular weight, surface charge of drug, hydrophilicity/lipophilicity and its interaction with keratin matrix of the nail.Hence for an effective penetration into the nail plate, an apparent balance between the physic-chemical properties of drug and biophysical properties of nail plate is desirable. A drug molecule with high permeability coefficient, acidic pH, unionized/ undissociated molecule, small size (<300Da) and low keratin affinity permeates the nail barrier.

Nail lacquer and its Potential

Nail lacquer is a varnish applied to nails for the treatment of nail infections namely, onchomycosis and psoriasis. It is a novel formulation solution to the problem of transungual drug delivery. Nail lacquers consist of solvents, film forming polymers which improve the adhesion and plasticizers make the nail lacquer flexible. A nail lacquer application to the nail forms an adhesive polymeric film on evaporation of volatile organic solvent. An active ingredient is incorporated in the nail lacquer for therapeutic action and is applied by a brush forming a film on evaporation of volatile solvent.Direct application of the nail lacquer onto the nail plate maintains optimal concentration of drug . The volatile solvent(s) of nail lacquer get evaporated and the drug concentration in the lacquer film residue thereby increases. The lacquer film residue acts as a drug reservoir since the drug remains with the infected nail for a longer duration of time. The potential advantages of nail lacquer can be gauged from the fact that they prevent reinfection in initial step along with the property of occlusion offered by the lacquer film, which further enhances nail plate hydration. The recurrence rates of infection is reduced as the drug by pass delivery from nail bed via matrix circulation. This is because the nail bed turnover is high depleting drug concentrations.The polymeric adhesive film formed by the lacquer ensures sufficient adhesion with the nail for continuous delivery of the drug and longer periods of time. The drug concentration in the film is much higher than concentration as compared to the nail lacquer.The formation of film has an additional benefit on the nail plate as it reduces water loss from the nail surface leading to hydration of the upper nail layers. The permeation enhancers present can cause sufficient nail

hydration by reducing pores obstructing drug diffusion.The water-insoluble films like methacrylic polymer and vinyl resin provide sustained drug release and water-soluble films like hydroxypropyl chitosan provide stronger adhesion and facilitate greater drug partitioning/release into the nail plate .The water-soluble films easily get washed on exposure to water. Hence, to combine the advantages of adhesion and drug release properties of water-soluble films with the occlusiveness of water-insoluble films.

Components of Nail Lacquer

The components of nail lacquer play a significant role in the transungual delivery.

Nail lacquer usually contains;Volatile solvent to solubilise the drug (65 to 75%)*Film forming polymer (10 to 20%),*Plasticizer to give flexibility and durability to the film.*Film suspending agents can be added to increase the viscosity of enamel, *Resins to improve adhesion of the film to nail and surfactants to improve drug's wettability and solubility (7 to 15%)*Humectants like sorbitol, glycerol can be added alternatively which on evaporation of alcohol leave a hydrated polymer film, hence; increasing drug solubility and thus permeation *Titanium oxide, mica, bismuth oxychloride, sedimentation retarders, chelating agents, antioxidants, silicates, aroma substances, wetting agents, lanolin derivatives, light stabilizers and antibacterial substances can also be added.

Ciclopirox Hydroxypropyl Chitosan (HPCH) Nail Lacquer

Ciclopirox 8% hydroxypropyl chitosan (HPCH) [Marketed in different countries as the following registered (®) brands: Ciclopoli, Fulcare, Kitonail, Myconail, Niogermos, Niogermox, Onytec, Ony-Tec, Polinail, Privex, Rejuvenail] is the first topical nail lacquer developed using innovative drug formulation technology. It is indicated for the treatment of mild-to-moderate fungal infections of the nails that are caused by dermatophytes and/or other ciclopirox-sensitive fungi, without nail matrix involvement. HPCH is a patented drug formulation technology for the delivery of active principles into the nails based on a hydrosoluble semisynthetic amino-polysaccharide biopolymer derivative of chitosan. The lacquer acts as a protective barrier against microbiological attack, physical damage and/or aggressive chemicals. In clinical studies in patients with mild-to-moderate onychomycosis, ciclopirox 8% HPCH was found to be more effective than the commercial water-insoluble ciclopirox 8% and amorolfine 5% lacquers, as indicated by higher complete cure, response and mycological cure rates at 48 weeks after treatment initiation. Ciclopirox 8% HPCH has been found to be generally well tolerated, with no treatment-related adverse events reported in patients using this nail lacquer.

Conclusions

Nail lacquers can be used for the topical treatment of nail fungus and psoriasis.There are only a few products on the market for now. There are nearly ten products in development phase.We look forward to new products

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FOLLOWING THE LATEST GUIDELINE IN 2021: WHAT'S NEW?

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The most used guidelines for managing Chronic Urticaria are; the American Academy of Allergy, Asthma, and Immunology (AAAAI) and the European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA2LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO). There are some differences between their recommendations however the main recommendations are remaining similar. The EAACI/GA2LEN/EDF/WAO updated their guideline for chronic urticaria in December 2020. There were many topics discussed in the 5th Global Urticaria Forum (GUF) and new recommendations were considered. As a UCARE and ACARE center from Kayseri, Turkey, we have also contributed by voting in the new guideline. However, the guideline for chronic spontaneous urticaria (CSU) is still under development however, we are waiting for some important changes.

If we summarize the expected suggestions:

1-To including the angioedema control test (ACT) as a tool for the assessment of patients with CSU who have angioedema,

2-To include the total IgE levels and IgG anti-TPO to be assessed by specialists in the workup of CSU,

3- To reduce the guideline algorithm into three steps: antihistamines, omalizumab, cyclosporine, and updosing of antihistamines and omalizumab will be included in the respective steps for treatment.

However, the core recommendations are expected to be similar. We are looking forward to the official guideline of the EAACI/GA2LEN/EDF/WAO.

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WHICH CAME FIRST? THE CHICKEN OR THE EGG?: THE ROSACEA OR THE DEMODEX SITUATION

Seray Külcü Çakmak

Rosacea and demodicosis are common conditions in dermatology practice. While demodicosis is clearly the result of infestation by the Demodex mite, the etiology of rosacea is unclear.

Rosacea is currently considered by most authors as a disease of the immune system, an inflammatory process including innate and then adaptive immune responses. There is increasing evidence to suggest that rosacea is an inflammatory continuum and that there is a key role for the Demodex mite in this inflammatory process.

Individuals with rosacea have been shown to have a higher density of Demodex mites on their facial skin compared to individuals without rosacea in studies performed with skin surface biopsy specimens, polymerase chain reaction and reflectance confocal microscopy.

In a metaanalysis of 23 case-control studies with 1513 rosacea patients it was reported that

rosacea patients were more likely to be infested by Demodex mites and had significantly higher Demodex density than did healthy control patients. Patients with erythemathotelengiectatic rosacea (ETR) and papulopustular rosacea (PPR) had significantly higher Demodex density (DD) than that healthy control patients, but DD tended to be lower in ETR than in PPR. It was reported that Demodex mites promoted the development of acute-inflammatory morphological elements, increased the duration of rosacea and the probability of recurrence.

Also the antiparasitic drug ivermectin, in the form of an external form, at a concentration of 1% has a high therapeutic efficacy in patients with rosacea associated with Demodex mites.

In rosacea it was proposed that increased numbers of Demodex mites could lead to blockage of the hair follicles and sebaceous glands resulting in cutaneous barrier disruption and tissue damage. The resulting increase in toll like receptor expression and recognition of the mite's chitin exoskeleton could trigger an inflammatory reaction. Disruption of the epithelium and recognition of exoskeletal chitin may also result in a Th2 and/or Th17 response leading to tissue damage as a result of neutrophil and macrophage activation. Studies also suggest that mites from rosacea patients harbour pathogenic bacteria and other microorganisms which drive inflammatory skin responses.

The potential role of the Demodex mite in the development of rosacea and the multiple clinical and histopathological similarities between demodicosis and rosacea also leads to diagnostic confusion between demodicosis and rosacea.

However most authors still think that proliferation of the Demodex mite in patients with rosacea is a secondary event, in which the initial inflammation, activation of matrix metalloproteinases, increased size of blood and lymphatic vessels, reduced levels of long-chain saturated fatty acids in the facial skin of patients with rosacea promotes the proliferation of Demodex, which then exacerbates the disease.

Also human Demodex mites, as a causative for rosacea, can not fulfill the Koch's postulates and the causative role of Demodex mites is limited considering Bradford Hills criteria for casual association including the strength of association (nearly 100 % prevalence rate of Demodex mites but up to 3% prevalence rate of rosacea in large-scale population surveys).

It can be thought that Demodex mites may enhance the disease progression in rosacea, leading to an increase in inflammation and eventually papulopustules.

So, although there are many studies indicating that the Demodex mites may play a significant role in rosacea by orchestrating the host immune status, more work needs to be done to determine the exact association between Demodex mites and rosacea.

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WHICH IS BETTER FOR HIDRADENITIS SUPPURATIVA: SURGERY OR MEDICAL TREATMENT

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Hidradenitis suppurativa (HS) is a chronic progressive disease that primarily affects the apocrine sweat glands. Its exact prevalence is unclear, ranging from 0.1% to 4%. Young adults and women are most affected from HS. A genetic background was reported nearly in 30-40% of HS patients.[1,2]

The disease initially appears around the pilosebaceous-apocrine unit with the obstruction of hair follicles by follicular hyperkeratosis, subsequently resulting in rupture of hair follicles and inflammation of the perifollicular areas and apocrine glands.[2] At early stages, inflammation is mainly characterized by involvement of proinflammatory cytokines, lymphohistiocytes, neutrophiles, macrophages, monocytes, and dendritic cells, leading to inflammatory nodules and abscess formation. During the chronic stage, with additional contribution of histiocytes, B cells, plasma cells, and giant cells, inflammation is complicated by formation of granulation tissue and granulomas, and subsequently extensive fibrosis.

Tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-17 are considered to be the most relevant cytokines, particularly in moderate-to-severe HS.[3,4] In addition, alterations in the cutaneous microbiome are common, with accumulation of biofilm-forming bacteria in lesional areas, such as *Corynebacterium*, *Porphyromonas*, and *Peptoniphilus* species.[1]

Depending on disease severity, HS may exhibit a wide variety of manifestations, including comedones (characteristically paired), papules, pustules, nodules, cysts, abscesses, sinus tracts, fistulae, and bridged scars in the flexural areas, e.g. the axillary, groin, anal, and breast regions.[5,6]

Among multiple scoring systems for disease severity, the Hurley Staging System is most common.[1] Hurley stage I, II, and III correspond to mild, moderate, and severe disease, respectively. Stage I is characterized by solitary or multiple recurrent nodules, abscesses, and minimal scars without formation of sinus tracts. Stage II is characterized by a single or a few sinus tracts and/or scar tissue as individual lesions. Stage III is characterized by multiple interconnected sinus tracts, abscesses and/or scar tissues entirely involving a certain area.[2,5,6] Progressive, chronic, painful, and debilitating features of HS inevitably lead to disruptions in the social and occupational lives of patients, and impaired quality of life.

HS may be accompanied by comorbidities, including cardiovascular conditions (myocardial infarction, ischemic stroke, and CV-associated death), hypertension, obesity, dyslipidemia, metabolic syndrome, smoking, thyroid disorders, arthropathies, psoriasis, inflammatory bowel disease, psychiatric disorders, and polycystic ovarian syndrome.[1]

Treatment of HS is designed by consideration of disease severity, comorbidities, and impact of the disease on patients' quality of life.

Despite the paucity of high-level evidence on optimal treatment of HS, multiple guidelines have been released guidelines during the past several years aiming to guide the treating physicians, the most relevant of which are the European S1 guideline, HS ALLIANCE working group recommendations, North American Clinical Management guidelines, and British Association of Dermatologists (BAD).[2,6-8]

Most guidelines recommend to assess disease severity based on the combined use of the Hurley classification system, a visual analog scale (VAS), and the Dermatology Life Quality Index (DLQI). After screening associated comorbidities and providing lifestyle recommendations, appropriate treatment is designed.[2,6-8]

Medical Therapies

In mild-to-moderate HS, topical treatment, e.g. clindamycin 1% solution, resorcinol 15% cream, chlorhexidine, zinc pyrithione, or other antibacterial creams or solutions, may prove to be beneficial. Additionally, oral antibiotic treatment with tetracyclines (doxycycline or lymecycline) over a 12-week course is recommended as the first-line systemic therapy. As a second-line alternative oral treatment, clindamycin and rifampin combination over 10-12 weeks is recommended. Another antibiotic option reported to be effective is the combination of moxifloxacin (400 mg daily), metronidazole (500 mg thrice daily), and rifampin (300 mg twice daily).

In cases in which antibiotic therapies are not efficacious, acitretin (0.3–0.5 mg/kg per day) or dapsone (25-100 mg/day) may be considered.

There are also ongoing experimental studies of hormonal agents to be used for all stages of HS, including estrogen-containing oral contraceptives, spironolactone, cyproterone acetate, metformin, and finasteride.

In moderate-to-severe HS, initially conventional systemic therapies (antibiotic therapies, acitretin and dapsone) are recommended. In refractory cases, biologic agents represent the second-line option, adalimumab followed by infliximab. When using adalimumab, if a reduction (³25%) in the overall count of abscesses and inflammatory nodules is achieved at 12 weeks, maintenance of adalimumab is recommended. Otherwise, switching to infliximab is considered. Other treatment modalities such as carbon dioxide laser therapy, laser hair removal, radiation therapy are reported to be beneficial in sporadic cases.[2,6-8]

Surgical Alternatives

Currently, data on surgical treatment of HS are sparse and sporadic.[2] However, there are quite a large number of moderate-to-severe cases in which no other alternative exists other than surgery. Various surgical methods have been reported, including incision and drainage, deroofing, electrosurgery, narrow-margin excision, and wide radical excision with closure by secondary intention, skin flap, or graft.[6-8]

In the treatment of painful abscesses and sinus tract formations no medical treatment alone is efficient; therefore, addition of surgical interventions is mandatory.

Hyperplasia of the follicular epithelium and healing of inflammatory lesions is often complicated by formation of fibrosis, scarring, hypertrophic tissue, bridging, and sinus tracts, which may facilitate local recurrences of HS and worsen patients' quality of life by restricting mobility. A meta-analysis investigating recurrence rates of HS after surgery reported varying recurrence rates: wide excision, 13.0%; local excision, 22.0%; and deroofing, 27.0%.[9] Another meta-analysis reported the average estimated recurrences as 26.0% for partial excisions and 5.0% for wide excisions.[10]

In conclusion, HS may require both medical and surgical treatment options depending on the disease severity, the stage of HS, and types of lesions. Therefore, these two treatment modalities are not alternative to, but complementary to each other.

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IS DIET REALLY IMPORTANT FOR ACNE?

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The relationship between acne and diet has attracted great attention for many years. The occurrence of acne in populations who did not historically have acne, after the shift from traditional diets to Western style diet, supports the role of diet in acne. So far many studies have been conducted on this relationship, however, there is still uncertainty regarding the role of some food in acne.(1)

In literature, several reports including meta-analysis and reviews focus on various dietary factors that can have positive or negative effects on the development of acne.(2) Dietary factors worsening acne include high glysemic index (GI)/ glycemic load (GL), dairy products, fat food and chocolate. Dietary factors reducing acne include fatty acids, fruit and vegetable intake.

Glysemic index (GI)/ glycemic load (GL)

Glysemic index (GI) is a value for foods based on how slowly or quickly foods cause increase in blood glucose levels. Glycemic load (GL) is the measure of foods' ability to raise blood glucose levels. Diets that have low GI/ GL include low carbohydrate, low processed meats and low refined food.(1, 3) Low GI/GL reduces free androgens and insulin like growth factor-1 (IGF-1) levels which lead to reduction of acne. Evidence from many studies supports the role of food with high GI/GL in promoting or aggravating acne.(1, 2, 4)

Milk and dairy products

Hormonal components and bioactive molecules of milk and dairy products mainly raise IGF-1 which increases mammalian target of rapamycin (mTOR) activity and sebaceous lipogenesis resulting with acne development.(5) Many studies have confirmed that there is an association between acne and milk and dairy products.(2, 5)

Fat food

Fried, oily food, fast food and saturated and trans fatty acids which are under the topic of fat food cause increase of IGF-1 followed by the well-known pathway of acne pathogenesis. The adverse role of fat food on acne is supported by several studies.(2, 6)

Chocolate

Consumption of chocolate was found to be associated with acne in various previous literature.(1, 2, 7) However, it is still uncertain whether chocolate's acne promoting effect depends on its high GI/GL, milk content or cocoa.(2) Further studies are needed to understand the impact of chocolate on acne.

Fatty acids

Omega-3 fatty acids have been shown to decrease IGF-1 levels and reduce inflammation.(1) Although beneficial effects of supplementation with omega-3 fatty acid and gamma-linoleic acid on acne is reported in a randomized-controlled trial (RCT)(8), further studies are need to confirm their utility.

Fruit and vegetables

There are reports indicating that frequent consumption of fruits and vegetables, more than 3 days a week, has a protective effect on acne. Their acne reducing effect is due to their anti-inflammatory and anti-oxidant activities.(2) Nevertheless, there are no RCTs evaluating the role of fruits and vegetables so far.

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WHAT IS DISCUSSED IN 2021 ON ISOTRETINOIN THERAPY

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Isotretinoin treatment has been used in acne treatment for over 40 years since 1980s. It is the only medication that eradicates and has an effect on all mechanisms. Despite an approximately %30 relapse, it comforts the rest of the patients significantly. It is used with FDA approval from 12 years of age, however, it can also be used in pediatric and infantile patients with severe acne. Although there have been several studies for many years, there are still some points that needs to be clarified and it is been discussed among authors. This speech will focus on these issues that are under discussion in 2021.

What are these issues discussed?

- What is the ideal dose of isotretinoin use? Is disease severity important for dosage?
- Is the completion of cumulative dosing compulsory? Does the severity of disease affect dosage?
- How often should lab examinations be conducted for patients using isotretinoin? What should the progress be like in case of hyperlipidemia, hepatotoxicity and hyper creatine-kinase emia?
- Is there an association between inflammatory bowel disease and isotretinoin use?
- Is there an increase of depression and suicidal thoughts or attempts in isotretinoin use?
- Can interventional applications and cosmetic treatments be implemented during treatment or right after treatment?
- What kind of an approach should be adopted in case of acne exacerbation or acne fulminans development?
- Does isotretinoin use have a positive or negative effect on rhinoplasty patients?
- Is there an association between Covid and isotretinoin use?
- What should be considered for patients using isotretinoin that will have a refractive surgery or wear contact lenses?

Challenging Cases

Psoriasis:

Psoriasis is a chronic inflammatory disease that can be highly severe. Biological treatments can be used in severe cases. These treatments respond really well in many patients, but some patients can experience side effects. Here, 4 specific psoriasis cases will be shared.

1st case: A psoriasis case experiencing erythroderma while using adalimumab treatment. Intact areas were observed in areas where the medication was used. Adalimumab was stopped and secukinumab treatment commenced. Why sucbutan injected areas remained intact will be discussed here.

2nd case: Tinea corporis was detected in a patient developing severe itchy plaques under ustekinumab treatment. Immunosuppressive treatments can lead to the development of several infections. These kinds of fungal lesions can be mistaken with psoriatic plaques and if corticosteroid is applied, this can cause tinea incognito development and diagnosis can be harder. Tinea infection should be considered in case of severe itchy lesion presence despite the treatment in psoriatic patients.

3rd case: Biological treatments, especially anti-TNF agents can lead to very different paradoxical reactions. Paradoxical alopecia, onycomadesis, an ankylosing spondylitis patient developing psoriasis and his successful response to antiL17 will be told here.

4th case: How long should the treatment be halted in psoriatic patients using biological treatment if operation is planned? This will be discussed with a case.

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THE ROLE OF FOXO1-GATA6 SIGNALING IN ACNE PATHOGENESIS AND TREATMENT

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The GATA family of transcription factors is of crucial importance during embryonic development, playing complex and widespread roles in cell fate decisions and tissue morphogenesis. GATA proteins are essential for the development of tissues derived from all three germ layers, including the skin. The zinc finger transcription factor GATA6 also known as GATA-binding factor 6 has gained great attention as a key regulator of the pilosebaceous follicle. Loss of GATA6 from the skin results in dilation of both the hair canal and sebaceous ducts [1]. Recently, Oulès and coworkers [2] presented fundamental research data demonstrating that the transcription factor GATA6, which is expressed in the upper pilosebaceous unit of normal human skin, is down-regulated in acne skin. GATA6 marks a population of cells of the human upper pilosebaceous unit that contributes to both the follicular (lower infundibulum/junctional zone/sebaceous duct) and upper sebaceous gland compartments [2,3]. GATA6 suppresses keratinocyte and sebocyte proliferation and reduces the expression of epidermal proteins critically involved in keratinization (comedogenesis) and sebaceous lipogenesis [2]. GATA6 is co-expressed with infundibular differentiation markers (involucrin and KRT79) and markers of differentiating sebocytes (FASN, KRT7, PPAR and BLIMP1), but not observed in mature sebocytes [2]. GATA6 controls the identity of the sebaceous duct lineage and specifies a lineage switch between sebocytes and sebaceous duct cells [3]. Furthermore, GATA6 suppresses androgen receptor expression [3], and controls the expression of inflammatory molecules such as IL-6, TLR2 and TLR4 [2], which are up-regulated in acne lesions.

Of importance, the transforming growth factor-β (TGFβ) pathway is activated by GATA6 [2]. In particular, GATA6 negatively regulates interfollicular epidermis/upper infundibulum fate through the induction of TGFβ signaling [2]. In a human sebaceous organoid model, GATA6-mediated down-regulation of the infundibular differentiation program is mediated by the induction of TGFβ signaling [2]. In addition, activation of the TGFβ signaling pathway is necessary and sufficient for maintaining sebocytes in an undifferentiated state. The presence of TGFβ ligands decreases the expression of genes required for the production of characteristic sebaceous lipids and for sebocyte differentiation such as FADS2 and PPARγ, thereby decreasing lipid accumulation through the TGFβ receptor 2/SMAD2-dependent pathway [4]. Of note, a genome-wide association study identified *TGFB2* as a susceptibility locus for severe acne associated with reduced TGFβ2 expression in lesional acne skin compared to non-lesional skin [5].

It is of critical importance that the expression of GATA6 is induced by the transcription factor FoxO1 [2], which plays a key role in acne pathogenesis [6]. Three putative FoxO1 binding sites have been detected on the *GATA6* promoter and inhibition of the transcriptional activity of FoxO1 diminishes both GATA6 transcription and GAZA6 protein expression.

Puberty, the major period of highest acne prevalence, is associated with increased insulin-like growth factor 1 (IGF-1) signaling. In addition, Western diet with excessive intake of hyperglycemic carbohydrates and commercial milk increases insulin/IGF-1 signaling resulting in AKT-mediated translocation of FoxO1 from the nucleus to the cytoplasm (**Fig. 1A**) [6]. In fact, decreased FoxO1 signaling with increased cytoplasmic FoxO1 expression has been demonstrated in sebaceous glands of acne patients [7,8]. Thus, Western diet with high insulin/IGF-1 signaling, which is superimposed on increased IGF-1 signaling during puberty, further impairs FoxO1-mediated GATA6 expression and consecutively GATA6-dependent TGFβ signaling disturbing sebofollicular homeostasis with comedo formation, hyper- and dysseborrhea.

In contrast, up-regulated GATA6 expression contributes to the therapeutic effects of *all-trans* retinoic acid (ATRA) [2]. In fact, GATA6 mediates the effects of ATRA on sebocytes [2]. Treatment of acne with isotretinoin, the precursor drug of ATRA, normalizes infundibular hyperkeratinization (comedo formation) and suppresses sebaceous lipogenesis via p53-mediated up-regulation of nuclear FoxO1 expression in epidermal keratinocytes, human SZ95 sebocytes and human sebaceous glands (**Fig. 1B**) [9,10].

Experimental and translational evidence supports the view that acne is a disease with diminished FoxO1-GATA6-TGFβ signaling commonly induced during puberty and aggravated by Western diet as well as genetically impaired TGFβ signaling. In contrast, treatment of acne with isotretinoin enhances p53-FoxO1-GATA6 expression and augments TGFβ signaling normalizing infundibular hyperkeratinization and dysseborrhea in acne vulgaris.

Thus, recent progress in the molecular pathology of acne allows a deeper understanding of acne pathogenesis, pharmacological and dietary intervention converging on the same road of signal transduction: the FoxO1-GATA6-TGFβ pathway (**Fig. 1**).

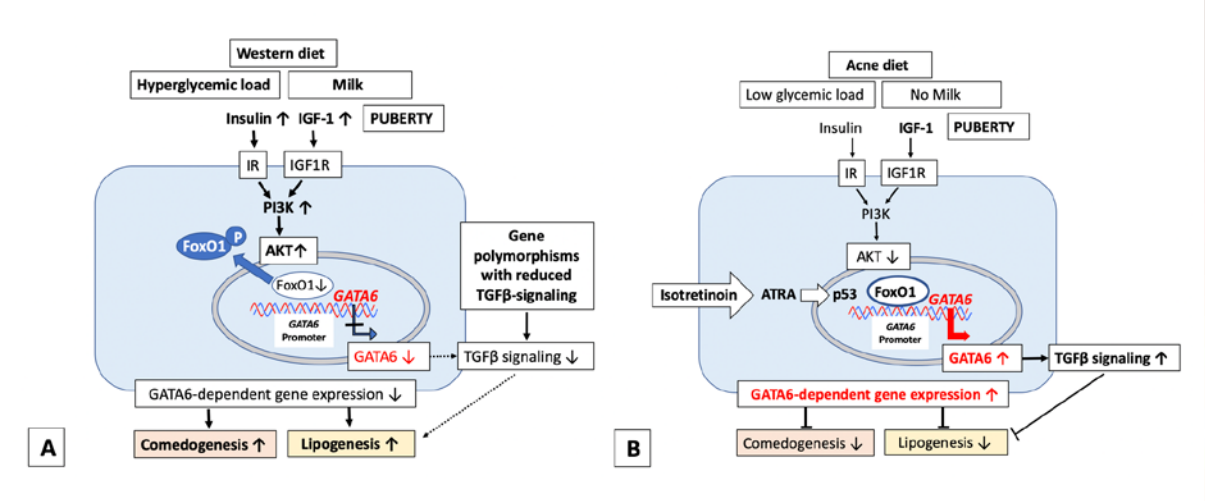

Fig. 1 A Acne pathogenesis: Impaired FoxO1-GATA6-TGFβ signaling during puberty and Western diet. Increased insulin-IGF-1 signaling decreases nuclear FoxO1 resulting in reduced GATA6 expression and diminished TGFsignaling disturbing follicular keratinization (comedogenesis) and enhancing sebaceous lipogenesis (hyper- and dysseborrhea).

B Acne treatment: Dietary intervention with reduction of glycemic load and milk intake reduces insulin/IGF-1 signaling increasing nuclear expression of FoxO1, which induces the expression of GATA6. Isotretinoin via ATRA-mediated over-expression of p53 augments nuclear FoxO1 expression, thus synergizes with dietary intervention in the treatment of acne. High GATA6 expression normalizes disturbed follicular keratinization and sebaceous lipogenesis. GATA6 stimulates TGF signaling, which is diminished in acne patients, especially those with gene polymorphisms of TGF pathway.

Abbreviations: IGF-1: insulin-like growth factor 1; IR: insulin receptor; IGF1R: IGF-1 receptor; PI3K: phosphatidylinositol 3-kinase; AKT: kinase Akt; FoxO1: forkhead transcription factor O1; GATA6: GATA6 transcription factor; TGF: transforming growth factor-.

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LASER, HIFU AND RF TREATMENTS IN HYPERHIDROSIS

Ahu Birol

Hyperhidrosis (HH) is a chronic disorder of excess sweat production that may have a significant adverse effect on quality of life. Treatment of HH depends on the etiology, localization, severity of the problem. Side effects of the treatment and the cost of procedure are other important issues.

Topical antiperspirants, oral agents, iontophoresis, botulinum toxin, devices and thoracic symphatectomy are the treatment options for hyperhidrosis.

Microwave thermolysis, high frequency ultrasound treatment, fractional microneedling, and laser treatments are recently used devices for axillary hyperhidrosis treatment.

Microwave thermolysis has been approved by the FDA for the treatment of primary axillary HH. It causes permanent destruction of both eccrine and apocrine sweat glands. The intervention ranged from a single administration to three times during the course of treatment. Overall efficacy of 90 % persisting for 12 months have been reported. Ultrasound therapy provides low levels of focused thermal injury to the eccrine and apocrine glands.

Short term adverse effects of microwave thermolysis and ultrasound; pain, edema, blister, burn, ulceration, irritation dermatitis and numbness. Long term adverse effect; altered sensation, skin sagging, hypotrichosis, hyperpigmentation, bumps, nodules, neuropathy.. All side effects resolve over the course of months after treatment.

Fractional microneedle radiofrequency involves the insertion of microneedles into the skin of bipolar thermal energy directly to the eccrine sweat glands with minimal epidermal trauma. Adverse effects include mild pain, swelling and redness.

Non invasive laser treatments using 1064 nm Nd-yag laser, diode laser have shown mixed results. Some resulting in reduced sweating and others exacerbating HH. Subdermal laser procedure treats HH by causing damage to eccrine glands.

All these HH treatments with devices need tumescent anesthesia to diminish pain. Patient satisfaction differs after treatments with the devices.

The evidence for the effectiveness and safety of device treatments for HH is limited..

INFLAMMATORY SKIN DISEASE & BOTULINUM TOXINS

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FDA approved cosmetic indications of botulinum toxin A (BoNT/A) are moderate to severe glabellar lines, and moderate to severe lateral canthal lines for Botox Cosmetic® (onabotulinumtoxinA, ONA) and glabellar lines for Dysport® (abobotulinumtoxinA, ABO).

In addition the above mentioned cosmetic benefits, according to a latest review, BoNT/A is used in different dermatological conditions associated with hyperhidrosis, including dyshidrosis pompholyx, bromhidrosis, chromhidrosis, hidradenitis suppurativa and Frey syndrome, in addition to skin diseases worsened by hyperhidrosis, such as Darier disease, Hailey–Hailey disease, inverse psoriasis, aquagenic palmoplantar keratoderma, pachyonychia congenita. Besides, BoNT/A showed efficacy in various eccrine gland abnormalities in some case series, such as multiple eccrine hydrocystomas, eccrine sweat gland naevi eccrine angiomatous hamartoma, and congenital eccrine naevus, and as a vasodilator in treating Raynaud phenomenon. BoNT/A improved the quality of life and alleviated pain in patients with painful cutaneous leiomyomas. It was proposed that other painful cutaneous conditions with and without neurological involvements, such as leg ulcers, anal fissures, lichen simplex, postherpetic neuralgia and notalgia paraesthetica, might benefit from BoNT therapy. BoNT/A has also shown therapeutic activity in patients with, lichen simplex, atopic dermatitis, plaque psoriasis, linear IgA bullous dermatosis, alopecia areata, androgenetic alopecia, facial erythema, flushing and various forms of itch.

Regarding to oily skin, in a latest analysis the authors concluded that most of the studies have suggested that intradermal injection of BoNT-A decreased sebum production and pore size. BoNT-A effectively decreased sebum production and excretion, and based on prior studies, this decrease could be achieved via blockade of cholinergic signaling and the neuromodulatory effect of BoNT-A on the arrector pili muscles.

For rosasea, inhibition of acetylcholine signaling has also been implicated in the prevention of erythema and flushing. There are several case studies of patients with recalcitrant rosacea. Two Caucasian patients received microdroplet intradermal injections of ONA into the glabella and/or cheeks at intervals of 0.5 cm. The total dose was 10 to 11 units. Patients reported an improvement in symptoms within 2 weeks of treatment, and the effects lasted for up to 4 months. In another study, two Korean patients underwent 2 treatment sessions with intradermal ONA at 1-week intervals. The total dose of ONA was 50 units across the 2 sessions for the first patient and 40 units across 2 sessions for the second. The cheeks, chin, and supra-eyebrow were injected at each session. Improvements in rosacea flushing were evident 1 week after the second treatment and lasted for 3 months. The only side-effect reported was mild pain during injection. In another proof-of-concept study investigated ABO in 15 patients with facial erythema of erythematotelangiectatic rosacea. Initially patients received intradermal injections to the nasal tip, nasal bridge, and nasal alae, but the protocol was altered to also include the cheeks, forehead, and chin. The mean dose was 25 units (range 15-45 units). Compared with baseline, erythema scores were significantly improved.

For atopic dermatitis, there is only one study with twenty-six patients. They found BTX-A as safe and effective therapy for atopic dermatitis of all grades (mild, moderate, and severe). However, being more ideal for patients with severe atopic dermatitis. Significant improvements were observed in the SCORAD score (mild, moderate, severe) were detected in all subgroups after treatment. In the placebo group, the mean SCORAD score did not change before and after therapy. There were no local or systemic serious side effects except for in six patients (29.2%) who reported injection site pain and three patients who experienced injection site swelling in the BTX-A therapy group.

Regarding to inverse psoriasis Zanchi et al used ONA (50-100 units) to reduce sweating and inflammation in 15 patients with inverse psoriasis. Treatment had been successful in 87% of cases. Ward et al demonstrated that ABO could induce remission of psoriasis in the KC-Tie2 transgenic mouse model of psoriasis. There two studies on plaque psoriasis, it was found effective in a study of 8 subjects, while a latest study with 20 patients did not see any statistical significant difference between case and control groups.

As a conclusion BoNT/A may be helpful in dermatological conditions associated with: hyperhidrosis, hyperseborrhea,

increased fibroblast and mast-cell activity, infiltration of cutaneous lymphocytes and acanthosis like hypertrophic scar, acne, erythematotelangiectatic rosacea, atopic dermatitis and psoriasis but a few more extensive multi□center RCT using a large sample is still required to determine the specific treatment mechanisms of BoNT□A, as well as the optimal injection techniques and doses.

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UNDERSTANDING THE DIFFERENCE OF EMOLLIENT, MOISTURIZER AND HUMECTANT

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Abstract

The word "emollient" is derived from the Latin verb *mollire*, to soften. It helps overall improvement of skin texture, eicosanoid production, membrane fluidity, cell signaling. Saturated and unsaturated hydrocarbons are examples of emollients. On the other hand, humect means "to wet", it consist of hygroscopic (hygro means moisture) low molecular substances. They absorb water by attracting water from dermis and a humid environment into the epidermis. More commonly they draw water from the dermis into the epidermis, making skin dryer. Combination with occlusives is highly recommended. Urea, sorbitol, panthenol, glycerol, propylene glycol, butylene glycol, hyaluronic acid, honey, gelatin and alpha hydroxy acids (glycolic acid, lactic acid, sodium pyrrolidine, carboxylic acid) are examples of humectants. Moisturizer and emollient are synonymous, even when occlusives and humectants are also part of it. Most moisturizers combine both emollients, and humectants.

Introduction

The first emollient recorded in human history is the cold cream invented by Galenus, Galen of Pergamon, a Greek doctor who worked in the Roman Empire. This cold cream was made mostly of natural oils and wax, and was used as surgical ointment rather than as a basic skin care product. From the 20th century people started to use soap to remove makeup, and basic skin care products evolved in order to supply lost hygro and soften the skin. After the World War II the industrialization of cosmetic ingredients and emollients spread, leading to the development of a wide variety of synthetic oils and semisynthetic oils made from natural oils. Today progress in chemical technology such as asymmetric synthesis has allowed the synthesis of a plethora of oils with different molecular weights using ceramides and other natural oils. Additionally, the variety of natural oils like organic certified oils are more commonly used, and this has become an alternative trend today.

Mechanism of moisturizers

There are four mechanisms: Occlusion, humectancy, hydrophilic matrices and photoprotection. The most occlusive moisturizer is petrolatum. For humentancy, the dermis possesses glycosaminoglycans, including hyaluronic acid, to function as humectants; however, other humectants include the following: glycerin, honey, sodium lactate, urea, propylene glycol, sorbitol, pyrrolidone carboxylic acid, gelatin, vitamins, and some proteins. These topically applied ingredients can draw water from the air; however, the moisturizer becomes sticky and unesthetic when this occurs. Glycerin is the most effective humectant. Hydrophilic matrices are a less popular form of moisturization characterized by the colloidal oatmeal bath where the oatmeal forms a physical protective coating over the skin preventing evaporation. Colloidal oatmeal is also used in moisturizers for much the same reason. Other high molecular weight substances that can provide a barrier to evaporation include proteins, such as growth factors and collagen fragments. Occlusion and humectancy are much more effective methods of moisturization than hydrophilic matrices. The sunscreen, whether organic or inorganic, is thought to prevent cellular damage and thus prevent dehydration.

Formulations of emollients and humectants

Creams and lotions are emulsions containing hydrophilic and hydrophobic ingredients. Creams generally have a higher viscosity, but there is no viscosity that defines a cream or a lotion. In either viscosity, the emulsion can be oil-in-water (O/W), where the oil is emulsified into the water, or water-in-oil (W/O), where the water is emulsified into the oil. O/W emulsions are the most popular for moisturizer use; however, emulsifiers are responsible for many of the problems associated with moisturizers as they can also solubilize intercellular lipids. Liquid crystal forming emulsifiers that do not damage the intercellular lipids include lecithin or hydrogenated lecithin. Other skin friendly emulsifiers include behentrimonium methosulfate and dicetyldimonium chloride. Ointments are anhydrous semisolid preparations composed of fats, waxes, animal and plant oils, and hydrocarbons. Because they do not include water necessary for

microbial growth, they can be formulated without preservatives or with a low preservative load. They are also waterproof; however, they possess poor esthetics because they are sticky and stain clothing. This moisturizer formulation may be preferred in patients with extremely dry skin or preservative allergies, but very few moisturizers and many therapeutic moisturizers fall into this category. A new formulation in moisturizers is the serum, a thin water or oilbased product applied to freshly washed skin. The serum provides minimal moisturization benefits but is used to apply an active agent to the skin beneath a moisturizer. As the serum formulation is not necessarily an emulsion, it does not require emulsifiers which could damage the active ingredient. Usually, the serum has few ingredients designed to optimize the availability of the active agent, which may be a vitamin, growth factor, botanical extract, etc.

Ingredents humectants

Squalane is a component of the human sebum. Properties such as permeability, and diffusivity to the skin are superior to other hydrocarbons and it is an ideal emollient. Most squalanes sold in the market today are obtained from deep-sea shark liver oil. However, due to the decrease of catch in recent years botanical squalene is also used. Natural moisturizing factor (NMF) is a commonly used scientific and cosmetic terms to delineate the combination of chemicals the body uses to regulate the moisture content of the stratum corneum. NMF has been synthetically formulated as a mixture of amino acids, derivatives of amino acids, and salts. Naturally occurring epidermal NMF contains amino acids, pyrrolidone carboxylic acid, lactate, urea, ammonia, uric acid, glucosamine, creatinine, citrate, sodium, potassium, calcium, magnesium, phosphate, chlorine, sugar, organic acids, and peptides. About 10% of the dry weight of the stratum corneum cells is composed of NMF broken down from filaggrin; however, formulations attempt to remoisturize the skin through synthetic NMF composed of ingredients and ratios mimicking the naturally occurring substance. One ingredient of synthetic NMF is sodium PCA, which is a sodium salt of 2-pyrrolidone-5-carboxylic acid. Synthetic sodium PCA has been shown to be a better moisturizer than glycerol and is found in several moisturizer products functioning as a humectant when used in concentrations of 2% or higher. Urea and lactic acid are also components of synthetic NMF and can diffuse into the outer stratum corneum disrupting hydrogen bonding exposing water binding sites on the corneocytes and facilitating increased hydration. This is especially important in calluses, which can be improved by foot products containing these ingredients to increase stratum corneum pliability in direct proportion to the amount of lactic acid or urea absorbed. Panthenol (also called pantothenol) is the alcohol analog of pantothenic acid (vit B5), In pharmaceuticals, cosmetics and personal-care products, panthenol is a moisturizer and humectant, used in ointments, lotions, shampoos, nasal sprays, eye drops, lozenges, and cleaning solutions for contact lenses. Hyaluronic acid is a glycosaminoglycan distributed widely throughout connective, epithelial, and neural tissues. Hyaluronic acid is a main component of the extracellular matrix, and has a key role in tissue regeneration, inflammation response, and angiogenesis, which are phases of skin wound repair. Promotes wound healing, however, show only limited evidence from clinical research to affect burns, diabetic foot ulcers, or surgical skin repairs. In gel form, hyaluronic acid combines with water and swells, making it useful in skin treatments as a dermal filler for treating facial wrinkles lasting about 6 to 12 months, a clinical treatment with regulatory approval by the FDA.

Ingredents of emollients

Saturated and unsaturated hydrocarbons are common examples of emollients. Common vegetable oils used in cosmetics are olive oil, avocado oil, sesame oil, almond oil, rice bran oil, safflower oil, shea butter, camellia oil, castor oil, macadamia nut oil. Common animal fats and oils used are beef tallow and egg yolk oil. Aliphatic higher alcohols and fatty acids are not effective emollients when used alone, but they show emollient effects when used with hydrophilic surfactants to form a self-organization called alpha gel. They have high occlusive and moisture-retaining properties. Endogenous ceramide synthesis is the first step in barrier repair. Ceramides are one of the main components of stratum corneum intercellular lipids, and are composed of 15% cholesterol ester, 5% cholesterol, 5% fatty acid, and 5% sugar ceramide. Nine different ceramides have been identified and synthetically duplicated for inclusion in moisturizer formulations distinguished by their polar head group architecture, as well as by their hydrocarbon chain proper.

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GUMMY SMILES AND TREATMENT

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A ''Gummy Smile'' or "excessive gingival display," is a smile in which the gums appear prominently and make the teeth appear smaller. This can be due to the gums, teeth, or jaw being out of proportion with the other sections, or due to the upper lip being hypermobile. The condition in which gingival tissue is located more on the cervical third of the crowns; resulting in teeth that appear shorter describes ''Gummy Smile''(1).

Also the condition chacterized by excessive exposure of maxilarry gingiva during smilling also called '' high smile line'' or '' gingival smile line'' (2). Oliveira, et al. defined 'gummy smile' as a continuous band of gingival display of more than 3 mm, during spontaneous smile (3). However, "Gummy Smile" is considered a descriptive term and not a diagnosis. Usually, the main cause of increased interlabial space is dentoskeletal dishormany (vertical maxillary excess and / or protrusion of upper incisors), which may or not be associated with anatomical and/or functional changes in the upper lip. A gummy smile is typically caused by genetics, though it can also be the result of certain medications. Diagnosing of Gummy Smile's muscular etiology is crucial for immediatelly recognizing the limitations of orthodontic threatment and aeshetic solutions. It has four types to be evaluated. The fourth type of lip line which is widely known as ''Gummy Smile'' show more than 4. mm of maxilliary gingiva in full smilling. It's biological mechanism appears to involve the combined effects of anterior vertical excess, an anincreased muscular capasity to raise the upper lip in smilling, short upper lip, and associated factors such as excessive inter-labial gap at rest and excessive overjet and overbite. Hyperfunction of the lip elevator muscles often results in excessive gingival display (EGD) and is the primary factor when lip lenght is normal and lower third of the face is proportional to the other thirds. Delayed eruption as a cause of excessive gingival display and require orthognathic surgery. However in most cases,some or all of these factors are correlated. Thus requiring complex treatment.

Gummy Smile can have a serious negative impact on overall self-confidence. People who are self-conscious about their smiles will often try to cover their mouths when they laugh or smile without showing their teeth. This is particularly true of people who worry about having gummy smiles — smiles that show too much of their gums, making their teeth look small. Luckily, there are options available to help these people feel more comfortable and confident in their smiles.

There is no technical definition for when a person has a gummy smile, given that so much of the diagnosis relies on perception. However, a smile is typically considered to be non-gummy if less than two millimeters of gum is visible between the top of your teeth and the bottom of your upper lip when you smile. If more than that is visible (typically more than three millimeters), then the smile is likely to be considered gummy. 14 percent of women and 7 percent of men have gummy smiles. However, those statistics are based on the number of people who come in to have their gummy smiles fixed — in reality, the numbers are probably higher. People often want to correct a gummy smile because it is affecting their enjoyment of life. Often a gummy smile can affect a person's overall confidence and well-being.

There are a number of options available for correcting a gummy smile, including a gingivectomy, crown lengthening, orthognathic surgery, lip repositioning, and botox. Figuring out which option is right for you largely depends on the root cause of your gummy smile. While there are many possible causes, the most common ones are gums that are long or enlarged, a short or hyperactive upper lip, teeth that are comparatively small, or an upper jaw that is overgrown and makes the gums bulge out. Different procedures tackle different root causes, so it's important to speak to a doctor before you begin correcting your smile.

Although correcting a gummy smile can be expensive and can involve some recovery time, the procedures are providing more than just a more beautiful smile — they're providing an improvement in your overall confidence and well-being.

There are different treatment options:

Gingivectomy: This procedure reshapes the excess gums to expose the natural shape of the teeth. It creates a nice balance between the gums, which are shortened, and the teeth, which are lengthened. The procedure is relatively painless and patients typically experience little post-operational discomfort.

Crown lengthening: In this procedure, the excess gum tissue and the underlying bone are cut and reshaped to expose the full length of the teeth. The process takes around an hour and usually does not require additional post-operative care.

Orthognathic surgery: This is a more intensive procedure that tackles a gummy smile that is caused by an excessively long upper jaw (as compared to the bottom part of the skull). During the procedure, the upper jaw is recontoured to the proper shape and then secured into a new position that reduces the amount of gumminess in the smile. Unlike the other procedures, orthognathic surgery involves general anesthesia and a hospital stay.

Lip repositioning: This procedure addresses a gummy smile caused by either a short or hypermobile upper lip that exposes too much gum when you smile. It is a simple and safe procedure that restricts the pull of the "elevator" muscles in your upper lip. It doesn't result in any external scarring given that all the work is done on the inner lip.

Botox: This is the least invasive and most short-term way of dealing with a gummy smile. Botox works by temporarily paralyzing the elevator muscles so that they don't drastically raise your upper lip. While this is a cheaper and faster fix than surgery, the results typically only last around three to four months — Botox needs to be repeated frequently for any long-term results. However, if you are considering eventual lip repositioning for a gummy smile, Botox can be a great way to test out what you will look like before undergoing surgery.

VISUAL LOSS IN AESTHETIC DERMATOLOGY

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Any impairment or loss of vision (temporary or permanent) secondary to central retinal or retinal branch artery occlusion occurring as a direct consequence of percutaneous injection for aesthetic treatment (4). Blindness after facial injection is extremely rare and was first reported by von Bahr2 over 50 years ago after scalp injection of a hydrocortisone suspension to treat alopecia (5). The first cases after aesthetic filler treatments were reported in the 1980s (four cases) and rose to at least 16 reported cases between 2000 and 2010, presumably related to the increase in the number of treatments being performed (4).

Depending on which artery is occluded, vision loss can be classified into six subtypes: (6–8)

1. Ophthalmic artery occlusion (OAO)
2. Generalized posterior ciliary artery occlusion with relative central retinal artery sparing (PCAO)
3. Central retinal artery occlusion (CRAO)
4. Branch retinal artery occlusion (BRAO)
5. Anterior ischaemic optic neuropathy (AION)
6. Posterior ischaemic optic neuropathy (PION)

There are also four subtypes of periocular complications associated with blindness following cosmetic filler injection (9):

Type I – Blindness without ophthalmoplegia (paralysis or weakness of ocular muscles) and ptosis

Type II – Blindness with ptosis but without ophthalmoplegia

Type III – Blindness with ophthalmoplegia but without ptosis

Type IV – Blindness with ophthalmoplegia and ptosis.

Based on previously reported case studies, improvement of visual acuity in patients with vascular occlusion after filler injection is extremely rare. By contrast, periocular symptoms such as ptosis and ophthalmoplegia recovered dramatically (9).

TREATMENT ALGORITHM FOR OCULAR PAIN AND BLINDNESS AFTER FACIAL FILLERS

Indications for treatment are sudden onset ocular pain and/or loss of vision. The goal is to quickly reduce the intraocular pressure to allow for the emboli to dislodge downstream and improve retinal perfusion (4)

1. Treatment must start within 90 minutes.
2. Stop treatment immediately.
3. Place patient in supine position (10)
4. Call emergency medical service and prepare to transfer patient to hospital setting as soon as possible.

TEARS TROUGH PROBLEMS AND FILLERS

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Tear troughs are a complex area to treat and should only be attempted by experienced injectors. When performed correctly, dermal filler in the tear trough can reduce the apperance of tiredness under the eyes and improve the sunken effect that happens as we age. Tear troughs treatment should only be undertaken by experienced practitioners. As you will see – problems can occur as a result of either poor filler choice, a lack of understanding of patients anatomy or poor patient selection.

1. **Overfilled tear troughs:** Tear trough swelling complication

Problem: Even as infants we have a subtle tear trough and the aim of treating the under eye area should not be to eliminate the trough entirely. Overfilling the tear trough can lead to lumps, often seen when smiling or when looking at the tear trough from above. As injectors we often see patients who have had filler poorly placed in the tear trough, often with a cannula, causing a sausage shaped lump under the eye.

Solution: Dissolve the filler and start again. As hard as this is to hear, overfilled tear troughs do not look good and it is best to dissolve the filler and build up the area again using less product.

2. **Blue/green discolouration under the eyes after filler. The 'Tyndall effect'**

Problem: The 'Tyndall' effect is a phenomenon seen when filler is injected too superficially under the skin. When we treat the tear trough the filler should be placed deep under the skin. If placed too superficially the filler can give a blue / green discolouration which is seen easiest in daylight.

Solution: Filler placed too superficially should also be dissolved. We can use an enzyme to break down the filler. After a week come back so we can place the filler in the correct area.

3. **Swelling under the eyes after filler**

Problem: Some patients can experience swelling in the mid cheek or under the eye after tear trough filler. The problem here is that the filler has been placed above the orbicularis retaining ligament or too superficially under the skin. Dermal filler attracts water and this can cause intermittent swelling under the eye if the filler is placed too closely under the skin.

Solution: Again, the solution here is to dissolve the filler.

The dermal filler should be placed deep under the skin, under the retaining ligament to reduce the chance of swelling. We have to be careful in our choice of dermal filler product as they vary in how much water they attract and how much they have the potential to swell.

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FAT PADS OF THE FACE AND AESTHETIC DERMATOLOGY

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Most of the facial fat compartments undergo atrophy with increasing ag however, the nasolabial fat compartment undergoes hyperthrophy with aging. The lateral fat compartment has a tendency to deflate in the forth decade; it is thin, fibrous and vascular. The middle fat compartment has a tendency to deflate in the forth decade as well; it is thick, relatively avascular and easy to dissect. The malar fat pads (superficial and deep) undergo defletion in the fifth decase. The superificial malar fat pad is vascular and fibrous along the transition between middle and malar compartments. The deep malar fat pad's halmark of deflation is the vertically long lower lid and the infraorbital V deformity. The jowl and the nasolabial compartments rarely undergo deflation, instead they are accenuated with the deflation of the middle and the malar compartments respectively.[1]

The face is arranged in five layers which are the skin; subcutaneous fat including the retinacula cutis (composed of fibrous connective tissue); superficial musculo-aponeurotic system (SMAS); deep fat and the periosteum or deep fascia. The thicknesses and number of layers depend on the region. Fatty tissue in the face is located in the superficial and deep compartments, seperated by the SMAS.[2]

The superficial compartments of the face are superficial lateral forehead compartment, superficial central forehead compartment, superficial upper temporal compartment, superficial lower temporal compartment, superficial nasolabial fat compartment, superficial medial cheek fat compartment, superficial middle cheek fat compartment, superficial lateral cheek fat compartment and the jowl fat compartment. The deep compartments are (deep) upper temporal compartment, (deep) lower temporal compartment, superior premasseter compartment, middle premasseter compartment, lower premasseter compartment, deep lateral forehead compartments, deep central forehead compartment, retro-orbicularis oculi fat compartment, medial suborbicularis oculi fat compartment, lateral suborbicularis oculi fat compartment, deep pyriform space, deep medial cheek fat compartment and deep lateral cheek fat compartment.[2,3]

One of the aesthetic procedures done using the fat compartments is the autologous fat injection. Here, fat compartments provide topographic guidance to optimize injection outcome. Fat harvesting is done by manual lowpressure lipoaspiration using a blunt 3-mm cannula. The inner thighs and abdomen are the ideal donor sites because they contain the highest concentration of stromal vascular cells and the procedure is less painful when perforemed there. Approximately 1 to 3 cc is injected into each compartment, followed by gentle massage to the malar region. Approximately 1 to 2 cc is injected into each side fort he chin. Approximately 1 to 3 cc is injected again in anterograde and retrograde fashion, with improvement of aesthetic line as the endpoint to the mandibular border. One cc is injected to the temporal line. One cc injection is then needed to correct the hollowing in a radial fashion lateral to the lateral eyebrow. Deep facial compartments are always restored first because they are the foundation of facial volumization.[4]

One of the most important characteristics of facial aging is the deepening of the nasolabial fold with reduced malar highlight caused by sagging of the midface. Midface lifting can be achieved by the use of polidioxanone threads. By way of the PDO cog threads, deep medial fat pad and inner layer of the superficial muscular aponeurotic system are lifted.[5]

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BLEPHAROPLASTY FOR THE DERMATOLOGIST

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Upper eyelid blepharoplasty is one of the most common procedures in oculoplastic surgery practice which is also being more commonly performed due to ageing population in recent years. In addition to being a major cosmetic procedure for periocular rejuvenation, decreased peripheral vision and visual field loss, impaired visual acuity, compensatory chin-up, backward head tilt, reading difficulties, eye strain and fatigue are functional indications for upper eyelid blepharoplasty. Upper eyelid blepharoplasty is also reported to provide significant relief for tension type headache and to improve headache related quality of life. While upper lid blepharoplasty is considered to be quite straightforward and safe, severe problems regarding not only the appearance but also the function of the eye and the quality of life may if it is performed improperly.

Careful patient selection is the first crucial step as in every surgical procedure. Patients with psychological problems, pre-existing dry eye conditions, active cicatrising skin conditions or history of keloids must be excluded at first. Detailed patient history should be obtained including chronic systemic diseases, autoimmune conditions, anticoagulant medications and drug allergies.

Next comes thorough preoperative examination with photographic documentation in addition to full ophthalmic examination including best corrected visual acuity, anterior segment examination for the evaluation of lacrimal function and possible dry eye disease, examination for pupillary reflexes, ocular alignment and extraocular motility tests. Standardized eyelid measurements are very useful for the evaluation of the case. These must include the measurement of vertical palpebral fissure, levator excursion, lid crease height, margin reflex distances (MRD 1 and 2) in addition to the evaluation of the strength of orbicularis oculi. Accompanying problems like eyelid ptosis, brow ptosis, lower lid laxity and lacrimal gland ptosis which might affect the surgical outcome should be carefully evaluated for optimal planning. Besides all these, understanding the expectations of the patient is one of the most important steps of the consultation before the procedure.

One of the most significant steps of the preparation phase is appropriate marking of the eyelids before surgery. Marking of the skin crease and skin for excision may be performed in sitting and/or supine position. Compass caliper is very helpful in case of lid crease asymmetry. After marking the skin crease, forceps pinch technique is used to determine the borders of the skin excision.

Local anesthesia with systemic intravenous sedation is the choice of anesthesia type but it depends on the preference of the patient and other possible simultaneous procedures. Local anesthesia including dilute epinephrine is always utilized, even in cases under general anesthesia.

For the surgical technique, skin incisions may be done with either scalpel blade, electrocautery, radiofrequency or laser. Haemostasis should be carefully obtained to prevent complications. Small medial opening of the orbicularis oculi should be adequate for fat removal which is typically medial. Gentle manipulation of the fat pads is crucial to prevent bleeding. Care should be taken for appropriate amount of fat removal avoiding overexcision. If necessary, lid crease fixation may be accomplished with separate absorbable sutures. Adjunctive procedures like levator surgery for ptosis, brow elevation and/or fixation for brow ptosis and lacrimal gland repositioning are performed according to the presurgical planning. Although closure of the skin may be performed with different suture materials and suturing techniques, running 6/0 prolene suture is of choice. Care must be taken to close the wound under minimal tension. Cold compresses are applied for two days after the procedure with topical antibiotic ointments twice a day. Sutures are removed on the 7th postoperative day.

Although upper lid blepharoplasty is generally a straightforward procedure for an experienced and careful surgeon, it is important to recognize potential complications and employ appropriate management. Most of these are not severe and may be managed with conservative care including prolonged bruising and swelling of the eyelids, mild lagophthalmos and exposure keratitis. Although vision threatening complications like retrobulbar haemorrhage causing orbital compartment syndrome and globe rupture are rare, they may end up with catastrophe. Infection, lagophthalmos, dry eye syndrome, lacrimal gland injury, ptosis, diplopia, sulcus deformity, incision problems like canthal webbing, scarring, asymmetry of the lid crease, skin, fat or brow position are other complications to be dealt with.

SIMULATION MODELS IN DERMATOLOGY EDUCATION

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Simulation-based training has gained favor as a means to teach technical skills without jeopardizing patient safety. The use of simulation to teach basic dermatologic procedures in dermatology training is expanding rapidly. It has been shown to directly improve

clinical knowledge, teamwork, communication, and procedural skills. In this talk, the scope and importance of simulation models in dermatology education will be reviewed and discussed.

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EHEALTH TECHNOLOGIES IN DERMATOLOGY

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E-health (also written ehealth) is a relatively recent healthcare practice supported by electronic processes and communication. The term can covers a range of medicine and healthcare services or systems including electronic health records, computerized physician orders, e-prescribing, clinical decision support systems, telemedicine, telerehabilitation, telesurgery, teledentistry, health informatics, virtual helathcare teams, m-health, medical research using grids, healthcare information systems. M-health referred to health applications and links on mobile phones. Although it is a common convention about the importance and potential benefits of e-health, the realisation of these benefits has generally been slower than expected hitherto. However, with the start of the pandemic in the last year, e-health has become more important than ever.

E-health can allow previously underserved populations to access services. Increasing population with more chronic diseases is challenging health services in both developed and developing countries. Today, prevention of diseases and encouragement of healthy lifestyles becomes even more important. E-health can be used to help positive behavioral changes, assist to latch on to a healtier life style, more active patient engagement and patient involvement. Access to e-health services may be easier than traditional services, and its usability has gained importance during the pandemic period as it provides social distance. It also helps lighten the burden on healthcare. It provides the opportunity to provide healthcare services to more people at a low cost.

In this lecture, a series of up-to-date dermatological studies from around the world that provide important information on key issues related to e-health services will be presented.

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BEST DERMATOLOGY SOFTWARE

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Computers and smartphones have become an essential part of our everyday life as well as our daily clinical practice during the last decade. These devices dramatically facilitate our complicated and challenging tasks by running various third-party software and applications that are consistently increasing in number and variety over the years. As medical care providers, we frequently use this software and applications on a daily basis during monitoring patients, diagnostic processes, treatment decisions and algorithms, educational and academic activities, calculating complex scoring systems, and storing and sharing clinical, dermoscopic, or pathologic images. On the other hand, patient-based applications may provide consultation of skin lesions to an expert, early cancer self-detection, and patient education.

Software technology has been rapidly developing every year. In parallel with that, the number and variety of software in the field of dermatology are increasing as well. Therefore, it is hard to make a decision which software is the best in dermatology. However, we can try to define the properties of the best dermatologic software. The best dermatologic software should completely fulfill its intended purpose, provide evidence-based information, be easy to use and access, safe, well organized and designed, understandable by all users, open to development, affordable or free of charge, have no conflict of or monetary interest. In this lecture, software and applications that could fulfill these criteria will be discussed in detail.

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INDUSTRY 4.0 / 5.0 AND DERMATOLOGY

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The terms like Industry 4.0 and Industry 5.0 are the names corresponding to Industrial Revoution. It is proceed towards more efficient life with the new technological developments in every field such as transportation, communication, daily life and health.

1st Industrial Revolution has began offically with the production of first mechanical loom in 1764. Steam machine invented by James Watt in 1776, caused big changes firstly in England and later all over the World. 2nd Industrial Revolution has started with the coming up energy sources such as electric and petrol towards the end of 19th century. 3rd Industrial Revolution called as digital revolution started in the middle of 20th century. The production and development of semi-conductor electronic pieces have accelerated with the invention of first transistor in 1947 and integrated circuit in 1959. 4th Industrial Revolution brought us newly terms like internet of things, industrial internet of things, cloud storage, artificial intelligence (AI) etc. All the machines communicate with each other, effect of human minimized, datas are handled in real time and digital twin can be formed. At the end industry 5.0 is the term for unmanned and public-oriented technologies. Although superior technologies produced in this manner.

Artificial intelligence is a kind of machine software which can imitate cognitive personal behaviours such as learning and problem solving. Learning of machines means completion and continuation of decision making process by learning and making changes (1). Artificial intelligence terms was first used in Dartmouth College Conference in 1956. In 1970's researchers reported that artificial intelligence can be used for health science (2). It has been seen that artificial intelligence can be used for medical image scanning, diagnostic aid, biotechnology, medical research and development. Artificial intelligence was not attracted attention in early periods and it could not find place itself for the applications. This is because comparatively data is not collected enough and the lack of parameters (3). The dermatological usage of artificial intelligence began later than the usage of radiological usage. Dermatology is a branch of science which is based on morphological features and visual pattern evalution. From this point of view dermatology is very suitable for artificial intelligence definition and diagnosis. In the study carried out in Stanford University 129,450 clinic images taken for different diseases and loaded to artificial intelligence was taught to recognize the illness in the light of these images. The results were compared with 21 board certified dermatologists, they were wanted to allocate keranitocyte carcinomas from benign seborrheic keratoses and malignant melanomas from benign nevus. It was seen that artificial intelligence evaluated the images as successful as the dermatologists in both groups (4). In another study carried out soon; artificial intelligence educated with 12378 dermastoscopes images and 100 melanoma images, 145 dermatologists evaluated the same images was compared and it was seen that the results of artificial intelligence was as true as dermatologists (5). Artificial intelligence is not limited to the images sent to itself; it also speeds up the sharing in regional internet by the way of data mining and the progress time which will be held with the way of adding database (6).

In recent years, many developed countries have developed new artificial intelligence strategies for the future. Among the examples for these strategies are; National Al Researches and Development Strategic Plan developed by United States, Growing the Al Industry in UK developed by United Kingdom, The State Council on Promoting Action Guidance for Internet+, A new Generation of Al Development Plan developed by China and The Age of Al:Towards a European Strategy for Human-Centric Machines developed by European Union.

There are some problems in clinical practice. Lack of image scale of skin disease, information sharing among centers and not to prove image standardisation are the problems. Another problem is decreasing the reliability of research results and the rate of artificial intelligence. The co-operation among computer science, biomedical and medical staff is very important. Privacy of personal data and legal issues appeared with artificial intelligence are the other problems. Should not be forgotten that images are not enough for diagnose. Additional information and anamnesis were needed to diagnose, to plan treatment and to determine prognosis. These steps must be applied by artificial intelligence (7). At the end artificial intelligence cannot replace the relationship between physcian and patient.

With the developments in mobile technology, smart phones are always there for end-users in every field of life. We can load third party applications for adding unlimited process apart from their own functions. Mobile applications can be used for diagnostic purpose by clinicians, educational purpose for the students and health status tracking purpose by the patients. Health applications known as mHealth, they are incerasing day by day. Diabetes Mellitus is the leader for mobile application count for a single disease (4). Teledermatology makes these applications popular and worthy for dermatology. The most popular dermatological applications are teledermatology apps and dermatological informative

applications (8). Mobile applications are also used for follow-up for diseases, treatment reminders, schedulers and co-operation between patient and physcian (9).

Mobile dermatology applications are generally effective for determining risk of skin cancer. After the patient's informations are loaded, they can predict the risk by using related lesion's image. It is not enough alone but it helps people by giving an idea. Here it is important to be known that mobile applications decisions are not always true; false positive decisons can be evaluated and corrected by clinicians but false negative decisions may cause delay for patients to get effective treatment (10). Masud et al. evaluated dermatology applications under four criterions; convenience for purpose, content, accuracy and design. 9 applications got high score and interestingly some of most downloaded apps were not in this top 9 . Download count must not be enough for decision (11).

How to choose right application? criterias are; (12)

1- Application must be supported for different platforms especially for android and IOS,

2- Free applications should be preferred more than the paid applications in view of multiplicity use and sharing,

3- User friendly applications should be preferred for longer usage,

4- Large amount of data storage and high reliabilty for application should be preferred because these applications include images and personal datas so; privacy rules must be read and approved carefully,

5- Comments about application should be read and the logical ones should be taken into account,

6- Regular update and easy feedback to developers should not be overlooked, both are necessary for app maintenance.

Conclusion

Artificial intelligence and computational neural networks are the new, exciting fields for diagnosis of skin diseases. It is seen that artificial intelligence is very effective about melanom and non-melanom skin cancers and other diseses. It was seen that the skin cancer evaluations made by neural networks as effective as the experts who have board certificate (D34). It is seen that artificial intelligence will be more entegrated with mobile apps in the future. Co-operation with dermatologists during development phases of application will increase reliability and accuracy.

Smartphones and applications are always with us. The new applications should be developed multidirectional and effective. The biggest concern about the applications is their scientific validity and the way of increasing scientific reliability is to study with expert dermatologists during the developing process of applications. Artificial intelligence based and customizable applications are seen as the future of dermatological applications.

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FLOW CYTOMETRY IN DERMATOLOGY

Emine Müge Acar

Flow cytometry is the measurement of physical or chemical characteristics of cells or other biologic particles as they flow through a fluid stream. Flow cytometry can be performed on a variety of tissues, including peripheral blood, bone marrow aspirates, skin biopsies, and tissue culture cell lines. Flow cytometry is used in multiple disciplines such as immunology, virology, molecular biology, cancer biology and infectious disease monitoring. In dermatology, flow cytometry is also used in the diagnosis and follow up of various skin diseases.[1]

Mechanism

Flow cytometry systems have five components including a laser light source, fluidics that allow the cells to stream as a single file through the laser, optics that collect the light generated by the cells in the beam, photomultipliers that convert the light signals to electronic data, the computer system processing the data.

The angle of light emitted from the analyzed cell gives optical information known as forward scatter (FSC) and side scatter (SSC). Forward scatter is light scattered at a small angle and detected by a sensor on the opposite side of the laser source. This provides information on the relative size of the cells. Light that scatters off the cell at a 90° angle is called "side-scatter," and gives information about the granularity of the cells. Light scatter is not related to fluorescence. A fluorophore, which is a fluorescent chemical bound to the antibody, is chosen according to the specific wavelength of laser existing in each flow cytometer. If the selected markers are present on the cell surface the laser energy will be absorbed by the bound antibody–fluorophore and subsequently a specific wavelength of light is emitted as the cells passthrough the laser. The emitted light is detected by an optical system, allowing for multiple surface markers to be read simultaneously and collected by a computer. [1]

A major application of flow cytometry is sorting cells for further analysis which makes possible to capture and collect cells of interest for further analysis. Therefore the cells can be analyzed microscopically, biochemically, or functionally. "Gating" is the term used to describe the selection of a subpopulation of cells for analysis.

Flow cytometry is used in various areas including in particle analysis (size distribution, refractility, concentration), cell sorting (cell enrichment, cell concentration, verification of analysis), oncology (cell classification, clone enumeration, proliferation rate, DNA quantitation), cell biology (DNA content, RNA content, chromosome karyotyping, protein content, enzyme activity, intracellular PH, membrane potential, viability, membrane fluidity), immunology (epitope density, epitope type). [1,2,3]

Cutaneous T-Cell Lymphoma

Cutaneous T cell lymphoma (CTCL) is a malignancy of phenotypic helper/inducer T cells which infiltrate the skin, migrate into the epidermis and localize in T-cell zones of lymphoid structures. The pathologic evaluation of mycosis fungoides (MF) is a challenging topic in dermatopathology. In addition to the histologic findings, immunohistochemistry and molecular studies are frequently used to support the diagnosis of MF.[1] Flow cytometry is an adjunctive method which is efficient and sensitive in detecting and enumerating MF/SS cells in the peripheral blood. [4] Grossly abnormal cells are often not present in MF and the lymphocyte compartment can be studied in greater detail with FCM. Lymphocyte typing of peripheral blood is also a valuable staging and diagnostic tool in the evaluation of newly diagnosed cases. FCM can also be used in the immunophenotyping of lymph node cells.

The first indication of hematogenous involvement in MF is an increasing CD4: CD8 ratio. This ratio will increase with both the increase of malignant CD4+ cells in the circulation and with the decrease of CD8 +cells, which also occurs in the progression of CTCL. In addition, patients with more normal CD4:CD8 ratios are more immunocompetent and this finding shows a favorable response to immunotherapy with photopheresis. The CD4:CD8 ratio increases before the white blood count is elevated. The best utilization of FCM in CTCL patients is to obtain baseline values at the time of diagnosis and these values should be reassessed every 6 months, In case of new cutaneous eruptions it is valuable to assess whether the peripheral subset status has changed.[1] Flow cytometry can also be applied to routine skin biopsies and contributes to the diagnosis and subclassification of cutaneous lymphoid lesions.[5]

HIV infection

HIV infects CD4 positive cells and leads to eventual cell death; this causes a marked decrease in circulating CD4+T cells. FCM can be used to analyse the treatment response of antiretroviral treatment which can be evaluated by periodical assesment of total CD4 and CD8 lymphocyte levels at the time of the diagnosis and in the follow up. [1]

Adult T-cell Lymphoma/Leukemia (ATL)

The characteristic finding of ATL is very high level expression of IL-2 receptor (Tat) by peripheral blood and skin-infiltrating lymphocytes. ATL can often be detected by the presence of an increased amount of CD25 (Tat, the high affinity IL-2 receptor) expression in the peripheral blood. With disease progression, the amount of CD25 expression increases and this parameter can be used in the follow- up of patients on therapy. [1]

Systemic Lupus Erythematosus

Two-color FCM analysis shows that the number of T4 + 2H4 + lymphocytes in SLE patients is reduced and this is exaggerated in patients with active SLE.[9] The T4 + 2H4 + subset is thought to be the subset of helper T-cells that play a role in the activation of CD8 cells. These findings also support the CD8-mediated suppression of antibody-producing B-cells which play a role in the pathogenesis SLE. [1]

Progressive Systemic Sclerosis

Increased CD4: CD8 ratios in progressive systemic sclerosis **(**PSS) patients were seen in younger patients with shorter disease duration and more extensive skin involvement than patients with a normal ratio. [1] In a study by Wohlfahrt, using flow cytometry, type 2 innate lymphoid cell counts, which are similar to Th2 cells in cytokine production,were found to be increased in patients with systemic sclerosis and was found to be correlated with the extent of skin fibrosis and the presence of interstitial lung disease. [6]

The circulating endothelial cells in patients detected by FCM, may point to endothelial disease and may be a promising new clinical marker for active systemic sclerosis**.** [7] In literature there are studies about the use of flow cytometry in several other cutaneous diseases. Sampaio et al. reported that detection of IgG anti leishmania antigen by FCM can be used as a diagnostic test for cutaneus leishmaniasis. Scarsi et al reported the use of FCM to detect the HLA-B*58:01 positive individuals to analyse the risk of allopurinol induced severe cutaneous adverse reactions. [8] In a study by Fernandes, flow cytometry based immunophenotypic analysis of bone marrow mast cells was found as the most adequate test for systemic mastocytosis due to its high sensivity.[9]

Flow cytometry seems to be a promising adjunctive technique in the diagnosis and follow up in dermatological diseases. As characteristics of circulating cells in these diseases are defined by further researches, FCM will have wider clinical applications in dermatology.

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BLUE LIGHT AND SKIN HEALTH

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Nowadays, we are moving from the idea that light is only for enabling us to see to the idea that light is more than that, since it is responsible for maintaining, and have a profound impact, on our circadian rhythm synchronisation. And this simple fact alerts us for the quality and quantity of light that we need in order to accomplish a good vision and, also, improve our health and wellbeing, not forgetting about our emotions.

Since becoming an industrialized society, we have introduced artificial lights in our life in order to extend "daylight" time, this is called Light Pollution.

Blue light is emitted visible light between the wavelengths of 400 to 500 nm. The main source of blue light is sunlight, but digital screens, light-emitting diodes (LEDs), and fluorescent lighting serve as additional sources. Concerns about the negative effects of blue light on the skin have rapidly increased over the past 15 years, and consequently, the urge to learn more about this topic is increasing as well (1). We spend most of our lifetime in indoor environments, thus we are under longer and more intense exposures to artificial light, and nowadays it is almost the same that saying that we are under blue light which has a significant impact in human wellbeing (2).

Exposure to blue light is unavoidable. Blue light sources are classified in two major group: Manmade blue-light and natural blue-light. Man made blue-light sources are digital screens like laptops-cell-phones-tvs etc, fluorescent lights and light emission diods (LEDs). The natural source is the sun, especially in cloudy weathers. Blue-light emitting intensity decreases from sun to TVs, monitors, laptops and cell-phones.

Blue-light affects circadian rythm changes, eye health, skin health and mood changes (3). Blue light has been shown to generate reactive oxygen species and induce oxidative damage in the skin similar to UV radiation. Blue light can penetrate deeper into the skin layers, induce cellular dysfunction and DNA damage. Negatively impacts photoaging and inflammatory skin conditions. Flavins are the main photosensitizers for blue light causing oxidative stress. These flavins produce superoxide which is the main free radical caused by exposure to blue light. Blue light exposure stimulates flavins. Flavins produce reactive oxygen species (ROS). ROS are significantly related with photo aging and carcinogenesis (4).

Blue light induces the enzymes matrix metalloproteinases (MMPs) in skin cells, contributing to photoaging. These MMPs not only degrade the present collagen, but also block new collagen formation and in turn prevent repair. Blue light also has a negative effect on collagen and elastin.

There are different suggestions for pigmentation mechanism caused by blue light. First theory is, exposure to blue-light makes decrease in carotenoids, decreased carotenoids causes formation of free radicals, and so oxydative stress on melanogenic precursors result in pigmentation changes. Pigmentation changes result in melasma and age spots. Another theory of pigmentation is blue-light exposure promotes opsin-3 signaling and thus increases formation of protein complexes result in hyperpigmentation. Darker skin types are more likely to generate hyperpigmentation from blue light exposure (5).

It's easy to use protector physical filters to avoid blue light exposure. Anti-glare screens and protectors, blue-light filters, mobile 3rd party apps and the glasses with digital light protection may help to protect from blue-light harms. There are numerous agents claim that they protect blue light's hazardous affects. Exogenous antioxidants administered topically and/or orally were shown to beneficial in the case of UV radiation; this effect has not been confirmed with blue light yet.

There are also beneficial effects of blue light in daily practice: Small doses of lower-energy blue light treatments are effective for; actinic keratosis, psoriasis vulgaris, eczema, acne vulgaris and photorejuvenation (1).

As conclusion; it is known that the blue light from the sun can cause skin damage and oxidation, blue light from devices may result in similar effects. The effects of blue light on the skin depend on the wavelength and the intensity of the exposure. Low exposure to high energy blue light can be used for aiding skin problems and help minimize

dermatological problems. Longer exposure to high energy blue light can increase the amount of DNA damage, cell and tissue death, and injury, causing eye damage, skin barrier damage, hyperpigmentation, and photoaging

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ELASTOGRAPHY IN DERMATOLOGY

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Palpation has played an important role in the general physical examination of patients because it provides information about the physical characteristics of the tissues. A loss of elasticity or increase in rigidity of organs or tissues has traditionally been associated with a poorer prognosis in inflammatory processes, which histologically tend to be associated with fibrosis, and in tumor processes, in which the elastic properties of healthy tissues decrease . Estimation of the elasticity or rigidity of tissues could therefore facilitate early, noninvasive monitoring and treatment of inflammatory and tumor processes.

Elastography is a technique in which ultrasound is used to detect changes in tissues. It was first defined by Ophir et al. as a method of determining the mechanical propperties of biological tisuues . Until today elastography has been used in various diseases, including tumors of the breast, thyroid and liver, as well as in inflammatory processes in the same organs.

In medical use, elastography is based on measuring the displacement that occurs before and immediately after mechanical stress is applied to tissues . To understand elastography technique, it is necessary to learn some concepts. When a tissue is subjected to pressure, it deforms and tends to recover its initial shape which is called *elasticity.* The resistance of the tissue to deformation is called *rigidity* or *stiffness*. The term *strain* describes the change in the relative length of a structure subjected to pressure with respect to the surrounding tissue. In addition to this physical phenomenon, a series of waves perpendicular to the displacement of the pressure wave which is hnown known as *shear waves* -are also generated in the tissue. Special equipment is required to detect small tissue displacements, as soft tissues in the body have a high water content and are virtually incompressible

According to the clinical guidelines on elastography published by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB), there are two basic types of elastography:

1. Strain elastography (SE), which assesses tissue deformation, a qualitative method
2. Shear wave elastography(SWE), which characterizes the shear waves, a quantitavi method

Today, elastography is used in the diagnosis and follow-up of various diseases in dermatology. The areas where elastography is used most frequently in dermatology can be summarized as follows:

Skin Tumors : The most widely investigated application in elastography of skin tumors is the differentiation of benign and malignant tumors. In tumors, the mechanical properties of the tissue are generally altered in a way that allows the tumor to be differentiated from the adjacent healthy tissue. Although benign subcutaneous tumors have a recognizable appearance in B-mode ultrasound, in doubtful cases elastography could play a useful role in the differential diagnosis. Elastography shows that malignant skin tumors are stiffer than the surrounding tissue. Elastography has been used to study melanoma. The melanomas were hypervascularized and had multiple vascular pedicles, it is shown that the lesions were stiffer than the adjacent skin. The lesions with the highest degree of vascularization had the greatest stiffness. The correlation between melanoma neovascularization and prognosis is well known in the literature. Therefore, lesion stiffness could be a prognostic factor in melanoma.

Lymph Node Enlargement : The aim of ultrasound assessment of lymph nodes is to noninvasively diagnose malignant lymph nodes in patients with clinically suspicious lesions. Lymph nodes have an elastic structure in which the cortex tends to be less rigid than the capsule and the hilum.Benign enlarged nodes generally tend to be soft, whereas malignant nodes tend to be stiffer. However, lymphomas are less stiff than metastatic nodes and similar in stiffness to inflamed nodes. Therefore, benign and lymphomatous nodes cannot be distinguished with elastography alone.

Inflammatory Skin Diseases : Elastography has been more extensively developed in fibrotic and sclerotic processes that are primarily cutaneous or systemic (morphea/systemic sclerosis), in which clinical measurement scales have very

limited sensitivity and specificity. Initial studies carried out in systemic sclerosis, have indicated that dermal stiffness is greater in patients with systemic sclerosis than in controls. However, the reproducibility of the technique at other sites, such as the fingers, was variable, perhaps because of the proximity of the bony surface of the phalanges. The authors concluded that elastography reduces inter- and intraobserver variability in the assessment of dermal thickness of the fingers in patients with systemic sclerosis.

Elastography has also been used in other fibrotic processes, such as cutaneous processes secondary to irradiation.

Other Skin Conditions **:** It ıs suggested that lower strain values in patients with lipodermatosclerosis than in patients with lymphedema, regardless of the degree of lymphedema, ın a study using elastography

Elastography has also been used to assess pressure ulcers. Experimental studies in phantoms and animals have found that the stiffness of the surface skin increases quickly after sustained pressure and that this could be an early marker for the detection of areas at risk of ulceration

As the conclusion, Elastography in dermatology is an emerging technique that has great potential in the physical characterization of the tissues of the skin. Dermatologists also have new tasks in integrating the rapidly developing technique into dermatology.

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CONTINUOUS-WAVE LASER HYPERTHERMIA IN DERMATOLOGY (THERMOTHERAPY)

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Introduction

Heat has been used as a therapeutic and curing modality throughout human history. There are ancient Egyptian medical papyri that describe the use of this method for treating strangulated hernias. Galen described the humors as warm, cold, moist, and dry. Keeping them in balance was the key to good health. In several cultures, hot spas, steam baths, hot tea and other hot drinks, heating pads and heat lamps have been used as local heat therapy. Heat treatment is useful for pain relief and for treating deep cutaneous infections. The theory is, heat increases blood flow and therefore speeds healing.

The heat is used in many areas and the frequency of dermatological use has increased lately. Thermotherapy is successful in the treatments of many skin diseases.

The use of thermotherapy in skin diseases	
Bacterial infections	**Viral infections**
Staphylococcal infections	Human papillomaviruses
Streptococcal infections	Herpes simplex viruses
Acne (P. acnes)	Kaposi sarcoma
Mycobacterial infections	**Skin tumors**
M. ulcerans	Melanoma
M. chelonae	Nonmelanoma skin cancers
M. marinum	Bowen's disease
M. avium complex	
Fungal infections	**Primary cutaneous anaplastic large cell lymphoma**
Mycetoma Sporotrichosis	**Postherpetic neuralgia**
Chromomycosis	**Pernio**
Parasites	**Cosmetology**
Cutaneous larva migrans	
Leishmaniasis	

Thermotherapy has mostly been used in infectious skin diseases, skin tumors, and cosmetics. Although there is evidence about thermotherapy has direct toxic effects on microorganisms and/or up-regulates the body's immune response, its anti-infective function is not completely clear. The most comprehensive experiences of thermotherapy has been in the treatment of leishmaniasis, sporotrichosis, and chromomycosis. It has been shown that local heat application in leishmaniasis lesions causes a systemic cytokine response that causes a decrease in interferon- α and tumor necrosis factor-α. Thermotherapy can lead to a variety of changes that affect the antimicrobial activity, immune system responses, and cytokine profiles. Thermotherapy has also been shown to have an antibacterial effect on Propionibacterium acnes, which is involved in acne pathogenesis. When exposed to heat and other stresses, cells can respond by induction of heat shock proteins that cause cell death. Therefore, thermotherapy plays a role in acne clearance through antibacterial effects. The term 'hyperthermia' also refers to various techniques of heat application administered as an adjunct to already established strategies in the treatment of cancer patients. In humans, a variety of superficial and deep tumors have been treated by hyperthermia with different degrees of success.

- superficial cutaneous tumors,
- recurrent breast cancer,
- recurrent malignant melanoma,
- head and neck squamous cell carcinoma, lymph node metastases,
- glioblastoma,
- cervical carcinoma

More recent studies have focused on the hyperthermia's effects on distinct cellular signaling pathways; particularly with those involved in 'heat shock response', cell cycle regulation and apoptosis. Furthermore hyperthermia influences tumor blood flow, oxygen and nutrient supply, as well as, the cellular immune response, by changing the microenvironment under in vivo conditions. The morphological changes associated with hyperthermia include endothelial swelling, the shift of plasma fluid into the interstitium, micro-thrombosis, and changes in the viscosity of blood cell membranes. All of these factors also reduce the oxygen and nutrient supply, as well as, intratumoral acidosis. One of the many studies investigating how hyperthermia acts on cell lines has revealed that heat reduces cell viability and proliferation in a time and temperature-dependant manner. Cell sensitivity to hyperthermia treatment varied among different cell lines, and a basal cell carcinoma (BCC) cell line turned out to be quite sensitive to heat. Several energy sources such as electromagnetic energy, microwaves, sonic energy, and laser energy from Nd:Yag laser—referred to as laserthermia have been used to produce local hyperthermia. The treatment rationale is based on the fact that diseased tissue is more sensitive than normal tissue to the effects of elevated temperature; therefore, it is less able to recover after heat exposure. No single mechanism of hyperthermia cytotoxicity has been generally accepted. One explanation is that cell death occurs as a result of the heat-induced accumulation of nuclear proteins that restrict the rejoining of DNA strand breaks. The use of physical methods in dermatoses and skin tumors is increasing in medical practice. In particular, laser-induced thermotherapy is used frequently. The mechanisms of the effects of laser radiation on tissues and the final biological effect of this interaction are determined primarily by the optical and energic properties of radiation, the ways of providing energy to the tissue, and the properties of the biological tissue itself. However, the literature data regarding the use of this method in the treatment of dermatological pathology are not systematic. Its advantages are low invasiveness, the high selectivity of cancer tumor damage, no risk of severe local and systemic complications, early diagnosis and organ-sparing treatment procedures, as well as simultaneous diagnosis and treatment. In the literature, there are case reports about laser-induced thermotherapy treatments in basal cell carcinoma, Bowen's disease, and resistant warts.

In a study, 37 BCC patients were treated with continuous-wave Nd: Yag laser hyperthermia at 6-week intervals. Following the treatment, 36 patients were reported to have recovered completely. It was stated that only one recurrence (2.7%) was encountered within the 3-5 year follow-up periods and that continuous-wave Nd: Yag laser hyperthermia could be an alternative treatment for BCC.

In another study, 77 superficial and nodular BCC patients, 31 of them were multiple carcinomas, were treated with laser-induced hyperthermia. The success rate in low stage cases was reported to be 97% and 78.3% in high stage cases.

In a case report, Nd: Yag laser hyperthermia treatment was applied twice with an interval of 6 weeks to a 54-year-old female patient with resistant warts on her hands. Complete regression was reported after 2 sessions.

In conclusion, laser-induced hyperthermia can be regarded as an effective, easy, non-invasive alternative procedure to treat dermatoses and skin tumors. Nd: Yag hyperthermia is particularly useful in areas that are more difficult to treat with other methods, such as BCCs in the nose and areas around the eyes. It showed an excellent cure and cosmetic rate with minimal complications.

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THERMOGRAPHY IN DERMATOLOGY

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Historically, body temperature has been described as an excellent indicator of health status since it was first noticed by Hippocrates around the 4th century BC. The human body is homeothermic, which means it can maintain a constant internal body temperature regardless of external influences. The human body keeps its temperature within a narrow limit by various physiological processes, called thermoregulation. Any change in temperature by a few degrees can be a sign of a possible illness.

Thermal imaging or thermography is a relatively new technology that allows observation of the thermal properties of objects. This technique is mainly based on the fact that any object at a temperature above absolute zero (>-273 °C) emits infrared (IR) radiation or thermal radiation, which can be detected by thermal cameras. Recent developments in thermal camera technologies have provided access to these devices much easier than it was before. Therefore, it has raised significant interest in the medical field. Undoubtedly, the greatest part of this interest has been experienced in the field of dermatology.

The skin is the largest organ in the human body and lies superficially, so it is an ideal target for thermography. Several diverse thermography applications have been performed in dermatology to monitor and assess different conditions such as inflammatory lesions, malignant and vascular tumors, bacterial and viral infections, allergic diseases, ischemic disorders, skin burns, and pressure ulcers.

In inflammatory skin lesions, an increase in temperature is usually observed due to an increase in vascularity. Thermography has been used in scleroderma and morphea patients to detect and monitor disease activity. Likewise, a decrease in IR radiation can be observed in psoriasis patients after treatment. Thermography has also been successfully performed in hidradenitis suppurativa (HS) patients to identify the severity of disease activity. Further application of thermography in HS is to help surgeons ensure disease borders during surgical excision.

Infectious conditions generally cause an increase in core and peripheral body temperature. Soft-tissue infections such as cellulitis and erysipelas are usually diagnosed by clinical examination; nevertheless, various disorders may resemble soft-tissue infections, called pseudo-cellulitis. Thermography has been performed to differentiate cellulitis from pseudo-cellulitis successfully. Another interesting application of thermography in infectious diseases in dermatology is to predict post-herpetic neuralgia in acute herpes zoster patients. It has been determined that as the temperature difference between acute herpes zoster lesions and normal skin increases, the risk of developing post-herpetic neuralgia also increases. In earlier studies, thermography has been used for the diagnosis of leprosy patients. It has been shown that cooler areas such as the ear and nasal rim region were heavily affected.

Doppler US and MRI are standard imaging techniques in the diagnosis of vascular malformations and tumors. However, these imaging modalities may not always be available and require trained personal. Thermography is more affordable, portable, and easy-to-use. In addition to identifying the lesion borders, as the temperature difference correlates with blood flow, it is possible to say the vascular lesion's flow characteristics by thermography.

Maybe the most vital application of thermography is to use in the detection, treatment, and monitoring of malignant skin tumors such as melanoma. There are several ongoing researches on this subject that will definitely help clinicians to be more comfortable in taking care of skin cancer patients.

In conclusion, thermography is still an emerging technology in dermatology. It is easy to use, mobile, relatively affordable, and open to improvement. Being aware of thermography's clinical applications will provide dermatologists more accurate precision of diagnosing, monitoring, and treating skin conditions in the future.

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CONFOCAL, USG, IMAGING METHODS IN DERMATOLOGY

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Although many dermatologic diseases can be diagnosed easily with "naked eye" examination,

there have been significant advances in ancillary non-invasive imaging technologies that aid in diagnosis, management and follow-up of some dermatological conditions and tumors. Digital dermoscopy, confocal microscopy, optical coherence tomography (OCT) and high-frequency ultrasound (HFUS) are the main examples of the technologies used in dermatological practice (1, 2).

Confocal microscopy is an optical technique that provides cellular resolution of skin and cutaneous structures. It can be performed in either reflectance or fluorescence mode. *Reflectance confocal microscopy (RCM)* highlights the refractive index differences of some skin structures in vivo to provide contrast. Confocal microscopes have an 830-nm (near-infra red laser). Melanin, keratin and collagen and inflammatory cells of the skin can provide contrast and have a strong refractive index, with melanin having the strongest. These structures appear bright white, whereas nonreflective structure appear dark when reflected light reaches the detector. Interplay between structures with different refractive indexes generates a black white image representing the area at the cellular level. On contrast to the classical histopathological sections, images created by CRM are parallel to the skin surface. The commercially available device is called VivaScope (Caliber ID, Rochester) and has two different probs: Vivascope 1500 and Vivascope 3000. Vivascope 1500 is the large prob of the device which is fixed to skin surface with a metal ring and automatic basic horizontal images of 0.5 x 0.5 mm are taken and stitched together to create a 2D mosaic images of 8x8 mm (VivaBlock). A specific point can be marked on a VivaBlock and series of consecutive single RCM images can be stacked vertically (Vivastack), from the skin surface to superficial dermis, at the same point in the tissue. Vivascope 3000 is handheld device that enables imaging of curved anatomic sites, such as face or flexures, and does not require fixation of the probe to the skin (3).

RCM has a wide range of use, specifically in the diagnosis of melanocytic and nonmelanocytic skin tumors, as the cellular resolution of the images are quite high and that is why it has been called "virtual biopsy". Its specificity is quite high in melanocytic tumors and it is an important tool to avoid unnecessary excisions. It can be used to determine pre-operative margins for skin tumors and in the follow-up of high-risk skin tumors to detect superficial recurrence early. Its main limitation is its penetration depth of 200-300 um (level of the papillary dermis), so it can not provide information for the deeper parts of the skin. It is also an expensive device and requires adequate training to analyze obtained images.

Ultrasound devices are used to create images using the reflection of ultrasound waves from the interfaces with different acoustic impedances (4). Transducers contain piezoelectric crystals that produce sound waves once stimulated by an electric voltage. The reflection/echoes generated by different skin structures are received back by the same transducer and converted in electrical energy which is later transformed into points of greater or lesser luminous intensities on a computer screen (B-mode image). Image brightness is determined by the amplitude of the echo reaching the transducer. Keratin, collagen, fascia and connective tissue are hyperechoic and appear white on the B-mode image. Dermatologist are interested in very superficial structures therefore the appropriate equipment is *high frequency ultrasound (HFUS*). Exploration probe is usually linear, as we are interested in the skin structures parallel to the body surface. When combined with Color Doppler, blod flow can be visualized by HFUS, so information about vascularization can be obtained.

HFUS might be used for several indications in dermatology. It can be used to determine disease activity in rheumatologic skin conditions like scleroderma or lupus, to evaluate disease extension in hidradenitis suppurativa, to visualize depth of affection in bacterial skin infections, to diagnose subcutaneous lesions, to characterize cutaneous vascular lesions, to delimitate malignant skin neoplasms, and to evaluate filler complications like granulomas. Other than skin itself, nail plate and nail matrix can also be evaluated by HFUS (4, 5).

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COLOURS IN DERMATOLOGY: WHITE, BLACK, BROWN, PURPLE, YELLOW, GREEN AND REDNESS

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Introduction

Dermatology is one of the most visual medical speciality, in addition diagnosis of most dermatological diseases depended on dermatologist's visual physical examination with or without equipments such as dermoscope and Wood's light. While performing dermatological examination, it is important to define skin lesions accurately. Lesion's size, distribution, arrangement and morphology should be determined correctly and particularly. Morphological features should be detailed with definition of primary and if present secondary elementary lesions and colour. Abnormal colours can be originated in consequence of different mechanisms such as alterations in pigment biosynthesis, altered blood flow, depositions, cell proliferations and infections.

The term 'chromophore' describes all chemicals and structural items that change colour of skin. The term 'pigment' should now be restricted to being used to describe melanotic chromophores, while 'pigmentation' is reserved for descriptions of skin colour and its abnormalities related to melanocytes and melanin. The colour of the skin as determined by two distinct groups of chromophores, those of the pigmentary system (i.e. melanin and melanocytes) and those composed of other elements (chromatics) of the skin, such as collagen, blood, carotenes.

In this review, we discuss importance of common colours of skin lesions in a pathogenesis-oriented manner.

Common Dermatological Colours: Which pathogenetic mechanism-Which colour?

1. White Colour

a. Hypomelanosis, hypomelanocytosis and amelanosis:

Hypopigmentation is the term used to define decreased melanin and depigmentation is the term used to define absence of melanin. Wood's light examination is also beneficial to distinguish hypopigmentation from depigmentation. Depigmented lesions seem chalky white under Wood's light.

Hypomelanosis, hypomelanocytosis and amelanosis can be underlying pathogenetic mechanisms of white skin lesions. Genetics, autoimmunity, chemical exposure, inflammation could be initial triggers. Hypomelanosis is the term used to define decreased melanin with normal number of melanocytes; in addition hypomelanocytosis is decrease of both melanin and melanocytes. In the absence of melanin using terms of amelanosis would be appropriate. All of these situations can be distinguish from each other histopathologically.

Both hypopigmented and depigmented skin lesions could be congenital or acquired; localized or generalized which could be easily detected with patient's history and physical examination. Examples for hypomelanosis: Focal dermal hypoplasia, hypomelanosis of Ito, naevus depigmentosus, tuberous sclerosis complex, oculocutaneous albinism, ataxia telengiectasia, Hallerman Streiff syndrome, histidinemia, homocystinuria, hypomelanosis of immundeficiency, Menkes kinky hair syndrome, oculocerebral syndrome with hypopigmentation, phenylketonuria, leprosy, sarcoidosis, drug-induced hypopigmentation, Kwashiorkor, hypopituitarism, idiopathic guttate hypomelanosis, progressive macular hypomelanosis, hypopigmented mycosis fungoides.

Examples for hypomelanocytosis: Waardenburg syndrome, Alezzandrini syndrome, piebaldism, vitiligo, lichen sclerosus et atrophicus, depigmentation associated with melanoma.

b. Disarrangement in dermal connective tissue:

Scar tissue represent a tissue response to dermal injury characterized by local fibroblast proliferation and collagen production. Keloids are fibrous growths that extend beyond the original area of injury to involve the adjacent normal skin. Hypertrophic scars may have a similar clinical appearance, but in contrast with keloids, remain confined within the

boundaries of the wound area and tend to regress spontaneously over time. Although keloids and hypertrophic scars are associated with increased fibroblast proliferation and excessive collagen overproduction; white colour is characteristic feature of mature scar tissue.

Anetoderma, also known as macular atrophy, is an uncommon disorder of elastic tissue that is clinically characterized by wrinkled and atrophic depressions or saccular outpouchings of the skin. Available evidence suggests increased breakdown of elastic fibers may play a primary role. Examination of the skin demonstrates skin-colored or white, wrinkled and atrophic depressions or saccular outpouchings that may herniate on digital pressure.

c. Decreased blood flow:

Insect bite reactions and urticaria can present with edematous, pale-white papule and plaques caused by excessive dermal edema in the superficial dermis mediated by cutaneous mast cells. Basophils have also been spotted in lesional biopsies. Mast cells and basophils release multiple mediators including histamine (which causes itching) and vasodilatory mediators (which cause localized swelling in the uppermost layers of the skin) upon activation. Naevus anemicus and Bier's spots are another clinical antity characterized with white macules. Naevus anemicus is a congenital, localized, cutaneous vascular anomaly presenting as a pale, irregularly shaped patch on otherwise normal skin, thought to be caused by a localized increased vascular sensitivity to endogenous catecholamines resulting in persistent vasoconstriction. Bier spots, also called physiologic anemic macules, is an uncommon benign vascular anomaly causes mottled skin which are thought to be an exaggerated physiologic vasoconstrictive response of the small cutaneous vessels to hypoxia induced by venous stasis or venous hypertension.

d. Epidermal proliferation:

Epidermal proliferation can be seen in malignant or begin processes and can be present with white plaques especially in mucosal areas such as lichen sclerosus, lichen simplex chronicus, squamous intraepithelial lesions and squamous cell carcinoma.

e. Microorganisms:

Candida infections are presented with white, easily removable white plaques. Pityriasis versicolor can be present with white macules in dark-skinned patients. Molluscum contagiosum present with white, umblicated papules.

2. Black Colour and Brown Colour

a. Necrosis:

Acute cutaneous necrosis is represented by a wide range of aetiologies and is associated with significant morbidity and mortality. Clinically, skin necrosis is characterized with black, well demarcated, dry, adherent ulcers. Warfarin and heparin administration, calciphylaxis, chemical/thermal burns, pyoderma gangrenosum, peripheral gangrene, embolic phenomena, purpura fulminans, brown recluse spider bite, necrotizing fasciitis, ecthyma gangrenosum, antiphospholipid syndrome, cryoglobulinemia and hypergammaglobulinemia are situtations that result in skin necrosis.

b. Hypermelanosis and hypermelanocytosis:

Hyperpigmentation is the term used to define increased melanin. Hypermelanosis and hypermelanocytosis are possible underlying pathogenetic mechanisms of brown to black skin lesions. According to Tyndall effect, superficial hyperpigmentations tend to seem blacker. Genetics, chronic ultraviolet exposure, inflammation could be initial triggers. Hypermelanosis is the term used to define increased melanin with normal number of melanocytes; in addition hypermelanocytosis is increase of both melanin and melanocytes. All of these situations can be distinguish from each other histopathologically.

Simple lentigo, solar lentigo, post-inflammatory hyperpigmentations, cafe au lait macules, melasma, acanthosis nigricans are hypermelanotic; melanocytic nevi, dysplastic nevi and malignant melanomas are hypermelanocytic lesions.

c. Exogen pigmentation:

Tatoos, radiation induced pigmentation, traumatic tatooing can present with black-brown macule, papule or plaques.

d. Microorganisms:

Erythrasma is a superficial skin infection caused by Corynebacterium minutissimum, a gram-positive, non-spore-forming bacillus which is a component of normal skin flora. Under conditions of moisture and occlusion, C. minutissimum propagates in the upper levels of the stratum corneum and presents as well-defined scaly plaques between the toes or erythematous to brown patches or thin plaques in intertriginous areas.

Pityriasis versicolor is a common superficial fungal infection caused by mycelial growth of fungi of the genus Malassezia. Patients with this infection often present with hypopigmented, hyperpigmented (especially in light-skinned individuals), or erythematous macules on the trunk and proximal upper extremities.

3. Purple Colour

a. Disruptions in vascular integrity:

Vascular integrity can be destroyed via trauma or inflammation (vasculitis). Petechias are milimetric red-purple macules. Purpuras are purple macules smaller than 1 cm, palpable purpuras are significant for vasculitis. Ecchymoses are purple patches or plaques bigger than 1 cm. Trauma, infections (i.e. Neisseria meningitidis), vasculitis, connective tissue synthesis disorders, clotting disorders, anticoagulant-antiaggregant useage.

b. Inflammatory skin diseases:

Inflammatory diseases such as lichen planus, contact dermatitis, psoriasis, cutaneous lupus erythematosus present with red-purple coloured lesions; purplish colour tend to be seem in dark-skinned patients.

c. Exogen pigmentation:

Tatoos can also be responsible for purple coloured lesions.

d. Malignity:

Kaposi sarcoma is an angioproliferative disease that is characterized by angiogenesis, inflammation and spindle cell proliferation. Clinical features are purplish or reddish blue macules, plaques, and nodules on the skin.

4. Yellow Colour

a. Jaundice (Icterus):

Jaundice is a sign indicating the presence of variable underlying diseases, including bilirubin overproduction, impaired bilirubin conjugation, biliary obstruction, and hepatic inflammation. Indirect bilirubinemia present with diffuse yellow discoloration in scleras and skin.

b. Endogen deposition:

Xanthelesma palpebrarum is the term used to define cholesterol deposition on eyelids. It presents with yellow, soft papule or plaques and often associated with hypercholesterolemia.

c. Dilated follicular infundibulum:

Dilated follicular infundibulum can easily filled with keratin and sebum; in addition it can be visualized with dermoscopy easily as yellow dots. Yellow dots are the most common and most sensitive features of alopecia areata, but are also seen in some cases of androgenetic alopecia and alopecia incognita.

d. Parakeratosis of nailbed:

One of the nail findings of psoriasis is “oil drop” sign that characterized as yellow dots on the nail occur as a result of parakeratosis of nailbed.

e. Microorganisms:

Onychomycosis is a fungal infection that may caused by dermatophyte, yeast, or nondermatophyte molded nail. Dermatophyte infections (also known as tinea unguium) are the most common and are estimated to account for 60-70 % of infections. Mycologic infiltration of nail plate results yellow discoloration, subungual hyperkeratosis and fragmentation of nailplate.

Impetigo is a common contagious superficial bacterial infection that may affects anyone but it is most frequently observed in children, especially those ages 2-5. It may be classified as primary impetigo (direct bacterial invasion of previously normal skin) or secondary impetigo (minor skin trauma such as abrasions, insect bites, or underlying conditions such as eczema). Lesions begin as papules that progress to vesicles surrounded by erythema. Subsequently they become pustules that enlarge and rapidly break down to form thick, adherent crusts with a characteristic golden appearance.

5. Green Colour

a. Microorganisms:

Pseudomonas aeruginosa is one of the most commonly considered gram-negative aerobic bacilli in the differential diagnosis of gram-negative infections. Patients with chronic onycholytic toenails who have prolonged immersion exposure to fresh water may develop a characteristic green discoloration called the green nail syndrome. The green color is due to the accumulation of debris below the nail and the pigment pyocyanin adhering to the undersurface of the nail plate.

b. Exogen pigmentation:

Tatoos can also be responsible for green coloured lesions.

6. Red Colour

a. Inflammation:

Inflammation is an adaptive response that is triggered by endogenous or exogenous noxious stimuli and conditions such as allergens, microorganisms, foreign bodies, malfunctioning cells and products of extracellular matrix breakdown. Pain, redness, edema, heat and loss of function are five cardinal signs of inflammation. Inflammation can occur either in acute or chronic process. Acute inflammation's clinical manifestations are vivid erythema, edema, serosity and sometimes blisters whereas chronic inflammation's are faded erythema, dryness and lichenification. Atopic dermatitis, contact dermatitis, psoriasis, erythema multiforme, cutaneous lupus erythematosus, erysipelas clinically present with erythematous lesions in acute phase.

b. Vascular malformations and tumors:

Vascular malformations are histologically characterized by an increase of dysplastic and dilated vessels. They are present at birth and grow proportionally as the child develops. Vascular tumors are composed of benign or malign proliferation of endothelial cells. They both present with red macules, patches, plaques or nodules such as infantile hemangiomas, congenital hemangiomas, pyogenic granuloma, hemangioendothelioma, capillary and venous malformations.

c. Microorganisms:

Erytrasma is an infectious disease caused by Corynebacterium minutissimum, present with well defined brown patches particularly in inverse areas. Erythrasma has spesific coral red reflect under Wood's light examination.

Conclusion

There are several elementary lesions and colours describing skin diseases in dermatology. This riot of colours are the clues of the diagnosis of dermatological disorders and these colours make dermatology enjoyable.

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DIAGNOSTIC CRITERIA IN DERMATOLOGY

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The art of medicine includes consecutive stages of assessment and judgement prior to providing recommendations. Assessment is the central step and several attempts to codify assessment have been undergone. In addition to improved patient care and research purposes, the accurate diagnosis of a particular disease is essential for billing and reimbursement. In other words in addition to academic reasons, economic, political and social forces also empower the development of diagnostic criteria (1).

The diagnosis process is more challenging in several disciplines including psychiatry, rheumatology and dermatology. Thus, diagnostic criteria are more favored in these disciplines and the Diagnostic and Statistical Manual of Mental Disorders (DSM) is likely the best-known example of diagnostic criteria.

During dermatological practice, rather than depending on a single ''gold standard'' method of a clinical, laboratory, pathological and/or radiological feature, patient reports and dermatological findings are admixed with advanced tests to determine the diagnosis. Additionally, the presentation, course and outcome of dermatological diseases tend to be heterogeneous.

Diagnostic criteria are fundamentally defined as a set of signs, symptoms and tests for use in routine clinical practice to guide the care of individual patients. Diagnostic criteria are generally broad and must reflect the different features of a disease in order to accurately identify as many people with the condition as possible including those with unusual features and presentations. Thus, the development and validation of diagnostic criteria can be quite challenging (2).

Diagnostic criteria for any condition must be both valid and clinically sensible. Different methods can be used to establish consensus among clinical experts for the content of a criteria set. Despite face-to-face communication may provide certain advantages over remote voting, in dermatology, the most preferred method for establishing consensus is Delphi method (3-6). Delphi is a completely anonymous process (7). The participants don't meet and ideas are expressed to the participants through a mailed questionnaire. Delphi method can be applied to high numbers of participants who cannot meet simultaneously for economical or logistic reasons. The participants may be either leaders in their clinical fields as evidenced by their roles as opinion makers within established organizations, authors who had papers directly concerned with the topic of interest in peer-reviewed journals or local physicians for regional diseases. The items of the questionnaire may be compiled from various resources including textbooks, published literature, personal communications with faculty members who have experience in assessing and treating the topic of interest. After the declaration of group responses to the first round, the second round is performed to drop or add items. Repeated iterations of the process are performed until the achievement of consensus (7). This consensus establishes what the criteria set should compromise and does not entirely ensure validity. Over the last decades, tremendous progress in focusing on measurement has been undergone and the development of diagnostic criteria is also evolving. Along with the evolution of clinical practice, the opinions of experts may also change. This is the rationale for the revision of existing diagnostic criteria sets that is inevitable owing to the improved understanding on disease pathogenesis and the development of new diagnostic tools.

The performance of diagnostic criteria is dependent on the prevalence of the disease in a given geographical area or clinical setting. Despite the sensitivity and specifity of diagnostic criteria sets are not influenced by disease prevalence, the predictive validity is altered. As an example, in Turkey where Behçet's disease is endemic(high pre-test probability), patients with recurrent apthous ulcers may be accurately diagnosed and treated even with few supporting criteria. Thus, in Turkey, the diagnostic criteria of Behçet's disease are implemented to patient identification during clinical research, however they are not strictly applied during routine patient care. On the other hand, in the United States (low pre-test probability) any set of diagnostic criteria will have a low positive predictive value. Diagnostic criteria will typically need

to be based on local prevalence of the disease and of other diseases in the differential diagnosis that is not a practical goal (2).

The feasibility, acceptability and available resources should be taken into account during the establishment of universally accepted diagnostic criteria. Stringent criteria that require a particular laboratory, pathological or molecular test could constitute a hurdle for patients and clinicians and has the potential to postpone the initiation of effective treatment.

Despite diagnostic criteria certainly provide improvement of patient care, the clinicians should be aware of the fact that diagnosis is a complex multi-step process that is difficult to accomplish with a single set of criteria.

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HYPO / HYPER / ABSENCE (A)-CONDITIONS IN DERMATOLOGY

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In dermatology, there are many diseases and symptoms that are characterized by hypo or hyper-conditions. The most common of these are hypopigmentations and hyperpigmentations. Some skin diseases and conditions may result in generalized or localized hypopigmentation (decreased skin color), or hyperpigmentation (increased skin color), or depigmentation (absent skin color). In this lecture, hypo-hyperpigmentations will be mentioned especially as they are more common, as well as hypo-hypertrichosis, hyper-hypohydrosis, hyper-hypo keratosis and hypoplasic conditions.

RED SCROTUM SYNDROME AND MALE GENITAL DYSESTHESIA

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The Red Scrotum Syndrome (RSS) is a condition characterized by persistent scrotal erythema associated with a burning sensation, hyperalgesia, and itching [1]. Its exact etiology is unknown, but suggested mechanisms may include rebound vasodilation after prolonged topical corticosteroid use, localized erythromelalgia (a triad of erythema, warmth, and burning pain), and neurogenic inflammation [1]. However, RSS was suggested to be a manifestation of corticosteroid misuse rather than a primary disease [2].

Diagnosis of RSS is usually a diagnosis of exclusion. Histopathological features are non-specific. The epidermis might show normal to spongiotic and atrophic changes. The dermis might show dilated blood capillaries with superficial perivascular lymphocytic infiltrate [3].

RSS is a chronic condition with several treatment options that have been tried with variable responses. Stoppage of topical steroid is necessary with therapeutic targeting of the proposed mechanisms including the rebound vasodilation, localized erythromelalgia, and neurogenic inflammation might be helpful [1]. Doxycycline showed 50-80% improvement of RSS within 2 weeks of therapy, with complete resolution of symptoms within 2-3 months [3]. Also, Doxycycline (100 mg twice/day) was used for 2 months, followed by once daily until complete resolution [4]. Oral pregabalin (50 mg 3 times/day) showed improvement in 2 cases [5]. It was suggested in a case report that doxycycline should be tried for 2 weeks as a first-line, and the use of gabapentin is recommended as a second line in case of doxycycline failure [6].

Also, oral and topical β-blockers have been tried. Topical timolol maleate 0.5% eye gel showed dramatic improvement after 2 weeks in a case report [7]. Oral carvedilol (6.25 mg/day) showed remission in 2 cases within 2-4 weeks of treatment, without reported systemic side effects [8]. Recently, oral ivermectin (12 mg/week) showed near resolution (>90%) of 3 cases of RSS after 1 month. Then, treatment was continued with topical ivermectin until the complete resolution of symptoms [9].

Prevention of RSS might be done through reduction of topical corticosteroid misuse and increasing the patients' awareness about the side effects associated with unmonitored use of these drugs [1]. It must be noted that data about treatment options come from case reports/and or series. Therefore, randomized controlled clinical trials with a large number of patients are needed.

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JOLLY ROGER SIGN IN DERMATOLOGY

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The "pirate brand" has long been tied to the skull and crossbones—the Jolly Roger—as a symbol of terror on the high seas.

The Jolly Roger sign stands for drugs used in dermatological therapy but are actually toxic.

The skull-and-crossbones symbol, consisting of a human skull and two bones crossed together behind the skull, is today generally used as a warning of danger of death, particularly in regard to poisonous substances.

The symbol, or some variation thereof, specifically with the bones (or swords) below the skull, was also featured on the Jolly Roger, the traditional flag of European and American seagoing pirates. The Workplace Hazardous Materials Information System (WHMIS) is Canada's national workplace hazard communication standard. The Jolly Roger is also part of the Canadian WHMIS home symbols placed on containers to warn that the contents are poisonous.

Potassium permanganate

Potassium permanganate is used as a medication for a number of skin conditions (1). This includes fungal infections of the foot, impetigo, pemphigus, superficial wounds, dermatitis, and tropical ulcers (2). For tropical ulcers it is used together with procaine benzylpenicillin. Typically it is used in skin conditions that produce a lot of liquid. It can be applied as a soaked dressing or a bath (1).

Side effects may include irritation of the skin and discoloration of clothing (1). If it is taken by mouth, toxicity and death may occur. Potassium permanganate is an oxidizing agent.The British National Formulary recommends that each 100 mg be dissolved in a liter of water before use (2).

Potassium permanganate was first made in the 1600s and came into common medical use at least as early as the 1800s. It is on the World Health Organization's List of Essential Medicines (3).

Uses include for fungal infections of the foot, impetigo, pemphigus, superficial wounds, dermatitis (eczema), and tropical ulcers. Typically it is used in skin conditions that produce a lot of liquid.For tropical ulcers it is used together with procaine benzylpenicillin for two to four weeks (1).

It can be used in children and adults. It can be applied as a soaked dressing or a bath. The U.S. Food and Drug Administration does not recommend its use in either the crystal or tablet form (4).

Side effects

Topical

Side effects may include irritation of the skin and discoloration of clothing (1). A harsh burn on a child from an undissolved tablet has been reported. For treating eczema, it is recommended using for a few days at a time due to the possibility of it irritating the skin (5). Higher concentration solutions can result in chemical burns. Therefore, the British National Formulary recommends 100 mg be dissolved in a liter of water before use to form a 1:10,000 (0.01%) solution (5). Wrapping the dressings soaked with potassium permanganate is not recommended.

By mouth

If taken by mouth it is deemed to be very toxic.Side effects may include nausea, vomiting, and shortness of breath may occur. If a sufficiently large amount (about 10 grams) is eaten death may occur (6).

Concentrated solutions when drunk have resulted in adult respiratory distress syndrome or swelling of the airway. Recommended measures for those who have ingested potassium permanganate include gastroscopy.Activated charcoal or medications to cause vomiting are not recommended.While medications like ranitidine and N-acetylcysteine may be

used in toxicity, evidence for this use is poor (7).

Arsenic

During the 18th, 19th, and 20th centuries, a number of arsenic compounds were used as medicines, including arsphenamine (by Paul Ehrlich) and arsenic trioxide (by Thomas Fowler) (8). Arsphenamine, as well as neosalvarsan, was indicated for syphilis, but has been superseded by modern antibiotics. However, arsenicals such as melarsoprol are still used for the treatment of trypanosomiasis, since although these drugs have the disadvantage of severe toxicity, the disease is almost uniformly fatal if untreated (9).

Arsenic trioxide has been used in a variety of ways over the past 500 years, most commonly in the treatment of cancer, but also in medications as diverse as Fowler's solution in psoriasis (10).

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INTESTINAL BACTERIAL OVERGROWTH IN DERMATOLOGY

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Small intestinal bacterial overgrowth (SIBO) is a condition characterized by an increase in the number and/or abnormal forms of bacteria in the small intestine. SIBO may occur due to disturbance of the gastric acid secretion and intestinal motility which normally inhibit bacterial growth, leading to frequent gastrointestinal symptoms including diarrhea, distension, malnutrition, and weight loss [1]. Diagnosis of SIBO can be made through intestinal aspirate which is the gold standard. However, breath tests by measuring the exhaled gas after ingesting either glucose or lactulose are a more commercially popular and non-invasive diagnostic tool. The breath test results depend on the bacterial metabolism of the ingested material the bacteria [2].

In addition to gastrointestinal (GIT) symptoms, SIBO might affect the gut/skin axis, and a potential link has been found between SIBO and numerous dermatological conditions including rosacea, psoriasis, and systemic sclerosis (SSc) [3]. Rosacea has been linked to SIBO and the treatment of SIBO with rifaximin which is a rifamycin derivative has shown to have beneficial effects [4]. After treatment of SIBO in rosacea patients, remission has been maintained in 44% of patients after 5 years of follow-up [5]. Treatment of the associated SIBO in patients with psoriasis showed improvement in psoriasis area severity index (PASI) [6]. In patients with SSc, SIBO is more prevalent as compared to control, and treatment of SIBO has been associated with GIT symptoms in those patients [7]. Therefore, special attention should be on the possible gut/skin axis which may carry a potential therapeutic modality for several dermatological conditions

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CUTIBACTERIUM IN DERMATOLOGY

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Recent phenotypic and genomic (16S RNAr and CoreGenome) investigations led to some modifications in the Propionibacterium genus taxonomy. Notably, specific genes were identified in these cutaneous species, and taxonomic reclassification was therefore proposed in which Propionibacterium acnes was renamed Cutibacterium acnes. This new name differentiates it from other environmental Propionibacteria species, including those present in dairy products and cattle rumen. So, since 2016, Propionibacterium species living on skin changed their denomination to Cutibacterium. The names in standard use are Cutibacterium acnes, Cutibacterium avidum, Cutibacterium granulosum, Cutibacterium namnetense and Cutibacterium humerusii. C. acnes strains also have been classified into several subtypes, currently, it is subdivided into six main phylotypes: IA1, IA2, IB, IC, II and III. Cutibacterium species are well known as a commensal belonging to the healthy skin microbiota but also as an opportunistic pathogen mainly involved in skin inflammatory diseases related to dysbiosis and implant associated infections. Other species from this genus such as Cutibacterium avidum are mostly found in moist environment, Cutibacterium granulosum is generally found in dry area and the two most recently described, Cutibacterium humerusii and Cutibacterium namnetense, exhibit dissimilar ecologies in terms of topography (dry, moist or sebaceous environments) and pathogenic power.

C. acnes, a common skin organism, is most notably recognized for its role in acne vulgaris. C. acnes is also found in other tissues such as intestine, stomach, lungs, mouth, conjunctiva, prostate and urinary tract. It also causes postoperative and device-related infections and has been associated with a number of other conditions such as sarcoidosis and synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO), progressive macular hypomelanosis (PMH), although its precise role as a causative agent remains to be determined. C. acnes produces a number of virulence factors and is well known for its inflammatory and immunomodulatory properties. On the skin surface, the microbial community is mostly constituted by bacteria belonging to the three main genera of Corynebacteria, Propionibacteria and Staphylococci. Interplay between members of this cutaneous microbiota is essential for the maintenance of a healthy skin. While the commensal bacterium C. acnes, predominant in sebaceous sites, is critical in the regulation of skin homeostasis and prevents colonization from other harmful pathogens, it can also act as an opportunistic pathogen in acne vulgaris. New findings on C. acnes reveal that, contrary to what was previously thought, its proliferation is not the trigger of acne but instead, a tight equilibrium between members of the skin flora and among C. acnes phylotypes might play a more critical role in acne onset. Loss of the skin microbial diversity together with the activation of the innate immunity might lead to this chronic inflammatory condition. Analyses showed that the load of C. acnes is similar among patients with acne and healthy individuals (87%–89%). Two major studies previously decrypted skin microbiota in acne context. These studies both showed that no clear difference was observed in C. acnes abundance between healthy and acne individuals, whereas recent evidence highlighted a loss of C. acnes subgroups diversity in severe acne. Changes in physiological conditions may lead to an imbalance between the different skin community members, called dysbiosis, and eventually to the selection of more pathogenic C. acnes strains. Acne might be triggered by the selection of a subset of C. acnes strains, including the acne-associated phylotype IA1. Biofilm formation and differences in virulence and inflammatory potential of C. acnes strains might enhance their pathogenicity.

In conclusion, after being underestimated and almost in variably considered as a contaminant of samples, C. acnes has been shown over the last decade to play a significant role, via its various subgroups, in several skin disorders. The development of new methods has revealed C. acnes not just as a commensal bacterium but also as an organism involved in various types of inflammatory dermatoses.

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IGF IN DERMATOLOGY

Ufuk Kavuzlu

Insulin-like growth factor (IGF) is a hormon with an insulin-like structure. IGF-1 and IGF-2 are proteins that play role in growth and also mediate some of effects of growth hormone. (1,2) There are various studies examining the effects of insulin-like growth factor on some dermatological diseases such as acne, alopecia or acrochordon. (2,3,4) This presentation summarizes role of IGF in dermatology

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GHRELIN IN DERMATOLOGY

Ufuk Kavuzlu

Ghrelin is a 28-aminoacid lipopeptide hormone secreted mainly from the stomach. (1,2). Ghrelin has antiinflammatory activities due to its effect on T cells and monocytes. (2,3) It increases appetite and stimulates fat storage. Ghrelin levels are low in obese patients. (3) There are some studies researching the relationship between serum ghrelin levels and some skin diseases such as psoriasis and acne. (2,4) This presentation summarizes role of ghrelin in dermatology.

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ULTRASTRUCTURAL AND HISTOPATHOLOGICAL CHANGES AFTER COSMETIC PROCEDURES IN HUMANS

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ABSTRACT

Cosmetic procedures such as fillers, botulinum toxin, lasers, microneedling, mesotherapy / PRP and radiofrequency cause various structural and histopathological changes in the human body. The purpose of this presentation is to show the effect of the mechanisms of cosmetic procedures and the changes they cause especially in the face.

Fillers show different effects according to their content and are metabolized in the body in different ways. For example; hyaluronic acid modifies the organization of the actin cytoskeleton, influencing fibroblast shape and orientation, poli-L-lactic acid increases fibroblast activity and stimulates collagen synthesis and calcium hydroxylapatite increases in histiocytes and associated fibroblasts appears to anchor down the microspherules as well as to induce new collagen formation as the aqueous gel is metabolized.[1,2]

Botulinum toxin causes distortion in muscle fibers, shortening of sarcomeres, disruption of the triad structure in tubules and mitochondrial degeneration.[3]

CO2 laser therapy was confirmed by significant histological improvement in the form of significant decrease in number of melanocytes, reduction in the degree of epidermal hyperpigmentation, decrease in number of melanophages and decrease in dermal perivascular edema. Fractional laser therapy also causes a decrease in the number of melanocytes.[4]

According to the studies, although mesotherapy does not cause a significant histological and structural change in the human body, PRP causes thickening in the reticular dermis and an increase in collagen and elastic fibers with an increase in the number of active fibroblasts.[5,6]

Microneedling increases in the mean of collagen types I, III, and VII through secondary fibroblast proliferation.[7]

Radiofrequency causes instant collagen denaturation and subsequent new collagen formation with the effect of heat.[8]

Knowing how cosmetic procedures work and what kind of changes they cause allow us to have a better understanding of the procedure.

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MICROCHIMERISM AND SKIN DISEASES

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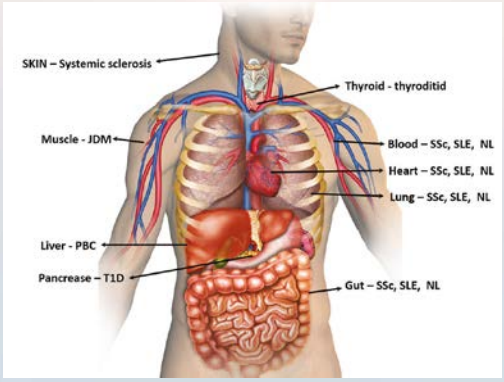
In Greek mythology, the chimera was a monstrous, fire breathing, female creature with the body of a lioness, a tail that terminated in a snake's head and the head of a goat that protruded from the center of its spine (Figure1).[1]

Today, the term is used to describe real-life entities that arise or are created as amalgams of previously separate entities in fields such as botany, genetics and molecular biology.[2] The term chimerism was first used by Liegeois et al. in the 1970s.[3] In genetics, microchimerism (Mc) is defined by the presence within an individual of a low level of cells or DNA derived from a genetically different individual. Yani, Chimera is a single organism that is made up of two or more different populations of genetically distinct cells that originated from different zygotes involved in sexual reproduction.[4] Chimeras are formed from at least four parent cells (two fertilized eggs or early embryos fused together). Each population of cells retains its own character and the resulting organism has a mixture of tissues.

There are two possible causes of microchimeric cells, natural and artificial. Pregnancy, miscarriage, twinning and sexual intercourse are natural, organ-tissue transplantation and blood transfusion are artificial causes. Among various forms of chimerism and pregnancy is the most common and natural cause (Figure 2). Fetal - maternal microchimerism occurs as a result of bi-directional exchange of hematopoietic cells through the placenta during pregnancy. It is now known that fetal-maternal microchimeric cells (F-MMcCs) can pass through tissues and organs such as peripheral blood, bone marrow, thymus, liver, lung, spleen, kidney, skin and brain. Therefore, we are all born as microchimera and nobody is pure.[5]



It is assumed that fetal stem cells that pass from the placenta to the maternal circulation can turn into various mature cells in the mother become active in time and react to maternal antigens. Researchers have investigated the role of microchimerism in some autoimmune diseases that primarily affect women. Autoimmune diseases, which they find a relationship with microchimerism, by detecting the fetal Y chromosomes that decades after pregnancy, are shown in the picture.

Microchimerism has been investigated in different autoimmune disorders such as GVHD, systemic sclerosis, systemic lupus erythematosus, dermatomyositis, Sjogren's yndrome autoimmune thyroid diseases, primary biliary cirrhosis, and juvenile inflammatory myopathies.

While microchimeric cells sometimes help suppress tumor growth by assuming an immune surveillance role, sometimes, they may act as cancer stem cells and contribute to the growth of tumors including squamous skin cell carcinoma.[6]

Identification of male fetal cells in maternal cesarean wounds that have healed after pregnancy suggests that fetal cells migrate or proliferate locally to the site of damage, including maternal tissue repair, possibly in response to signals generated by maternal skin injury during cesarean section.

Recent research data have demonstrated the promising role of microchimeric cells in maternal response to tissue damage by differentiating many lineages. Therefore, a better understanding of fetal-maternal microchimerism can help predict its effects on disease as well as more general women's and children's health problems.

Microchimerism has been investigated in lichen planus[7,8], psoriasis[9], alopecia areata[10] and Behçet[11] disease, apart from autoimmune conditions; There was evidence that it may be associated with the last two diseases.

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MAS-RELATED G PROTEIN-COUPLED RECEPTOR X2 (MRGCRX2) AND ALLERGY

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Allergy: Allergy is an **a**bnormal reaction by the immune system in response to foreign substances called allergens. A wide variety of substances can be allergic. Allergens cause the release of inflammatory substances via the high affinity IgE receptors (FceRI) from mast cells upon activation.

Mast cells: Mast cells are long-lived mononuclear cells that reside in tissues near external surfaces, *e.g.,* in skin or mucosa, and thereby are among the first cells of the immune system (Galli et al., 2011; da Silva et al., 2014).). These cells fulfill their tasks in innate and adaptive immune responses by secreting different kind of mediators including histamines and various inflammatory and immunomodulatory substances (Galli et al., 2011). There are two populations of mast cells are available. 1) Mucosal type, which is found predominantly at mucosal surfaces contain only tryptase (MC_T). 2) Connective tissue type, which contains tryptase, chymase, carboxypeptidase A and cathepsin G, (MC_{TC}) located within connective tissues including skin. Total tryptase level in blood is used as an indirect parameter of mast cell burden and activation. Following activation, mast cell release both preformed mediators and newly synthesized compounds.

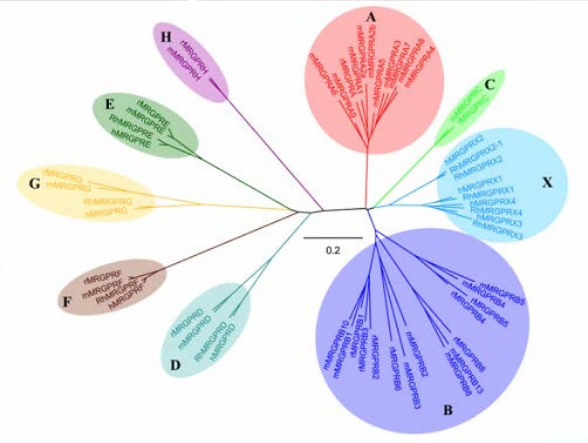
Mast Cell Activation and Degranulation: There are three activation mechanisms of mast cells:

1) IgE-dependent activation: Mast cells are activated through the crosslinking of antigen-specific IgE receptors (FceRI), which causes the release of numerous mediators. In addition, these cells can also be activated by antibody-independently in response to a range of cationic substances, which include peptides and amines such as substance P, mast cell-degranulating peptide, neuropeptide Y, mastoparan, and compound 48/80, etc. (Bischoff, 2009).

2) Monomeric IgE-dependent activation: This has been taken place by binding of monomeric IgE to the high affinity IgE receptor, even in the absence of cross-linking by allergens.

3) Non-immunological activation *(e.g., through MRGPRX2)*: There are a huge number receptors on mast cell membrane, which make these cells respond to a diverse range of stimuli, including via IgE-independent mechanisms. Downstream pathways of each individual receptor are not fully understood but ultimately lead to MC degranulation (Bischoff, 2009; Solinski et al., 2014).

MAS-Related G Protein–Coupled Receptors X (MRGPRX2): MRGPRX2 is a novel G protein-coupled receptor activated by endogenous prodynorphin-derived peptides and opioid compounds (Lansu et al., 2017). MRGPRs are also known as sensory neuron-specific receptors. MRGPR-encoding genes have been detected in mammals. The mammalian family of MRGPR can be subdivided into nine separate subfamilies (A–H and X) being X is specific to primates including humans, macaque, and rhesus monkey.



(Fredriksson et al., 2003;Katritch et al.,2013)

Human Mas-related G protein-coupled receptor X2 binds promiscuously to structurally diverse peptides and small molecules that tend to have basic properties (basic secretagogues), resulting in acute histamine-like adverse drug reactions of injected therapeutic agents (Grimes et al., 2019). MRGPRX2 is the main receptor related to pseudo-allergic reaction, which occurs quickly and can be life-threating. The MRGPRX2 subtype has several peptidergic ligands being the most characterized ligand the cortistatin-14 peptide (Robas et al., 2003; Kamohara et al., 2005). This receptors are widely expressed in the body, i.e., from primary sensory neurons to several brain areas, from mast cells to the adrenal medulla (Kamohara et al., 2005). Apart from cortistatin-14, adrenomedullin has also been shown to activate MRGPRX2 (Kamohara et al., 2005; Córdoba-Chacón et al., 2011). MRGPRX2 was also shown to be involved in mast cell activation by a set of structurally similar, endogenous (Subramanian et al., 2016) or exogenous (Subramanian et al., 2011). Substance P, somatostatin, mast cell degranulating peptide, neuropeptide Y, VIP, mastoparan and compound 48/80 etc have high affinity binding sites for MRGPRX2. This receptor is also activated by antimicrobial peptides such as the cathelicidin, LL-37, human b-defensins, which can be released from epithelial cells in response to infectious agents (Subramanian et al., 2011, 2016). Hence, MRGPRX2 can integrate paracrine input from various cell types by detecting alterations of the local milieu and inducing mast cell degranulation. MRGPRX2-mediated responses seem to be more rapid, but transient in comparison to IgE-triggered events.

MRGPRX2 is closely related to pseudo-allergic reactions, which are adverse, non-immunologic, anaphylaxis-like sudden onset reactions that are mediated through an IgE-independent pathway. These reactions are hypersensitivity reactions mediated via a non-IgE-dependent mechanism, thus, they do not require prior exposure to the sensitization process of antigens, causing mast cell degranulation directly. G protein-coupled receptors (GPCRs) are seven transmembrane domain receptors that convert extracellular signals into biological responses. MRGPRX2 is a newly discovered MRGPRX family member that, can be activated by a diverse range of basic ligands, leading to non-immunologically induced mast cell degranulation (Subramanian et al., 2011, 2016; Bischoff, 2009). At present, only few drugs are available to treat allergy conditions and symptoms. The available clinical drugs mostly inhibit the downstream effectors of anaphylaxis. Some medicines, such as immune suppressors, mast cell stabilizers, and antihistamine drugs, can only alleviate suffering as a result of anaphylaxis and help relieve allergic symptoms. Furthermore, these medicines have a number of adverse reactions. Among the antibody-independent substances that can uniquely activate mast cells are a number of cationic amphiphilic substances. In addition to the prototypic compound 48/80, other cationic mast cell activators include a variety of pharmacologic agents (tubocurarine, atracurium, icatibant, ciprofloxacin, and other fluoroquinolone antibiotics), components of insect venom (e.g., mastoparan and kinins), antimicrobial peptides (eg, a- and b-defensins and cathelicidins), secreted eosinophil products such as eosinophil peroxidase and major basic protein, and neuropeptides (namely, substance P, vasoactive intestinal peptide, neuropeptide Y, somatostatin, and cortistatin) (Olivera et al., 2018)

MRGPRX2-mediated mast cell degranulation depends on PTX-sensitive G proteins (Bischoff, 2009; Subramanian et al., 2011). It has been demonstrated that MRGPRX2 activation by LL-37 or human b-defensin-3 involves two different signaling cascades that act synergistically on degranulation. One is $G_{i/o}$-induced PKC activation, and the other is PTX-insensitive pathway leading calcium influx and release from internal stores (Subramanian et al., 2011, 2016). Another possible downstream signaling mechanism involves the activation of Rho-GTPases (Zang et al., 2020).

There is a cross-talk between sensory neurons and mast cells in that the neurons release a number of peptides such as substance P, VIP, CGRP etc, which can lead to mast cell degranulation. So this neuron-to-mast cell signaling results in neuroimmune interactions that eventually may contribute to chronic pain (Zuo et al., 2003). Since some basic secretagogues e.g., substance P, vasoactive intestinal peptide (VIP) etc can be secreted by primary sensory neurons, it is plausible to postulate that MRGPRX2 may also enhance neuron-to-mast cell signaling and hence resulting in neuroimmune interactions. This has pharmacological relevance as mast cells contribute to chronic pain, so the inhibition of such a paracrine signaling circuit would be an interesting approach for future analgesic therapy (Solinski et al., 2014). The receptor that mediates above-mentioned interaction seems to be mostly MRGPRX2. Therefore, it can be postulated that MRGPRX2 could be a target for pharmacological control of pain and itching (Solinski et al., 2014). Isoliquiritigenin is a chalcone isolated from the roots and stems of *Glycyrrhiza glabra, G. uralensis, and G. inflata*. Liquiritigenin is used in common foods as an alternative medicine, and its derivative-ISL is utilized as a food additive (Peng et al., 2015). This compound inhibits IgE-independent allergy through the interaction with MRGPRX2 (Hou et al., 2018).

MRGPCRX2 Activators: There are a number of activators of MRGPRX2 with a diverse chemical structure. The following are the agents demonstrated to cause pseudoallergic reactions so far through the activation of MRGPRX2. However, number of this list is likely to be expanded over time due to its promiscuity.

- Cortistatin-14
- Somatostatin, substance P, VIP
- PAMP(9-20), PAF, PACAP
- Neuropeptide Y
- Cathelicidin, b-defensin
- Mast-cell degranulating peptide
- Mastoparan (component of *hymenoptera* venom)
- GnRH analogues (cetrorelix, leuprolide, sermorelin)
- Angiotensin-converting enzyme inhibitors (ACEIs)
- Certain antibiotics such as fluoroquinolons (e.g., ciprofloxacin)
- Neuromuscular blocking agents (NMBAs)
- Opioids, antipsychotics phenothiazines
- Thimerosal
- Icatibant
- Octreotide

Inhibitors of MRGPRX2-mediated mast cell degranulation: Some compounds may inhibit mast cell degranulation through the inhibition of MRGPRX2 either directly or the signal transduction mechanism downstream of the receptor activation as follows:

- Shikonin and paeoniflorin *(Chinese herb-derived compounds)*, (Wang et al., 2020)
- Piperine *(a long pepper-derived alkaloid),* quercetin (plant-derived flavonoid) and saikosaponin A (one of the major active compounds inRadix bupleuri) (Ding et al., 2019; Wang et al., 2018)
- Tripeptide, QWF (glutaminyl-D-tryptophylphenylalanine)
- Roxithromycin (Zang et al., 2020)
- Isoliquiritigenin (Hou et al., 2018)

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HEALING PLANTS FOR SKIN DISEASES

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Scientific studies have shown that phytochemicals with antioxidant, anti-inflammatory and antimicrobial activities are common in herbal medicinal products (HMP). Therefore, plant-based products, i.e., plant extracts or phytochemicals etc. are used for thousands of years in dermatology, including wound healing, inflammatory skin problems, skin infections, and beauty products, i.e., against hyperpigmentation or sunburns and antiageing, etc.

Among the HMP in dermatology flowering aerial parts St.John's wort (*Hypericum perforatum*) has a unique place. Its naphthodianthrone type components "hypericin, pseudohypericin" in oily extract have been shown to act as a potent wound healing by increasing the collagen synthesis, fibroblast migration and infection resistance anti-inflammatory activity. Therefore St.John's wort oily extract is popularly used to reduce the healing period as well as scar in wounds and even in decubitis ulcers.

Carotenoids and triterpene alcohols in dried flowers of Marigold (*Calendula officinalis* or *C. arvensis*), flavonoids and volatile components in flowers of German chamomile (*Matricaria recutita*), sesquiterpene lactones in dried flowers of Arnica (*Arnica montana*), triterpene saponins in the aerial parts of Centella (*Centella asiatica*) and seeds of Horse chestnut (*Aesculus hippocastanum*) are the other popular wound healing HMPs.

Licorice roots (*Glycyrrhiza glabra*) also rich in triterpene saponins; glycyrrhizin, glycyrrhetinic acid. These components are shown to be effective in atopic dermatitis, inflammatory dermatosis and recurrent aphthous stomatitis. Recent investigations have shown that another group of components in the roots "prenylated isoflavonoids," i.e. glabridin, "chalcones," i.e. isoliquiritigenin to possess tyrosinase inhibitory activity and these have been formulated against hyperpigmentation.

Aloe gel is the jelly part in the middle part of *Aloe vera* leaves which is composed of polysaccharides. Aloe gel finds a widespread application in various dermatological problems; burns, wounds, skin inflammations, skin ulcers, aphthous wounds and also reported to increase the skin absorption rate of the chemical agents such as hydrocortisone.

Evening primrose oil, is obtained from the seeds of *Oenothera biensis*. Due to its rich Gamma-linolenic acid composition, it has been prescribed against atopic dermatitis to reduce symptom scores (pruritus, cortication, size) and increase recovery period.

Psoriasis is another severe dermatological problem with limited treatment options. Several HMP have been reported to reduce the disease symptoms. Among these, liposomal Turmeric rhizome (*Curcuma longa*) extracts (Meriva) was shown to increase filaggrin and involucrin levels and reduce phosphorylase kinase and proinflammatory cytokines (IL-17, TNF-α). Another possible beneficial HMP is Olibanum (*Boswellia serrata*) resin. Its active triterpenic acid component 3-acetyl-11-keto-beta-boswellic acid (AKBA) has shown to reduce the "psoriasis area severity index" (PASI) significantly on 12-week external application by inhibition of PGE_2, VEGF, TNF-α and $LTN\text{-}B_4$. St.John's wort oil has also been shown to reduce the PASI by its anti-inflammatory activity as well as by reducing the cell proliferation, TNFα expression and increasing the calcium influx, TRPC6 expression and cell differentiation.

For skin infections essential oils have been shown to possess a good antibacterial, antifungal and antiviral potentials. Particularly 1,8-cineol (Eucalyptus, Sage, Teatree oils), eugenol (clove oil), thymol/carvacrol (thyme, oregano oils) and bisabolol (German chamomile oil).

As conclusion, a wide range of plant metabolites, phenolics, flavonoids, procyanidins, triterpenes, volatile oils, polysaccharides, as well as essential oils or fatty oils are used in dermatology for various skin problems. Their activity profiles and mechanisms of actions are proven by detailed experimental and clinical investigations.

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KETOGENIC DIET IN DERMATOLOGY

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Ketogenic diet is a kind of diet program which contains very low carbohydrate, moderate protein and high fat diet designed to induce hepatic production of ketone bodies as an alternative fuel source. There are several participants in the world and raising its popularity day to day . This diets users says that it's very good for health and has no side effect for their body. With the increase of holistic medicine applications in the recent years, many medical doctors have been recommending this diet to the patients(1-6). Moreover, there are no large-scale studies of the ketogenic diet, there is no verified standardization in iniating and monitoring it. There are anecdotal methods (1).

The historical evidence shows us that the diet was offered by Hipoccrates as well. In early ancient times, physicians gave the diet to their patients for epilepsy and other neurological system (1,2). Today, it is widely used in childhood and adult epilepsy, Alzhiemer's Dementia, Parkinson's disease, brain and other cancers, Autism Spectrum Disorder.

Ketogenic diet and its effects are also investigated in inflammatory disorders, cardiovascular disease, management of diabetes mellitus, metabolic diseases, and malignacy (3-5).

Some adverse effect have been reported. The only known absolute contraindications to a ketogenic diet are porphyria and pyruvate carboxylase deficiency secondary to underlying metobolic disregularity. Metabolic cytooathies and carnitine deficiency are relative contraindications. Possible side effects are dehydration, acidosis, hypoglycemia, dyslipidemia, and electrolyte imbalance. These side effects are temporary and can be easily managed (5).

Ketogenic diet reduces IL-1 beta levels by suppressing NLPR3 inflammasome. This provides clinical improvement in inflammatory conditions such as Behçet's disease, hidradenitis supurativa, gout, sunburn, contact hypersensitivity, and metastatic melanoma (1). Very-low-calorie balanced ketogenic diet results in fewer produced reactive oxygen species (ROS) and provides an increase in the nicotinamide adenine dinucleotide ratio produced by the mitochondria, and with this mechanism, cellular energy can be provided through the mitochondrial system. Another hypothesis is that the levels of glutathione, a powerful antioxidant, increases in the body as a result of the ketogenic diet (1).

Other therapeutical effects are antioxidation effects, possible effects on mammalian target of rapamycin (mTOR) regulation, and exploitation of the Warburg effect. It suggested that ketogenic diet may play improvement on disease states through hormonal normalization, and improvement of metabolic risk factors (1).

There are no clear proven clinical results from the ketojenic diet in the dermatology. Further, other diets have shown benefit for many other disesase and health promotion purposes (1).

In recent years, it has been accepted that acne vulgaris is a metabolic disease of sebaceous glands (6). It is known that insulin resistance, obesity, type 2 diabetes, cancer and Alzheimer's disease develop through the pathway of a kinase termed mammalian target of rapamycin complex 1 (mTORC1). Acne vulgaris is also suggested to occur through the same pathway (6). It is claimed that by regulating the mTOR pathway, it can heal diabetes, obesity and related cardiovascular problems. A ketogenic diet results in very little insulin secretion. Ketons also have anti-inflammatory effects by itself. Therefore, many clinicians have adopted the opinion that ketogenic diet should be given in addition to medical treatments in acne patients (6).

The relationship between acne vulgaris and high carbonhydrate diet has been researched for years, but there are conflicted publications. Mediterranean type is adopted if the diet stoppes the inflammation on acne vulgaris. Karadag and collegues studied acne and they found a positive correlation with chocolate, bread, green tea, milk, white sugar, ripe banana, ice cream, apple, orange, and red meat consumption. The authors suggested that there was statistically significant relationship between acne severity and dietary factors such as chocolate, dairy products such as milk, sunflower seed consumption within the geographical regions (7) .

In a study Castaldo and their collegues investigated the effects of ketogenic diet with stable chronic plak psroriasis. They follow the obesity-psoriasis patient with only very-low-calorie ketogenic diet within 10 weeks. The authors reported a significant decrease in PASI scores, a decrease in itching score, and an improvement in the Dermatology Life Quality Index score with significant weight loss. They suggested that a balanced, hypocaloric, Mediterranean-like diet, may be an effective first-line strategy to reduce psoriasis severity (8). At the same time, ketogenic diet is recommended

to obese psoriasis patients by Barret et al (9).

Another common condition we as dermatologists see is skin disease due to diabetes mellitus. Ketogenic diet is recommended in the control of conditions such as bullosis diabeticorum, diabetic dermopathy, varicose ulcers, acanthosis nigricans, pruritus, necrobiosis lipoidica diabeticorum. Improvement has been shown to be due to reduced glycation end products and free radicals, increased insulin sensitivity, and decreased inflammation, along with low sugar entry into the body (1).

Prurigo pigmentosa may occur after severe ketogenic diet. There have been many notifications in recent years. In this case, the patients improved by adding carbohydrates to their diet (10). It is thought that ketosis was caused by fasting, and that diet may contribute to the pathogenesis of prurigo pigmentosa. Clinicians should keep this situation in mind and question it in the anamnesis.

There have been no large scale, randomized, controlled studies on the relationship between dermatological cancers and the ketogenic diet yet. There are hypotheses that cancer cells do not and may not metabolize ketone. It is suggested that adding this diet to the treatments can slow down cancer growth (1).

It is thought that the ketogenic diet will be beneficial in inflammatory skin diseases such as acne, psoriasis, allergic skin reactions and drug-related photosensitivity as it decreases tissue inflammation, increases glutathione and reduces free oxygen radicals (1).

It is known that intermittent fasting, coffee consumption, low level aerobic activity also puts the individual in a ketogenic state.

Conclusion :

Ketogenic diet may be used in dermatology practice, such as acne and similar eruptions, psoriasis, seborrheic dermatitis, pruritus. It can be given in addition to medical treatments as adjunctive, (safety, tolerable, low-cost) treatment. It is important to select appropriate patient.

Key words: ketogenic, skin , inflammation, dermatology and diet.

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DO VITAMINS WORK FOR SKIN DISEASES?

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Vitamins are important constituents of diet and they are classified as water-soluble (B group and C) and fat-soluble (A, D, E, K). They are essen¬tial for the maintenance of body and as well as skin functions. They play roles in skin health by exerting different actions such as antioxidant activity, synthesis of collagen, regulation of sebum and keratinisation, collagen synthesis, photoprotection and extracellular matrix homeostasis (1,2).

Vitamins are used in prevention and treatment of numerous dermatological diseases including skin cancers, atopic dermatitis, psoriasis, alopecia, vitiligo, acne and photoaging. They can be used both topically or systemically (1,3-5).

Biotin, nicotinamide, folic acid, vitamin A, C, D and E are used in dermatology practice (3, 6). Especially the role of vitamin D in dermatological diseases has a growing interest. Vitamin D supplementation is recommended in psoriasis, atopic dermatitis, ichthyosis congenita, acne, hidradenitis suppurativa, vitiligo, systemic lupus erythematosus, polymorphic light eruption, alopecia areata, melanoma and nonmelanoma skin cancers (7).

Supplementation of vitamins may also have some risks such as teratogenicity, interactions with drugs, allergic reactions, and others. Physicians should warn patients on these risks (8).

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DOES PHYTOTHERAPY REAL OR NOT FOR SKIN THERAPY?

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Phytotherapy is a herbal treatment approach in which standardized pharmaceutical formulations (tablet, capsule, cream etc.) which consist of medicinal plants and their active compounds (drugs) are employed in order to prevent diseases or to support conventional medical treatment (1). It has been applied in dermatology for a long period of time. However, there are very few scientific research of which clinical effects are proved through evidence-based methods on phytotherapeutic agents.

Dermatologists to be the authority being consulted and giving exact information in the field is inevitable with regard to avoiding potential complications; considering negative experiences of patients on dermatological diseases with a chronic course, the faith of patients on complementary therapies, and their increasing demands.

Although phytotherapeutic agents are applied in the treatment of many dermatological diseases; hyperpigmentation, vitiligo, psoriasis, acne vulgaris, and anogenital warts can be counted among dermatological entities supported by evidence-based studies.

Several botanicals such as, flavonoids in silymarin, pycnogenol, soy extract, licorice suppress melanogenesis by inhibiting reactive oxygen species formation and tyrosinase enzyme Botanicals most effectively treat acute forms and superficial (epidermal) forms of hyperpigmentation. They obtain a very low level of efficiency in cases of post inflammatory hyperpigmentation, drug-induced and dermal pigmentation (2).

In vitiligo cases, Polypodium leucotomos extract, a species of shield fern, with a content of such bioactive components as phenolic acid, benzoate, cinnamate, and ferulic acid, reduces UV radiation-mediated oxidative DNA damage, demonstrating antioxidant and immunomodulatory effect. It has been shown that whereas PLE stimulates repigmentation of NB-UVB / PUVA combination, it also lowers the risk of side effects via photoprotective effect (3).

It has been indicated that %52.3 of psoriasis patients are not satisfied with existing treatment, and %51 of them turn to complementary methods despite the lack of studies on their efficiency and reliability (4). In plaque psoriasis and psoriatic nails, Indigo naturalis with indirubin as its active component has an antipsoriatic effect with the regulator of keratinocyte proliferation and differentiation, and IL-17 inhibitor (5). Hyperforin, the major lipophilic active ingredient of St. John's wort (Hypericum perforatum (L.)), shows anti-inflammatory effects, and stimulates calcium influx into psoriasis keratinocytes. It also activates TRPC6 expression, reduces cell proliferation, and promotes proper cell differentiation. With the usage of 5% St. John's wort extract, it has been reported that a significant recovery was observed in patients with psoriasis, erythema, extension and the psoriatic plaques thickness (6).

Epigallocatechin gallate (EGCG) (Polyphenon E ointment), which is obtained from dried leaves of green tea (Camellia sinensis L.) is the first herbal medicine to get approval in the treatment of condyloma acuminata. Its mechanism of action is to reveal antiangiogenic activity suppressing vascular endothelial growth factor (VEGF) stimulated by TNF-a, and IL-8-mediated inflammation (7). It has been shown that EGCG provides regression in inflammatory and noninflammatory lesions, inhibiting Propionibacterium acnes' activity increase, hyperseborrhea, and follicular dyskeratinization steps involved in the pathogenesis of acne vulgaris (8).

Ingenol mebutate has an active component of macrocyclic diterpene ester which is found in Euphorbia peplus (milkweed). It received approval of FDA in the cases of actinic keratosis on the face, scalp, body, and extremities. Its efficiency has been shown by many randomized controlled studies (9). Ingenol mebutate is found on the market as the trading name of Picato gel at a concentration of 0.015% and 0.05%. Its mechanism of action is not completely known. However, it has been estimated that it operates via a kind of chemo-ablation, triggering direct and rapid cell death over sharp cytotoxic and neutrophil-mediated inflammatory effect (10).

As a result, the usage of phytotherapeutic agents in the field of dermatology has gathered speed nowadays. Nevertheless, it is not likely to come to a clear conclusion on its efficiency since it has been employed in different methodological approaches, and active ingredients are not in similar concentrations and standardized formulations. Thus, phytotherapy taking its place in dermatology can only be possible with trainings included in positive sciences, and enhancing the knowledge and experience of medical attendants in terms of effects, side effects and its interaction with conventional treatments, being supported by evidence-based studies.

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INTEGRATIVE APPROACHES OF PSORIASIS AND PSORIATIC ARTHRITIS

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Psoriasis and psoriatic arthritis are immune-mediated diseases with skin and joint involvement, but not limited to these areas. These diseases have an increased risk of cardiovascular and metabolic diseases.

Psoriatic arthritis (PsA) is a heterogeneous, erosive and systemic inflamatory disease. Main clinical domains are peripheral and axial joints, enthesitis, dactylitis, skin and nails. Psoriatic arthritis (PsA) affects up to 30% of patients with psoriasis.

The first complaint of psoriatic arthritis patients is mostly skin lesions, and dermatologists are the first physicians who see these patients. It is important for dermatologists to refer patients with critical symptoms to the rheumatology department in order to avoid delay in diagnosis.

There are lots of new therapies available for PsA. Basic treatment of PsA is NSAIDS and traditional disease-modifying anti-rheumatic drugs (DMARDs). However, these treatments have not been shown to prevent radiographic progression. For this purpose, anti-TNF agents are good choices. Other alternetive medications are oral phosphodiesterase 4 inhibitor, apremilast; a Janus kinase (JAK) inhibitor, tofacitinib; and several new biologics that target the IL-23/IL-17 pathway including secukinumab, brodalumab, ixekizumab, and ustekinumab.

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MANAGEMENT APPROACH TO PSYCHOCUTANEOUS DISORDERS

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Psychodermatology is a growing specialty which is gaining momentum in different parts of the world. It focuses on the connection between skin and psyche. Psychocutaneous conditions are characterized by those disorders where stress is the key element in exacerbating skin conditions or flare ups of dermatoses like psoriasis and atopic dermatitis. There is a direct relationship of stress with the course, and prognosis of the skin disease. In some situations, there is no skin condition but the lesions are self-inflicted and such disorders are always associated with underlying psychopathology or psychological conflicts. Sometimes emotional problems are more prominent as a result of having skin disease and the psychological consequences may be more severe than the physical symptoms. Management of these conditions require a combination of psychpharmacology, psychotherapy and liaison clinics of psychiatry and dermatology. This presentation focuses on the common management approach which can be adopted by deramtologists in treating patients with psychodermatological disorders, improving doctor-patient relationship and therapeutic bond. An optimal jnowledge of psychotropic medications and basic psychotherapeutic techniques is vital in the long term mnagement of these patients.

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TATTOO AND PSYCHOLOGY

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Tattoos have become increasingly popular in recent years .The possession of the oldest known tattoo belongs to Iceman Ötzi who lived 5300 years ago and is recognized as the oldest mummy of the world. Tattoos are not just an ink, figure or drawing on the body, but a tool for individuals to express themselves and to construct self-identity. They have symbolic meanings for emotions and they may be a clue for individuals behavior patterns. Consequently, tattooing is a complex practice and a subject of psychodermatology.

PERSONALITY DISORDERS IN DERMATOLOGY

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There is a significant psychiatric comorbidity that exists in multiple dermatological conditions, stemming from the patient's own psychological make up. Patient's childhood experiences, family structure and family dynamics during developmental years play a significant role on patient's personality. This presentation focusses on personality disorders and their types, which influence the course and prognosis of several psychodermatological disorders. Self-inflicted skin lesions, for example, are usually associated with obsessive-compulsive behavior, but they also share connections to Narcissistic and Borderline personality disorders. Body dysmorphic disorder is another psychodermatological condition seen in dermatology, aesthetic, and cosmetic surgery clinics, which is influenced by patient's personality type. In general, there is a significantly high proportion of personality disorders seen in aesthetic and cosmetic surgery. The management of patients with personality disorders is challenging, but joint liaison between psychiatry and dermatology has proven helpful and can provide patients with the best care for their psychological needs and dermatologic care.

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BULLOUS DISEASES

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Bullous skin diseases are a group of potentially life-threatening dermatoses include the clinical features are blisters, bullae and erosion in the skin and mucous membranes (1). Bullous skin diseases can be divided into autoimmune and non-autoimmune bullous skin (ABD) diseases (2, 3). Pemphigus and bullous pemphigoid (BP) are the most prevalent ABD. Pemphigus encompasses a group of autoimmune intraepidermal blistering diseases classically divided into two major variants: pemphigus vulgaris (PV) and pemphigus foliaceus (PF). Pemphigus herpetiformis, IgA pemphigus, paraneoplastic pemphigus and IgG/IgA pemphigus are rarer forms. The pemphigoid group represents a group of autoimmune disorders characterized by subepidermal blistering. This group includes mainly BP, linear IgA disease, dermatitis herpetiformis, and epidermolysis bullosa acquisita. ABD run a chronic course and are associated with significant morbidity and even mortality (2-5). In this lecture, treatment of bullous diseases will discussed with four challenging cases, we have seen in our clinical experience.

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VASCULITIS

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Vasculitis (also called angitis) is a general term for several conditions that cause inflammation in blood vessels (1-3). The type and size of the vessels involved are taken into consideration in the classification of vasculitis, Skin involvement rarely develops in large vessel vasculitis and is seen as diffuse necrosis of the skin. Livedo reticularis, retiform purpura, nodules, ulcers, infarcts and necrosis are observed in medium sized vessel vasculitis.. Palpable purpura, macular purpura and urticarial papules are most commonly observed in small vessel vasculitis. Small and medium sized vessels are involved in ANCA-associated vasulitis (AAV) and also small and medium-sized arterioles in the upper layers of the skin and in the deeper subcutaneous tissues are involved in AAVs Therefore the clinical examination spectrum includes findings related to vasculitic involvement of these vessels. (4). Palpable purpura is the most common cause of clinical signs of small and medium vessel involvement in AAV. When evaluating a case with a suspicion of vasculitis for the presence of palpable purpura, the patient should be assessed systemically, laboratory tests and ANCA tests should be performed, biopsy and histopathological examination is required and additional skin sample should also be taken for direct immune fluorescence analysis method that determines the accumulation of immune reactant /deposits. Additional studies should be conducted for classification. (5-6). AAVs are classified as granulomatous polyangitis (GPA), microscopic polyangitis (MPA) ve and eosinophilic granulomotosis with polyangitis (EGPA). This group of vasculitits is quite rare, they involve various organ systems and cause severe systemic vasculitis. Skin involvement is a common finding in AAV, it is approximately found in %47 of GPA, %44 of MPA and %40 in EGPA (1-3). Unlike immune complex vasculitis, vascular damage develops directly in AAVs. Vascular damage is mediated by neutrophils, therefore AAVs are also called "pauci-immune" vasculitis. The formation of ANCAs in this group of vasculitis also causes impairment in neutrophil apoptosis resulting in a long-term opportunity for autoantibody development. Cutaneous symptoms are common and variable in GPA, EGPA and MPA and 50% of the cases with skin involvement have more than one cutaneous symptom. The most important and common cutaneous finding is petechiae and purpura and should be considered a sign of systemic vasculitis. Cutaneous involvement is observed more frequently in EGPA and GPA than MPA and there is a significant relationship between skin involvement and systemic involvement severity in these diseases. Skin involvement increases the risk of systemic involvement of the disease. In EGPA and ANCA (-) patients, non-vasculitic skin findings such as itching, urticaria, maculopapular rash can be observed. In this talk, a case with marginal zone lymphoma later diagnosed with eosinophilic granulomotosis with polyangitis (EGPA) will be discussed.

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HOW CAN WE TREAT CHALLENGE CASES? PRURITUS

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Pruritus is a difficult condition to treat with a significant effect on quality of life.1 Several diseases could be the cause of pruritus such as atopic dermatitis, mycosis fungoides, bullous pemphigoid, scabies.

Atopic dermatitis is a chronic disorder characterized by intense itching and recurrent eczematous lesions. Although it usually starts in infancy, senile onset atopic dermatitis is seen in patients older than 60 years old. Pruritus is the dominating symptom of atopic dermatitis.2

Cutaneous T Cell Lymphomas are the most common primary cutaneous lymphomas and pruritus is frequent in these patients. It is unrelieved by emollients or oral antihistamines. It interferes with sleep. Water could worsen the situation. In the advanced stages, patients generally define a severe and diffuse pruritus that may resemble “burning pain”.3

Bullous pemphigoid is an autoimmune subepidermal blistering disorder, characteristically presents with tense bullae. Intense generalized pruritus is reported by the patients and in atypical cases, pruritus could be the only sign of the disease without bullous lesions. These cases require a high degree of clinical suspicion.4

Scabies is a common parasitic skin infestation characterized by severe pruritus. Scratching and encrustation could be recognized. Pruritus is the prominent symptom of scabies and it is generally difficult to manage.5

When the patients’ complaint is only pruritus, it is going to be difficult to make the diagnosis. Many dermatological conditions are included in the differential diagnosis for the pruritus and atopic dermatitis, mycosis fungoides, bullous pemphigoid, scabies are the diseases among them. We should consider these diseases in differential diagnosis in patients with pruritus. If we make the correct diagnosis, we can treat challenge cases.

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HIGHLIGHTS OF THE CURRENT TOPICAL ANTIBIOTIC GUIDE IN INFECTION DISEASES

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Topical antibiotics are widely used in skin diseases and they have many indications. However, bacterial resistance has developed against many antibiotics due to unnecessary use or long-term use in some diseases. This situation leads to the development of resistance in bacterial colonization in the host as well as resistance in the treatment of diseases. In this presentation, principles regarding the use of topical antibiotics in superficial skin infections are presented along with the literature. As a dermatologist, our primary goal is to prevent antibiotic resistance with rational approaches by preventing unnecessary use of drugs as well as the correct and adequate use of drugs for appropriate indications. Correct and rational use of antibiotics is very important, as well as starting the patient in need on time, stopping the drug on time, and deciding on which indication to be given topical and which systemic treatment is very important. In this presentation, respectively, under the guidance of the current topical antibiotic guide; the principles of topical antibiotic use and indications for systemic treatment in impetigo, ecthyma, folliculitis, furuncle, carbuncle, abscess, erysipelas, cellulitis, paronychia, ingrown toenails and corynebacterium-associated skin infections will be discussed. Topical antibiotics commonly used in superficial skin infections are; mupirocin, retapamulin 1% ointment; a new class of topical antibiotic, effective against bacteria with multiple antibiotic resistance, fusidic acid; which has increased resistance rates due to its widespread empirical use recently, oxytetracycline and polymyxin B combination, bacitracin and neomycin combination and ozenoxacin cream. In cases where Gram-negative infections are predominant, topical gentamicin and nadifloxacin are preferred. In addition, the use of topical clindamycin, erythromycin, mupirocin, fusidic acid and benzoyl peroxide comes into prominence in clinical pictures such as erythrasma, pitted keratolysis and trichobacteriosis, which develop under appropriate conditions depending on the corinobacterium species.

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ORAL PRESENTATIONS

OP-01 [Urticaria, Angioedema]

The Relationship Between Uric Acid Level and Disease Duration and Disease Activation in Patients with Chronic Urticaria

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INTRODUCTION & OBJECTIVES: Chronic urticaria is characterized by spontaneously appearing itchy wheals anywhere on the body.If autoantibodies or unknown causes induce the disease,it is called chronic spontaneous urticaria(CSU). Uric acid is a metabolic marker whose importance has been better understood in recent years.It has been reported that high uric acid levels are associated with metabolic syndrome. Because high uric acid levels are an indicator of oxidative stress and inflammation.In the current literature, uric acid has never been studied in patients with chronic urticaria.It was aimed to evaluate the relationship between the level of uric acid and disease duration and urticaria activation score in chronic urticaria patients.

MATERIAL & METHODS: We prospectively selected patients who admitted to the Dermatology outpatient clinic between March 2020-January 2021 and did not use any medication diagnosed with CSU.The necessary approval was obtained from the local ethics committee.

RESULTS:Atotalof131participants,62CSUand69controls,were evaluated in the study.33 of 62 chronic urticaria patients included in the study were female(53.2%),and 36(52.2%) of 69 control group patients were female.The mean age was 35.53±12.15 in the urticaria group and 35.54±11.57 in the control group.There was no difference between the two groups in terms of age and gender. CRP values were 4.46±5.57mg/L in the CSU group and 1.98±1.54mg/L in the control group.CRP was statistically significantly higher in the CSU group(p<0.001).The mean UAS7 score in CSU patients was found to be 20±8.8.There was no correlation between the UAS7 score and CRP(p=0.98). The uric acid value was 4.95±1.37mg/dl in the CSU group and 4.35±0.99mg/dl in the control group.Uric acid levels were found to be significantly higher in the CSU group(p=0.015).In correlation analysis, there was no correlation between UAS7 score and uric acid increase(p=0.25).Disease duration in CSU patients was found to be 21±15.9 months.Uric acid levels were correlated with the increase in disease duration(p=0.001).The data of the CSU and control group are summarized in Table1.

CONCLUSIONS:Urticaria is divided into two classes as acute and chronic(lasting more than 6 weeks).It is known to be associated systemic inflammation with CSU.It has been reported that high sensitive CRP(hs-CRP) is a better marker than standard CRP in diseases with low systemic inflammation.We could not find a correlation between CRP and UAS7 scores in our patients.We thought that the reason we could not find a correlation with CRP might be that we looked at the standard CRP level in the study. Uric acid value was found to be significantly higher in CSU cases than in the control group.Again, we found that uric acid level not correlated with the UAS7 score,but correlated with the increase in the duration of the disease.Our findings can show that the increase in disease duration rather than disease severity(UAS7) increases metabolic complications in CSU.

Keywords: Urticaria, uric acid, metabolic comorbidity, urticaria activity score 7 (UAS-7)

Table 1

	CSU group	Control group	p value
Age	35.53 ± 12.15	35.54 ± 11.57	>0.05
Gender, woman n(%)	33 (53.2%)	36 (%52.2)	>0.05
CRP (mg/L)	4.46 ± 5.57	1.98 ± 1.54	<٠,٠٠١
Uric acid (mg/dL)	4.95 ± 1.37	4.35 ± 0.99	0.015

The comparison of the CSU and control group

OP-02 [Autoimmune Connective Tissue Disorders]

Macrophage Activation Syndrome Due to Juvenile Amyopathic Dermatomyositis with Atypical Onset

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INTRODUCTION: Macrophage activation syndrome (MAS) is a life-threatening condition associated with rheumatic diseases. It has been rarely reported in juvenile dermatomyositis. Whereas classic dermatomyositis usually presents as classical skin findings accompanying myopathy, atypical onset and misdiagnosis are common in juvenile amyopathic dermatomyositis (JADM), since skin lesions are generally more atypical than in adults, and myopathy is not observed. Because of the atypical onset, we reported a case of eight-year-old girl with JADM misdiagnosed as psoriasis, and rapidly progressed to MAS.

CASE: A eight-year-old girl admitted to the pediatric rheumatology outpatient clinic with joint swelling and psoriasiform plaques on the dorsal surfaces of her elbows. She was diagnosed with psoriatic arthritis, and methotrexate therapy was started. Three months later, the patient

readmitted with intermittent fever, fatigue, weight loss, and arthralgias. On physical examination, body temperature was 38.5°C. Hepatosplenomegaly was observed. Muscle strengths were 5/5. On dermatological examination, facial edema, generalized maculoerythematous rash and xerosis were present. Erythematous-violaceous papulosquamous plaques were seen on dorsal surfaces of the elbows, metacarpophalangeal and proximal interphalangeal joints. Laboratory examination revealed cytopenia, hyperferritinemia, and hypertriglyceridemia. Antinuclear antibody titers were positive. On histopathological examination of the skin marked vacuolar degeneration was observed in the basal layer. Based on clinical and laboratory findings, according to the diagnostic criteria of hemophagocytic lymphohistiocytosis (HLH)-2004 which include fever, splenomegaly, cytopenia, elevated triglycerides/decreased fibrinogen, increased ferritin, histological demonstration of hemophagocytosis, decreased NK cell function, and increased soluble IL-2 receptor levels, the patient was considered MAS secondary to JADM. The cutaneous manifestations seen in MAS are not specific but depend on the underlying rheumatic disease. In the literature, the most common skin findings in patients with MAS secondary to JDM are heliotrope erythema, Gottron's papules, Gottron's sign, and periungual changes. The cytokine storm seen in MAS may cause more atypical skin lesions, such as facial or generalized edema, severe xerosis, and generalized maculoerythematous rash. heliotrope rash wasn't present. Poddighe et al. reviewed the JDM cases developing MAS; two out of 12 patients were diagnosed with amyopathic forms. The mortality rate in JDM might resemble quite similar to MAS in other rheumatic diseases. Unlike sJIA and SLE, MAS was usually the onset presentation of JDM.

CONCLUSION: MAS may result in a progressive multi-organ failure and, if not timely treated, it can be fatal, so early diagnosis is critical. In MAS with atypical skin findings, even if myopathy is not accompanied, JADM should be considered in the differential diagnosis.

Keywords: Macrophage Activation Syndrome, Dermatomyositis, Connective Tissue Diseases, Psoriasis

Figure 1

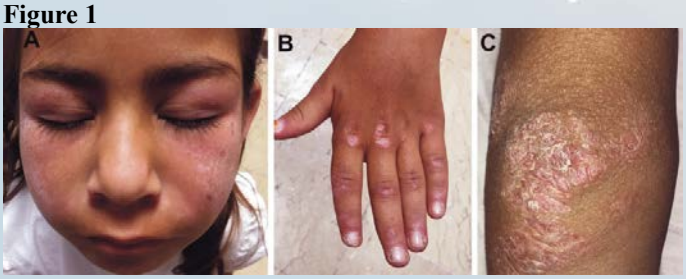

Figure 1: On second hospital admission, the patient presented with (A) facial edema, maculoerythematous rash, and xerosis on the face, (B) erythematous-violaceous papulosquamous plaques on dorsal surfaces of the metacarpophalangeal and interphalangeal joints, the cuticle was hypertrophic, (C) erythematous-violaceous papulosquamous plaques on dorsal surfaces of the elbows.

Figure 2

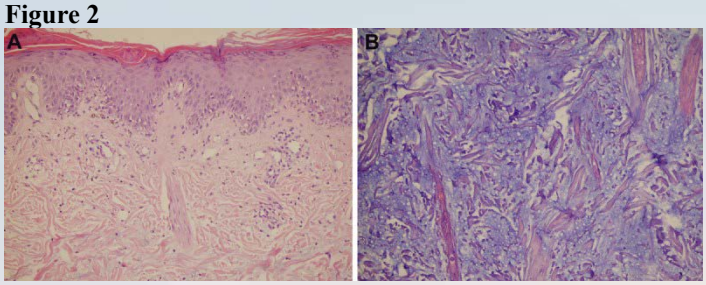

Figure 2: Histological images of the skin biopsy specimen from a papulosquamous plaque on the elbow. Histopathological examination showing (A) mild spongiosis, necrotic keratinocytes, vacuolar degeneration of basal layer, mild perivascular lymphohistiocytic infiltration (Hematoxylin-eosin stain; x 200), (B) increased dermal mucin highlighted by Alcian blue stain (x 200)

Laboratory investigations

Investigations	Patient	Normal range
WBC (103/dL)	3.7 (58% neutrophils, 28% lymphocytes)	3.8-8.6
Hemoglobin (g/dL)	10	11.1-17.1
Platelets (103/dL)	89	140-360
ESR mm/h	39	0-20
ALT (IU/L)	133	<40
AST (IU/L)	618	<40
GGT (IU/L)	200	<55
LDH(IU/L)	337	120-246
Total protein (g/dL)	6.9	6.6-8.7
Albumin (g/dL)	3.2	3.5-5.3
Ferritin (ng/mL)	968	2-276
Fibrinogen (mg/dl)	202	170-420
CK (IU/L)	86	24-195
Triglyceride (mg/dL)	205	40-180
CRP	3.2	<5
ANA	Positive (1/100, granular pattern	

Abbrevations: WBC, White blood cell count; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; ALT, Alanine transaminase; AST, Aspartate transaminase; GGT, Gama glutamil transferase; LDH, Lactate dehydrogenase; CK, Creatine kinase; ANA, Antinuclear antibody.

OP-03 [Allergology and Immunology]

COVID-19 infection in patients receiving omalizumab treatment due to chronic urticaria

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INTRODUCTION & OBJECTIVES: The prevalence of chronic urticaria is reported as 0.5-5% in the literature. The second-generation H-1 antihistamine drugs are the first step in the standard treatment guidelines for chronic urticaria. Although second-generation H 1 -antihistamines are the mainstay of symptomatic therapy in chronic spontaneous urticaria, up to a quarter of patients remain symptomatic, even increasing the dose up to four-fold above licensed doses. For these refractory patients, omalizumab is suggested in the guidelines. Omalizumab may cause additive anti-inflammatory and immunomodulatory effects by restoring the capacity of human plasmacytoid dendritic cells and downregulation of high-affinity Ig E receptor to produce IFN-α, lead to increasing antiviral activity.

MATERIALS & METHODS: Thirty-two patients (22F, 9M) between the ages of 21-59 were included in the study who received regular omalizumab treatment for antihistamine resistant chronic urticaria during the pandemic period in Adana City Hospital Allergy Clinic. They were asked whether they have been infected by SARS- Cov-2 since the beginning of the pandemic period. Patients with COVID-19 disease were evaluated according to the disease severity (e.g., hospitalization, pneumonia severity, or other manifestations). The patients' information about infection was obtained from records retrospectively. In case of an active infection, the treatment of omalizumab was discontinued until recovery.

RESULTS: Five (4F, 1M) of thirty-two patients between the ages of 36-47 had a documented SARS-CoV-2 infection until now. Two of the female patients had pneumonia detected by thorax computerized tomography (CT). A diffuse ground glass appearance was detected in CT of the two patients, who presented with back pain first. One of those who had pneumonia had hypertension and diabetes mellitus. They easily recovered despite widespread lung lesions. The other three patients with Covid-19 İnfection (1M, 2F) had myalgia and headache. None of them had an urticarial attack, and all of the patients recovered in the outpatient clinics. Six patients (5F, 1M) had negative results even they had a close contact history with the positive family members. Other patients had no history of COVID-19 disease.

CONCLUSIONS: Omalizumab therapy used in anti-histamine-resistant chronic urticaria may also have antiviral efficacy.

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Keywords: chronic urticaria, omalizumab, anti-viral efficacy

OP-04 [Acne and Related Disorders, Hidradenitis Suppurativa]

Evaluation of the laboratory parameters in hidradenitis suppurativa: Can we use new inflammatory biomarkers?

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BACKGROUND: HS is a chronic, recurrent, and debilitating skin disease. Increasing evidence suggests that HS involves dysfunctional immune responses in both adaptive and innate immune systems. This may affect the leukocyte types in circulation. Recent studies showed that inflammatory biomarkers, such as neutrophil–lymphocyte ratio (NLR), platelet–lymphocyte ratio (PLR) and Lymphocyte/HDL ratio (LHR), Neutrophil/HDL ratio (NHR), Monocyte/HDL ratio (MHR) are an indicator of inflammatory diseases and may be associated with disease severity and disease activity. There are few studies on this subject in HS.

AIM: To investigate NLR, PLR, LHR, NHR and MHR in HS patients. In addition, to compare erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complete blood count, leukocyte profile and biochemical parameters between the control and the patient group.

MATERIALS-METHODS: Clinical and biochemical data of patients and healthy subjects were collected from medical records, retrospectively. In total, 166 patients with HS and 124 control subjects were included.

RESULTS: Average disease duration was 6.01 years. The most common affected area was axilla and groin in HS group. Triglyceride ($p < 0.001$), total cholesterol ($p < 0.001$), LDL ($p < 0.001$) were significantly higher in patients, while HDL ($p < 0.001$) was significantly lower in the patient group. We found no significant difference in NLR ($p=0.207$) and PLR ($p=0.257$). LHR ($p < 0.001$), NHR ($p < 0.001$) and, MHR ($p < 0.001$) were significantly higher in the patient group. No positive correlation was found between any of these markers and disease severity according to Hurley staging system. However, MCV (Mean corpuscular volume), RDW (Red cell distribution width) and CRP showed a significant positive correlation with disease severity. Among these markers, only MHR was

positively correlated with disease duration.

CONCLUSION: Our study shows that CRP still maintains its value for HS patients compared to new inflammation markers. Unlike the studies in other inflammatory diseases, no significant relationship was found with most of these inflammatory parameters. MHR may be more useful in patients with HS as an indicator of inflammation compared to other parameters.

Keywords: C-reactive protein, hidradenitis suppurativa, inflammation, leukocyte profile, monocyte/high density lipoprotein ratio, neutrophil-to-lymphocyte ratio

OP-05 [Nail Disorders/Diseases]

Clinical and demographic characteristics of patients with ingrown nails

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İngrown nail describes the puncture of periungual skin by its corresponding nail plate,resulting in a cascade of foreign body,inflammatory, infectious and reparative processes.The hallux nails are most often involved.It is highly uncomfortable and painful for the patient and leads to workforce losses.The most predisposing factors for ingrown nails are factors such as incorrect nail cutting habit,poorly fitting shoes,obesity,skeletal or nail deformities,pregnancy,medications,bad foot hygiene and hyperhidrosis.The soft tissue in the nail sulcus is not normally in contact with the nail edges.The balance between the lateral nail sulcus and nail body is impaired by the factors that cause ingrown nails.There is not enough comprehensive study of the clinical and demographic characteristics of ingrown nail. Therefore,this study was planned in order to observe at which stage our patients experienced the ingrown nails mostly, the factors causing the ingrown nails and our treatment approaches. This retrospective-study was approved by the Ethics Committee of Yozgat Bozok University.The study was performed with 300 patients at 2-89 age with ingrown nails.The type of ingrown nail was evaluated in 3 stages.The mean age was 32 years.152 women(50.66%) and 148 men(49.33%) were included in the study.The female to male ratio(FMR)was 1.02.Ingrown nail was determined in 256 patients(85.33%) on single hallux,in 39 patients(13%) on both of hallux,in two patients(0.66%) on hallux and on the third finger of foot,in one patient(0.33%) on fingernail,in one patient (0.33%) on all fingernails and in one patient on both of hallux and on the first finger of hand. Ingrown nail was in stage 1 in 117 patients(39%-45 female&72 male,FMR: 0.62),in stage 2 in 95(%31,66-54 female&41 male,FMR:1.31,in stage 3 in 88(%29,33-53 female&35 male,FMR: 1.51).Sixteen patients(5.33%) had a previous history of nail extraction in the same or another nail.Four patients had ingrown nail during pregnancy.A total of 16 patients(5.33%) with ingrown toenail,ten of whom were at stage 1 and six of whom were at stage 2,had onychomycosis also.In a 41-year-old psoriasis patient stage 1 ingrown nail was observed in the second month of cyclosporine treatment.Ingrown nail in four patients was observed during isotretinoin treatment.Incorrect nail-cutting habits(71%),poorly fitting shoes(22.33%),excessive angulation of the nail plate(7.66%),obesity(12%),trauma to the feet(10%),pregnancy(2.63% of women),bad foot hygiene(20.66%) and hyperhidrosis(4%) were associated with ingrown nails.The other studies have often focused on the treatment of ingrown nails,therefore we think that these study data will be useful in the prevention of ingrown nail by revealing and then eliminating conditions creating a predisposition to it.

Keywords: Ingrown nails, Epidemiology, Infections

OP-06 [Psoriasis]

Evaluation of systemic treatment approaches in Psoriasis Vulgaris: A single center retrospective study

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In this cross-sectional study, 3049 psoriasis patients who applied to Sivas Cumhuriyet University Faculty of Medicine Department of Dermatology between 2006-2021 were retrospectively analyzed. It was observed that 606 (19.8%) patients received systemic treatment. Of these patients, 1452 (47.6%) were male and 1597 (52.4%) were female. Adalimumab was started in 87 (14.3%) patients, acitretin in 96 (15.8%) patients, etanercept in 7 (1.1%) patients, infliximab in 26 (4.2%) patients, ixekizumab in 2 (0.3%) patients, methotrexate in 438 (72.2%) patients, secukinumab in 30 (4,9%) patients, certolizumab in 1 (0.1%) patient, cyclosporine in 10 (1,6%) patients, and ustekinumab in 85 (14%) patients. It was found that the treatment of 9 patients from acitretin to adalimumab and 2 patients from adalimumab to acitretin were changed. It was found that the treatment from etanercept to adalimumaba was changed in 6 patients, and the treatment of none of the patients was changed from adalimumab to etanercep. It was found that the treatment of 10 patients was changed from infliximab to adalimumab, and none of the patients' treatment was changed from adalimumab to infliximab. It was observed that 5 patients switched from adalimumab to metotrexate, 24 patients switched from metotrexate to adalimumab and 2 patients used adalimumab and methotrexate together. It was observed that 4 patients switched from adalimumab to secukinumab, 3 patients switch from secukinumab to adalimumab, and 1 patient switched from cyclosporine to adalimumab, 22 patients switched from adalimumab to ustekinumab, and no patient switched from ustekinumab to adalimumab. As a result, when systemic treatment approaches initiated in psoriasis vulgaris were evaluated, it was found that there was a transition from conventional agents to biological agents, and an increase in the transition from TNF alpha inhibitors to IL17 and IL12-IL23 inhibitors among biological agents.

Keywords: psoriasis, systemic treatment, biological agents

OP-07 [Inflammatory Skin Diseases]

Assessment of inflammatory parameters in patients with lichen planoplaris

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INTRODUCTION & OBJECTIVES: Lichen planopilaris (LPP) is a rare inflammatory condition causing progressive, permanent hair loss with patches on the scalp. There is no exact data on the presence of systemic inflammation in LPP, and little is known about its relationship to disease activity. In this study, we evaluated the clinical role of inflammatory parameters in patients with LPP.

MATERIALS & METHODS: Data of individuals applying to Dermatology outpatient clinic between January 2001 and January 2011 were retrospectively reviewed. Study participants were divided into two groups; the patient group consisted of 49 subjects who were clinically and histopathologically diagnosed with LPP, while 49 of similar age and gender, applying to dermatology outpatient clinic with any complaint, formed the control group. Those with systemic / cutaneous inflammatory or autoimmune disease and a history of infection in the last month were not included. Demographic characteristics and white blood cell (WBC), neutrophil, lymphocyte, platelet counts, neutrophil / lymphocyte ratio, platelet / lymphocyte ratio, mean platelet volume (MPV) and red blood cell distribution width of both groups were recorded and, after that, statistically analyzed. Ethical permission was obtained from the Clinical Research Ethics Committee (21-KAEK-038). The collected data were analyzed using Statistical Package for the Social Sciences (SPSS) version 19 (IBM SPSS 19.0, SPSS Inc).

RESULTS: Both groups, composed of 98 participants, 49 (F / M: 33 / 16) of the patient group and 49 (F / M: 34 / 15) of the control group, were statistically similar in gender distribution ($p > 0.05$). Mean age, where the patient group was 44.40 ± 14.71 years (19-65 years), and control group was 43.97 ± 13.39 years (18-64 years), did not differ significantly between groups ($p > 0.05$). Five patients, whose inflammatory parameters showed no statistically significant difference compared to those without lichen planus (LP) skin lesions ($p > 0.05$), had LP skin lesions; none had oral mucosa and nail involvement. WBC, lymphocyte counts, and MPV values appeared to be significantly higher in the patient group than in the control group ($p = 0.030$; $p = 0.013$; $p = 0.020$, respectively) (Table 1).

CONCLUSIONS: Taking all these findings into consideration, we suggest that high WBC, lymphocyte counts, and MPV values, parameters, in addition to clinical signs, also contributed to assessing disease activity in LPP patients, predict the presence of systemic inflammation. It is hoped that this study can provide an essential insight into the relevant issue in the field.

Keywords: Lichen planoplaris, inflammatory parameters, neutrophil, mean platelet volume, white blood cell.

Table 1. Inflammatory parameters of lichen planoplaris patients and healty controls

Parameters	Lichen planoplaris (n=49)	Healty controls (n=49)	P value
WBC count (mean ± SD)x103	7.30±1.62	6.60±1.51	0.030
Neutrophil count (mean ± SD)x103	4.23±1.12	3.85±1.15	0.097
Lymphocyte count (mean ± SD)x103	2.36±0.65	2.05±0.55	0.013
Platelet count (mean ± SD)x103	256.53±49.49	250.78±51.66	0.575
NLR (mean ± SD)	1.85±0.51	1.99±0.73	0.273
PLR(mean ± SD)	115.61±32.87	250.78±51.66	0.076
MPV(mean ± SD)	9.55±1.44	8.93±1.11	0.020
RDW (mean ± SD)	13.86±1.61	14.01±1.48	0.630

WBC: White blood cell; NLR: Neutrophil / lymphocyte ratio; PLR: Platelet / lymphocyte ratio; MPV: Mean platelet volume; RDW: Red blood cell distribution width.

OP-08 [Dermatological Practice Management]

Epidemiological and Clinical Characteristics of Psoriasis Patients Admitted to Outpatient Clinic During Initial Period of COVID-19 Pandemic (March-June 2020) and Effects of Pandemic on Treatment Preferences

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OBJECTIVE: Psoriasis is a chronic inflammatory immune-mediated skin disease affecting around 2% of the worldwide population. There is a concern that drugs used in the treatment of some patients with psoriasis may increase the risk and severity of infection with COVID-19. The decision on whether continue or withhold psoriasis treatment was uncertain for dermatologists at the beginning of the COVID-19. We aim to evaluate clinical characteristics of psoriasis patients that admitted to our outpatient clinic during COVID-19 and the effect of the pandemic on treatment preferences.

MATERIALS-METHODS: This is a retrospective descriptive study. Psoriasis patients that had admitted to Ankara University, Dermatology Department, Outpatient Clinic between March 2020 and June 2020 when the first restrictions had been imposed by the government, were included in the study. Epidemiological and clinical characteristics of patients, admission reasons, subsequent admissions, treatments they received on admission and treatment plans on admission were recorded from patients' charts.

RESULTS: Of the 71 psoriasis patients (41 males and 30 females),

the average age was 41.7±15.7 years. The majority of the patients were between 18-64 years old (81.7%) and 71.8% of the patients were follow-up patients. Forty patients (56.3%) had subsequent admission during the study period. Thirty-one patients(43.7%) had systemic treatment at admission and 83% (n:26) of those were immunosuppressive or immunomodulatory drugs. Eighteen patients (25.3%) had biological treatment including etanercept(n:3), adalimumab(n:4), ustekinumab(n:6), and secukinumab(n:5), and eight patients(11.2%) had conventional treatment including methotrexate(n:6) and cyclosporine(n:2). Twenty of the patients who received immunosuppressive or immunomodulatory therapy continued their treatment according to physician's decision, after excluding COVID-19 by PCR test and/or questioning of specific symptoms for COVID-19. For two patients, cyclosporine treatment had switched to biological treatment, ustekunimab for one patient and secucinumab for one patient. For six patients, the dose of treatment was reduced or discontinued due to the risk of COVID-19 or the patient's clinical well-being. While one patient was given biological treatment again 3 months after.

CONCLUSION: Stopping immunosuppressive or immunomodulating treatment in psoriatic patients unaffected by COVID-19 could lead to exacerbation of the disease and reduced response at re-treatment. Because of the lack of evidence of adverse effect of biologics on severity and outcome of COVID-19 in psoriatic patients, treatment of psoriatic patients with biological agents has been suggested in literature. Our daily practice was similar to literature, and according to our knowledge, mortality due to COVID-19 has not occurred in our patients that under immunosuppressive or biological treatment.

Keywords: Psoriasis, COVID-19, biologic, immunosuppressive, treatment

OP-09 [Dermatopathology]

Red faced girl

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[2]Department of Dermatology, Mersin University, Mersin, Turkey

A 26-year-old female patient presented with facial erythema and mild itching past 2 weeks. She has get treatment with Humira (Adalimumab), Methotrexate, Prednol, Folic acid due to clinical diagnoses Rheumatoid Arthritis.

Widespread sharply limited erythema, scaling, follicular prominence and Demodex mites were seen on dermatological examination.

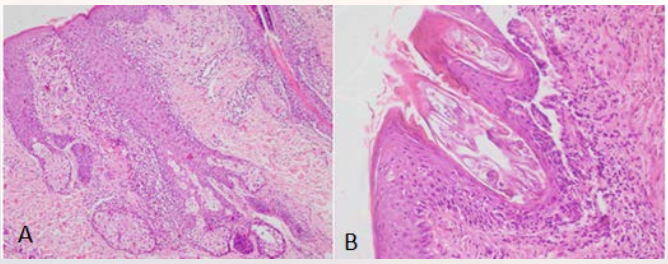
Microscopic examination revealed mild hyperkeratosis, irregular acanthosis, spongiosis and follicular plugging. And also Demodex follicularum took attention on microscopic examination. Heavy mononuclear inflammatory cell infiltration was observed around the hair follicul and ectatic vascular structures. The diagnosis of Rosacea was confirmed by these histomorphological findings. Rosacea is a common inflammatory skin disease. Rosacea presents with erythema, recurrent flushing, edema, telangiectasia, papules, pustules, rhinofima on facial convex region. Its etiology is not clearly understood. Enviromental factors, genetic factors, Demodex mites, H.pylori, neurovascular abnormalities,drugs have roles in development of Rosacea.

Keywords: rosacea, facial erythema, recurrent flushing, anti-TNF agents

Figure 1

Widespread sharply limited erythema, follicular prominence

Figure 2



A- Mild spongiosis, inflammatory cell infiltration around the hair follicules and sebaceous glands (H&EX200). B- Demodex mites (H&EX400)

OP-11 [Dermatopathology]

Fungal Infection Associated Erythroderma

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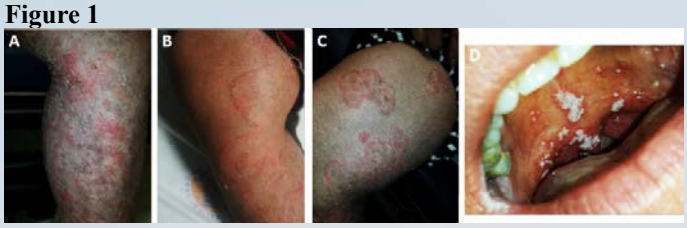
[2]Department of Dermatology, Mersin University, Mersin, Turkey

An adult female patient applied to the dermatology clinic with complaints of wounds for 1 month. Her wounds started first in the arms and then in the mouth spread to the whole body. She described widespread marginal edged rashes on the legs since 2014. Exacerbation of a chronic condition, which had persisted for more than five years. Her peeling, red skin gets very itchy and more extensive recently. She was concerned about recent skin changes and decided to seek medical attention. She had no personal or family history of either dermatitis or psoriasis.In dermatologic examination the whole body is erythrodermic and there are targetoid lesions on the legs. Erode areas with white plaques on the oral mucosa were seen. An incisional biopsy was performed by dermatology clinic with the preliminary diagnosis of erythema multiforme and Steven Johnson syndrome. In the histological serial sections hyperkeratosis, parakeratosis, intracorneal neutrophile leukocyte infiltration was observed in the epidermis. Subepidermal edema, congestion and mixed inflammatory cell infiltration containing dense neutrophil leukocytes were seen. At high power view fungal spore and hyphaes was noticed in the intracorneal pustules. Periodic acid-Schiff (PAS) and Gomori mehtenamin Silver (GMS) stains revealed positive hyphae in the stratum corneum, thereby confirming a diagnosis of tinea infection. She experienced complete resolution of her erythroderma after antifungal therapy. Erythroderma or exfoliative generalized dermatitis is a disease characterized by peeling and redness that involves more than 90% of the body surface. Systemic diseases that commonly cause erythrodermia; drug eruptions, dermatitis (especially atopic dermatitis), psoriasis (in case of treatment and discontinuation of systemic steroids), pityriasis rubra pilaris. Diseases that cause this condition less frequently include contact dermatitis, stasis dermatitis (venous eczema), seborrheic dermatitis, staphylococcal scalded skin syndrome, fungal infection, pemphigus, bullous pemphigoid, Sezary syndrome). Erythrodermic patients with chronic dermatophyte infection have been described in three clinical settings. One of these scenarios is: erythroderma that is a direct consequence of only the tinea corporis infection. The second situation of erythroderma-related chronic tinea includes individuals whose erythroderma is multifactorial; may be secondary to a paraneoplastic phenomenon or an ‘id reaction’. The third setting of erythroderma-associated chronic tinea occurs in patients with congenital disorders characterized by erythroderma who subsequently acquire a persistent dermatophyte infection.

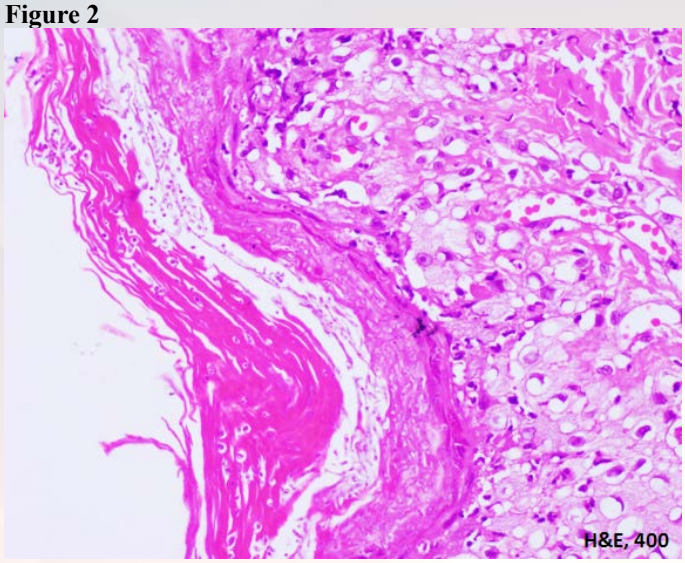
Keywords: Erythroderma, fungus, exfoliative, dermatitis

Figure 1



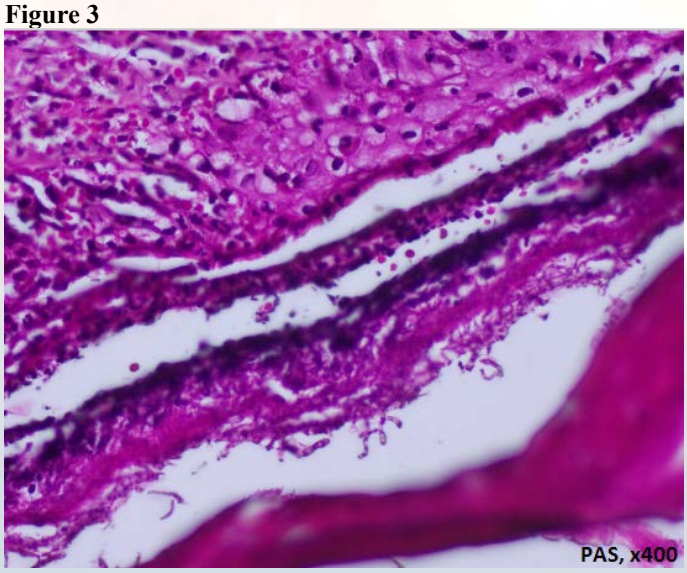
A, B. Erythrodermic skin lesions. C. Targetoid lesions on the leg. D. Erode areas with white plaques on the oral mucosa

Figure 2



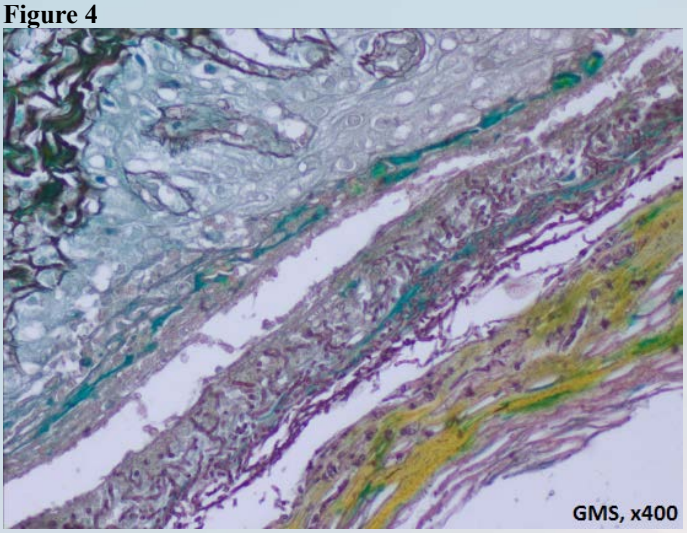
Intracorneal fungal spores and hyphaes are shown here (H&E, x400)

Figure 3



Intracorneal fungal spore and hyphaes with PAS histochemistry stain, septas can be seen in the hyphaes (PAS,400)

Figure 4



Intracorneal fungal spore and hyphaes with GMS histochemistry stain (GMS,400)

OP-12 [Dermatopathology]

A difficult case with recurrent erythroderma

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A 28-year-old female presented to the dermatology outpatient clinic with skin lesions characterized by red-colored rashes on the arm, leg and trunk. It is known that the case is followed up with diagnosis of ichthyosis vulgaris and retinoid therapy was given for several times.

Dermatologic examination revealed desquamed lesions on erythematous background. Biopsy performed from the lesions and non-spesific findings were observed in the histopathological examination. The lesions decreased after the cyclosporine treatment, then just in a few days the eruption had begun with erythema of the trunk and legs and than extensive scaly and pustular plaques appeared. A second biopsy was planned from the new lesions, for the presence of a second entity that could cause erythroderma in the patient who did not benefit from the treatment totally.Histopathological examination revealed hyperkeratosis, thin granular cell layer, suprapapillary thinning in the epidermis. Accompanied neutrophil leukocytes a mixed type inflammatory cell infiltration was observed in the dermis. Neutrophilic pustules were seen in subcorneal and intraepidermal location. Pustular psoriasis was considered with these histomorphological findings. Ustekinumab treatment was started after clinical evalution. She benefited from the treatment and erythroderma regressed just in a week. Erythroderma also known as exfoliative dermatitis is a clinical presentation of many different diseases. In erythroderma, eritema and scaly lesions must be present in more than %90 of the body surface. Common causes of erythroderma are skin diseases such as psoriasis, contact dermatitis, mycosis fungoides, malignancies, drug reactions and others. In our case, recurrent erythroderma and pustulosis in the patient who was followed up with the diagnosis of ichthyosis suggested a second entity. The skin biopsy revealed pustular psoriasis and ichthyosiform changes in the background. In the literature, the physiopathological connections of these two entities were investigated. In these articles, ichthyosiform erythroderma accompanied by pustular psoriasis are presented. Although it is known that they have the same genetic basis, it can not excluded yet, if pustular psoriasis can be a result of ichthyosis. In the presence of erythroderma in patients diagnosed with ichthyosis, the possibility of a second entity should come to mind when there is no response to treatment, even if the findings are non-specific.

Keywords: Erythroderma, Pustular psoriasis, Ichtyosis vulgaris

Figure 1

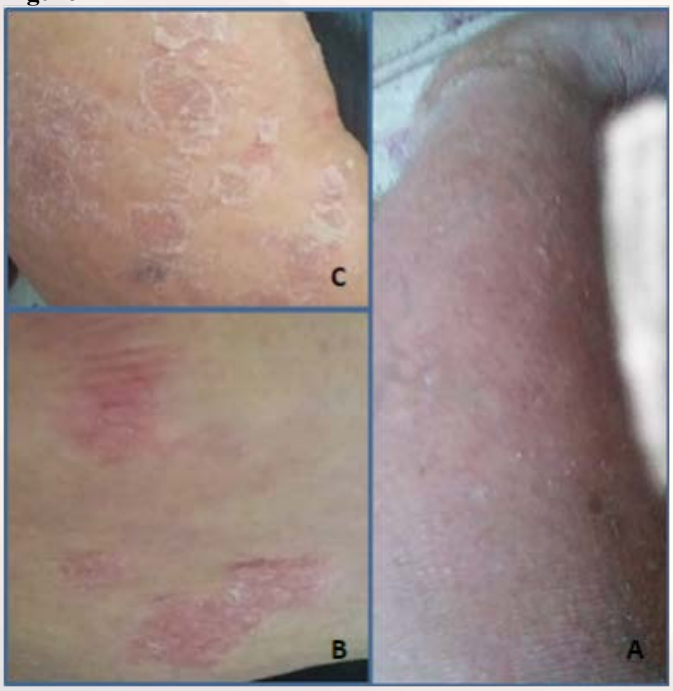

Figure 1: A: Lesions characterized by hyperkeratosis on extensive erythrodermic background. B:Erythematous background C:Hyperkeratotic plaques on erythematous ground

Figure 2

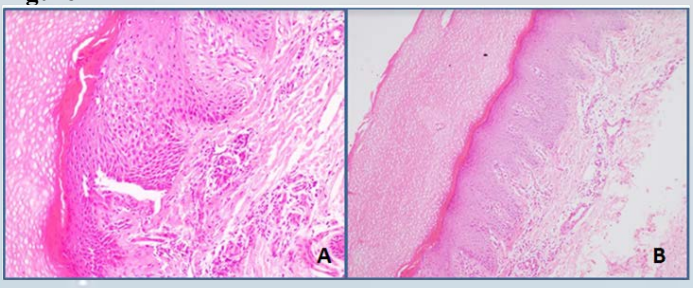

Figure 2: A: Areas where granular layer is absent and epidermal plates are thin. There are lymphohistiocytic

inflammatory cells around the vessels in the dermis (H&E x200). B: Compact hyperkeratosis and psoriasiform hyperplasia of the epidermis (H&E x40).

Figure 3

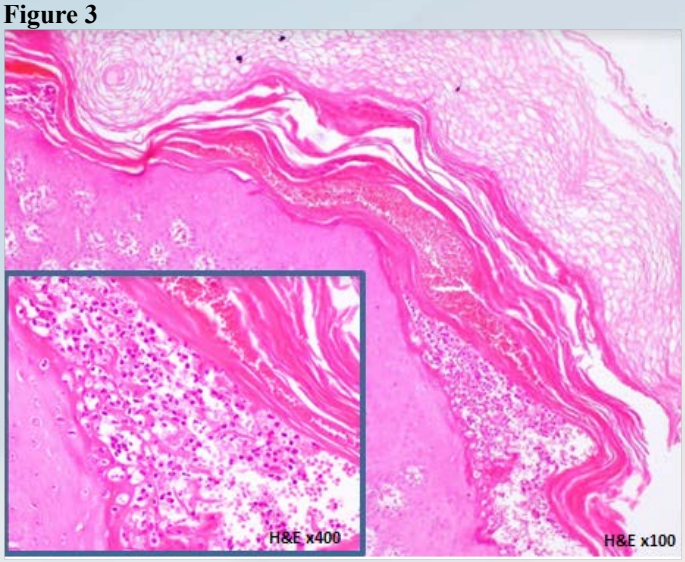

Figure 3: İnflammatory infiltrate consisting of neutrophil leukocytes in the intracorneal area.

OP-13 [Dermatopathology]

A Case of Pediatric Mycosis fungoides

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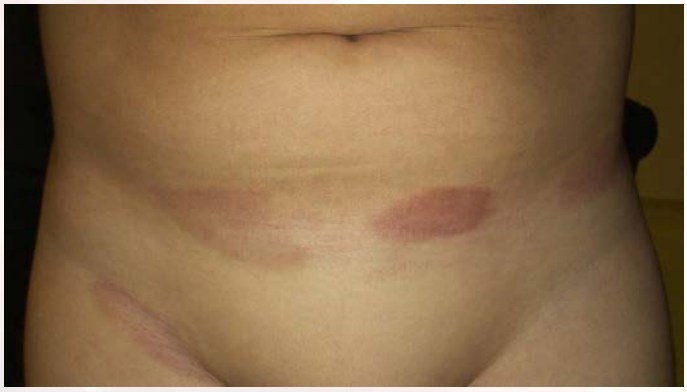
[2]Department of Dermatology, Mersin University, Mersin, Turkey

A 9-year-old male patient presented with a non-itching red swelling on lower abdomen for two months. There is no medical illness in the medical history of his family and himself. It was initially treated as tinea by family physician then he was sent to our hospital for the persistence of the plaque. In dermatological examination, there are two 4*2.5 and 4*1.5 cm annular erythema plaques in the suprapubic area, 3*2 cm in the right inguinal region and 4*2 cm in the left lumbar region. Biopsy was performed and the histomorphological examination of the biopsy specimen, orthokeratosis and follicular plugging were observed in the epidermis. Lymphocytes that fill the papillary dermis also lie transepidermally. These lymphocytes have significant cytological atypia such as nuclear enlargement, nuclear contour irregularity and perinuclear halo. In the immunohistochemical study, strong cytoplasmic staining with CD3, CD4 and CD5 in lymphocytes which filling the dermal papillae, showing alignment at the dermoepidermal junction and spreading transepidermal in patches was observed. Some of these lymphocytes showed strong cytoplasmic staining with CD8 and the ratio CD4/CD8 was 4. Most of the lymphocytes that filling the dermal papillae showed loss of expression with CD7. Moderate cytoplasmic staining was seen in very few lymphocytes in the dermal papillae with CD30 and CD20 positivity was not observed. The diagnosis of mycosis fungoides was confirmed by these histomorfologycal findings. Mycosis fungoides, which is characterised by infiltration of the skin with malignant T cells is the most common primary cutaneous lymphoma in adults and children. It comprises approximately %65 of all primary cutaneous lymphomas in pediatric patients.Similar to adults, children may have an indolent clinical course that is difficult to distinguish from inflammatory skin conditions. In adults, classic MF presents initially with scaly erythematous patches that may progress into infiltrated plaques and tumors in %35 and %20 of patients. The incidence of classic MF in children is approximately %41. Unlike adults, the majority of children with MF present with nonclassic variants of the disease, which include hypopigmented, hyperpigmented, folliculocentric, and poikilodermatous forms. Hypopigmented form is >%50 of pediatric cases. According to the studies conducted for the last 10 years, the most common treatment method is phototherapy. The patient was threated with phototherapy (narrow-band UVB two times a week). Significant improvement was observed clinically after the current treatment.

Keywords: Pediatric mycosis fungoides, erythema plaques, primary cutaneous lymphoma, phototherapy

1



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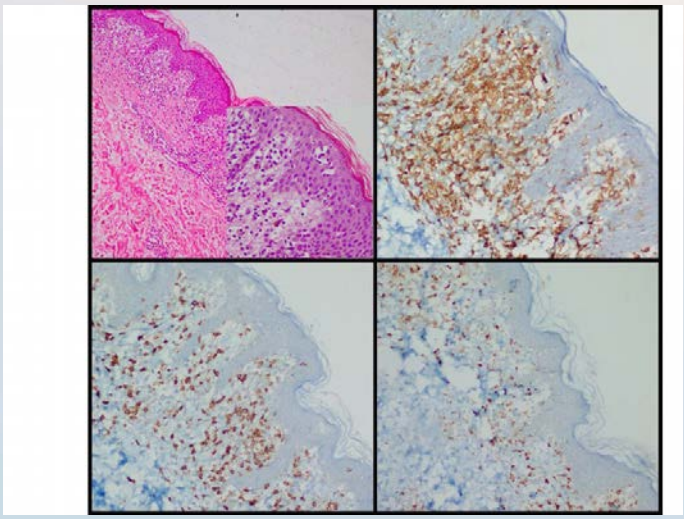

OP-14 [Corrective, Aesthetic and Cosmetic Dermatology]

Retrospective Analysis Of The Onabotulinum Toxin-A Patients Applying To The Cosmetology Unit Of A University Hospital

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İstanbul Üniversity-Cerrahpaşa, Cerrahpaşa Medical Faculty, Department of Dermatology

INTRODUCTION AND OBJECTIVES: Onabotulinum toxin-A is the combination of toxins produced by the bacterium Clostridium Botulinum. It has been long used for cosmetic purposes by paralysing facial expression muscles and thus reducing the fine wrinkles.1 In this study our aim is to anaylse the demographic characteristics of the patients applying to the cosmetology unit of İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, which is a public university hospital.

PATIENTS AND METHOD: The patients who have applied to the cosmetology unit of İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Dermatology Department and who received Onabotulinum toxin-A injections from January 2020 to January 2021 were included in this study. The gender, age and session count of each patient were noted from the patient files retrospectively. The gender distribution, average ages and application frequency were analysed.

RESULTS: A total of 153 patients applied to the cosmetology unit for Onabotulinum toxin-A treatment within the last year. Of these patients, 142 (92.8%) were female and 11 (7.18%) were male; female patients were treated significantly more. The mean of the age of all patients was 43 years; the mean age of male patients was 40 years and the mean age of female patients was 43 years. Twenty-one of the patients received two applications within the last year and 2 patients received three applications. The average number of applications was 1.16.

CONCLUSIONS: This study showed that female patients applied more for Onabotulinum toxin-A injections than the male patients and that the patients of both genders were of middle age. Furthermore, an average of 1.16 injections per year was requested by patients.

REFERENCES: 1- Satriyasa BK. Botulinum toxin (Botox) A for reducing the appearance of facial wrinkles: a literature review of clinical use and pharmacological aspect. Clin Cosmet Investig Dermatol. 2019 Apr 10;12:223-228. doi: 10.2147/CCID.S202919. PMID: 31114283; PMCID: PMC6489637.

Keywords: botox, cosmetology, wrinkles,

OP-15 [Allergology and Immunology]

Methotrexate monotherapy for idiopathic granulomatous Mastitis

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BACKGROUND: Idiopathic granulomatous mastitis is a rare benign chronic inflammatory breast disease of women of reproductive age.There is not yet a complete consensus on IGM's treatment algorithm. its aetiology has not been fully elucidated. Although it is benign, abscess, fistula and sinus formation in the course of granulomatous inflammation cause deformities in the breast. Surgical procedures (such as mastectomy and excision) cause tissue loss and cosmetic problems in the breast.These can lead to the deterioration of body image and mental disorders in patients.The good response of IGM to steroids points to the role of autoimmunity in the development of this disease. There are limited data on the use of mtx in the treatment of IGM. In this study, we evaluated the clinical effectiveness of mtx therapy for IGM.

PATIENTS and METHODS: Data from 15 patients who were histopathologically diagnosed with IGM and referred to an immunology clinic between 2018-2021 were retrospectively examined. The patients were divided into two groups as mtx and conservative.

RESULTS: Fifteen patients who did not get a complete response from surgery and antibiotic treatment were re-evaluated in immunology. The patients were divided into two groups as mtx(methotrexate) and conservative. Data of six patients treated with MTX were compared with 9 patients on conservative follow-up. MTX monotherapy was started at 7.5-10 mg / week. MTX treatment was applied for 6-12 months. No serious side effects were observed during the treatment, and no recurrence was observed in any patient during the 12-month follow-up period. Three of the 9 patients followed-up conservatively had a recurrence.

CONCLUSIONS: Mtx monoterapy is a safe and effective treatment in patients with igm.

Keywords: Idiopathic Granulomatous Mastitis, Methotrexate Therapy, Mastitis

Clinical characteristcs of patients (Methotrexate 7.5-10 mg/ week oral route)

	Age (year)	Lactation (mounth)	Number of child	O.C use	ANA	Abscess drainage	Lesion size (mm)	AB	Mtx treatment (month)	Follow-up period (month)
1	43	24	2	+	-	+	20	+	12	24
2	42	48	5	-	-	+	30	+	12	24
3	30	12	3	+	-	+	70	+	6	20
4	30	12	3	+	-	+	25	+	6	22
5	33	14	2	-	-	+	50	+	8	18
6	33	13	2	+	-	-	30	+	6	16

ANA, Anti-Nuclear Antibodies, Oc:Oral contraceptive, AB Antibiotic treatment

OP-16 [Dermatopathology]

Alopecia neoplastica due to metastatic epithelioid sarcoma

Mustafa Anıl Yılmaz[1], Vali Nasirov[2], Umit Tursen[1]
[1]Department of Dermatology
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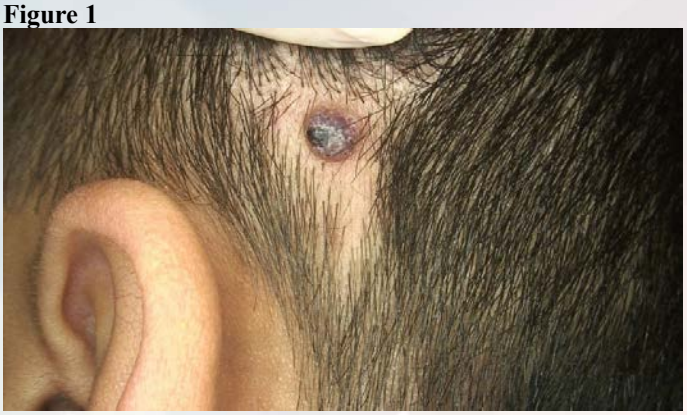
ABSTRACT: Alopecia neoplastica is defined as hair loss secondary to a visceral malignancy that has spread to the scalp.. We present a 22-year-old female patient reporting lesions at the scalp, and who was asymptomatic with a six months evolution. The patient reported prior epithelioid sarcoma and was undergoing chemotherapy at the time of consultation.We aimed to improve the knowledge on alopecia neoplastica, highlighting that in case of alopecia neoplastica due to epithelioid sarcoma.

Keywords: Alopecia neoplastica, Epithelioid sarcoma,Scalp Metastasis

Figure 1



Cicatricial alopecia area around the red crusted nodule on postauricular scalp

OP-17 [Nail Disorders/Diseases]

Evaluation of Nail Findings in Patients with Covid-19 Infection History and Wood's Lamp Examination

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INTRODUCTION & OBJECTIVES: Various skin findings due to coronavirus have been identified. Yet there is no literature knowledge on nail findings of the disease excluding few case reports. We aimed to document the nail findings of the Covid-19 survivors and shed light on the interesting sparkling seen under the Wood's light.

MATERIALS & METHODS: A total of 231 volunteers diagnosed with Covid-19 infection in the last 100 days were grouped in terms of the agents used in the treatment, as laid down in the protocol released by the Turkey Ministry of Health. Routine examination findings of the nails were recorded and Wood's lamp examination results were compared.

RESULTS: Volunteers treated with favipiravir had a significantly higher positivity of sparkling sign (p:0.0001), while it was negative in those who did not receive favipiravir treatment. A significant correlation was observed between the time passed over the infection and the distance of the sparkling sign from the lunula (p:0.0001). The most common nail finding in volunteers was splinter hemorrhage (13%), followed by leukonychia (12%), and longitudinal ridges (7.9%). One picture of the sparkling sign has been illustrated in Figure 1 along with a normal nail appearance under Wood's light in Figure 1.

CONCLUSIONS: The sparkling sign may be seen due to accumulation of favipiravir or its excipients on the nails. Accordingly, this accumulation may be seen in the vital organs. The most common finding was splinter hemorrhages in the volunteers with Covid-19 infection history. We think that coagulopathy and microvascular vasculitis associated with Covid-19 infection may have promoted the development of the splinter hemorrhages.

Keywords: Covid-19 infection, nail findings, wood findings, favipiravir, splinter hemorrhage, sparkling sign

Figure 1

Sparkling sign on the proximal third of the nail (Picture on the left) along with a normal nail (Picture on the right) appearance under Wood's light

OP-18 [Lasers]

Treatment of lip-localized venous lakes with long-pulsed Nd:YAG laser

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BACKGROUND / OBJECTIVE: Venous lakes are papules or nodules, which are dome-shaped, ranging from dark blue to purple, finger-compressible in middle-aged and elderly people, often found in areas exposed to the sun such as the face, ear, and lips. In histopathology, the papillary dermis contains dilated venules consisting of a thin layer of endothelial cells and thick fibrous walls. Since venous lake does not tend to regress spontaneously after it occurs, treatment is important both to improve the cosmetic appearance and to prevent bleeding complications. Different treatment methods including surgical excision, sclerotherapy, cryosurgery, electrocoagulation, and more recently, intense pulsed light and various lasers have been described. In this study, we aimed to examine the effect of Nd:YAG laser on venous lakes.

MATERIALS AND METHODS: Ten patients with lip-localized venous lake were treated with Nd:YAG laser between 2019-2020 in our clinic. 1064 long-pulse Nd:YAG laser was applied to all patients with 3 mm spot size, 55 ms pulse width and 200-250 joules / cm² energy. Depending on the size of the lesion, 1 to 3 shots were made without overlapping. Clinical response was determined by the lesion's hardening, mild whitening, and an audible popping sound. According to the clinical response, Nd:YAG laser was applied in a single session or two sessions with one month interval.

RESULTS: Eight male and 2 female patients, aged between 35 and 71 years, were included in this study. All lesions were located in the lip, nine of them were in the lower lip and one was in the upper lip. Lesions ranged in diameter from 4 mm to 10 mm. Complete recovery was observed in 7 of 10 patients (70%) with a single session and 3 (30%) of them with two sessions of Nd:YAG laser application. There were no complications other than mild pain and edema.

CONCLUSION: Laser treatment has become a preferred method in the treatment of venous lakes due to its easier application and less side effects compared to other treatment options. The effectiveness of long-pulse Nd:YAG laser in the treatment of venous lakes is ensured by the absorption of 1064 nm wavelength by methaemoglobin and its deep penetration and thus, they show more effect than short wavelength lasers in deep and thick lesions. Consequently, the long-pulse Nd:YAG laser is a simple, non-invasive, effective and safe treatment option that can be preferred in lip-localized venous lakes.

Keywords: Laser, Lip, Nd:YAG laser, Venous lakes

OP-19 [Genetics]

A rare vascular and lymphatic syndrome- A late-diagnosed case of Hypotrichosis–lymphedema–telangiectasia syndrome with new clinical findings

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INTRODUCTION: Hypotrichosis–lymphedema–telangiectasia syndrome (HLTS) is a rare vascular and lymphatic malformation. Cardinal features include a generalized lack of body hair, lymphedema of the extremities, and scattered cutaneous telangiectasias. Less commonly observed vascular defects include enlargement of the ascending aorta and renal failure from chronic microangiopathy of the glomerular and extraglomerular vasculature. Here we described a patient with cutaneous telangiectasias, congenital upper right extremity lymphedema, localized hypotrichosis and lymphangioma. To the our knowledge, upper limb localization and lymphangioma coexistence in HLTS has not been reported.

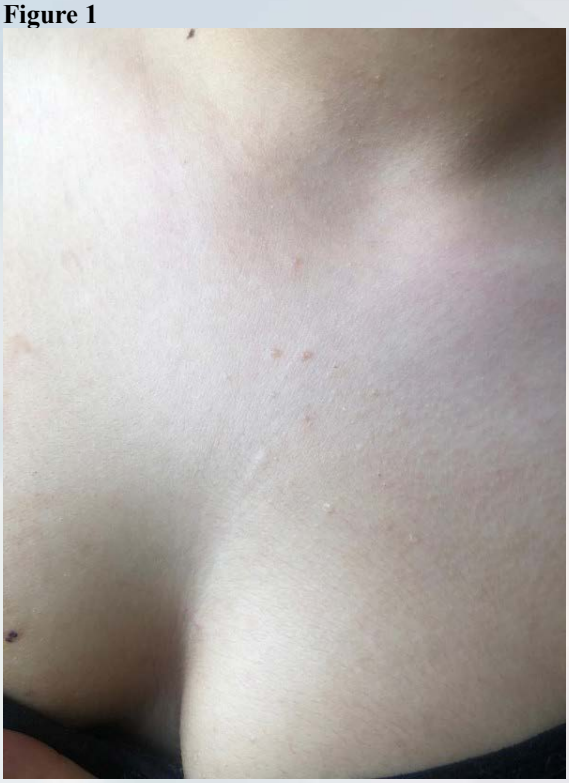
CASE REPORT: A 20-year-old female patient presented to the dermatology clinic with a history of multiple painless lesions on neck and chest since approximately four years. On dermatological examination, there were multiple translucent papules on neck and chest (Figure 1). Dermoscopic examination revealed multiple white-yellowish well circumscribed roundish lacunaes (Dermlite DL4, polarized, x10). She had congenital lymphedema on right arm and right hand (Figure 2). There were telangiectasias on right neck, right thoracic and lumbal region and, right upper extremity (Figure 3). There was hypotricosis in her right arm (Figure 4). Other physical examinations were normal. She had no drug history or systemic disease. There was no dysmorphic facial appearance. Hair growth was normal on the scalp. Neurologic exam was normal. Her parents were non-consanguineous and healthy. There was no known family history or of any dermatological condition. There were no renal or pulmonary abnormalities on laboratory examinations. Upper extremity MR showed lymphedema. No lymphatic flow was observed in the right upper extremity with lymphoscintigraphy. Transthoracic echocardiogram and abdominal ultrasound ruled out aortic dilation and kidney malformations. A punch biopsy was performed from translucent lesions. Histopathological examination demonstrated; enlarged lymphatic ducts and vascular structures.

DISUSSION: HLTS combines features that represent failure of proper vascularization, angiogenesis and hair formation. Dysfunctional development of blood vessels results in cutaneous telangiectasias and dilations of superficial vasculature, while disturbances in the maintenance of the lymphatic system are

manifested by lymphedemas. The third constituent of this syndrome involves defects in hair follicle development, leading to progressive scalp hair loss and absence of eyebrows and eyelashes (3). In our case, there was no involvement of scalp and head and neck, and hypotricosis was only limited on the right arm. Lymphedema was limited to the right upper extremity. There were multiple lymphangiomas on trunk and neck. We wanted to present our case because it is a rare syndrome and shows different clinical features has not been reported yet.

Keywords: Hypotrichosis–lymphedema–telangiectasia syndrome, vascular syndrome, lymphatic syndrome, lymphangioma

Figure 1



Multiple translucent papules on neck and chest.

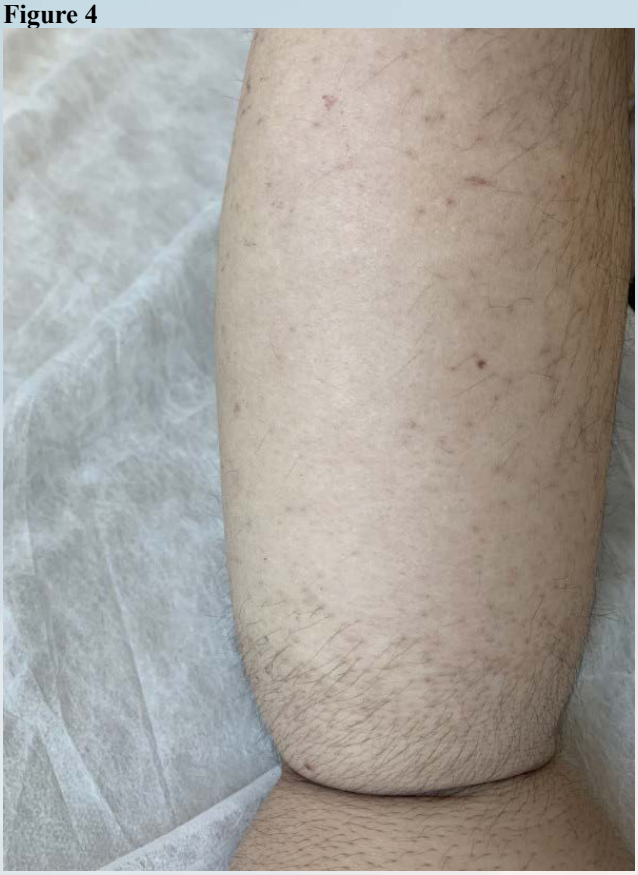
Figure 2

Lymphedema on right arm and right hand.

Figure 3

Telangiectasias on right upper extremity.

Figure 4



Hypotricosis on her right arm.

OP-20 [Dermatopathology]

The Role of CD1a expression in the diagnosis of cutaneous leishmaniasis, its relationship with Leishmania species and clinicopathological features

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BACKGROUND-OBJECTIVE: Leihmaniasis is a chronic infectious disease caused by different protozoan species of Leishmania. Although histopathological examination plays an important role in diagnosis, donovan bodies may not always be detected in biopsies. Few studies have shown that the CD1a marker is useful in detecting amastigotes. Our aim is to investigate the contribution of CD1a to diagnosis, especially in cases where pronounced donovan bodies are not observed.

METHODS: 84 cases suspected for cutaneous leishmaniasis were included in the study. Histopathologically, the presence of granuloma and giant cell, the selectability of amastigotes in hematoxylin eosin were investigated. Immunohistochemical study was performed with CD1a.

RESULTS: While donovan bodies were easily detected in hematoxylin eosin in 18 of 84 cases, fewer donovan bodies were seen by detailed search in 43 cases. Donovan bodies were not observed in hematoxylin eosin in 23 cases. In 60 (%71.4) of 84 cases, CD1a staining was detected. Expression was observed in all 18 cases containing donovan bodies that were easily detected in hematoxylin eosin. CD1a positivity was detected in 32 of 43 cases. Positive staining with CD1a was observed in 10 of 23 cases in which donovan bodies could not be seen in hematoxylin eosin. In these cases, very few donovan bodies became evident with CD1a.

CONCLUSION: In our study, high positivity was found with CD1a. However, donovan bodies that could not be seen in hematoxylin eosin were detected with CD1a. Therefore, we think that the use of CD1a makes an important contribution in the diagnosis of leishmaniasis.

Keywords: Leishmania, Cd1a, leishmania species

OP-21 [Autoimmune Bullous Diseases]

The management of bullous skin disorders in the era of COVID-19 pandemic: A single center, retrospective, cross-sectional study

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BACKGROUND: COVID-19, a serious pulmonary illness caused by the highly contagious novel coronavirus, is a global pandemic.

OBJECTIVE: In this retrospective study, we aimed to demonstrate the COVID-19 prevelance and treatment course of the patients with bullous skin disorders.

METHODS: A total of 151 patients with bullous skin disorders who admitted to our department between the dates of October 2019-October 2020 were enrolled in this study. The statistical analysis was performed with the SPSS-21.

RESULTS: One hundred twenty five patients were taking systemic steroid treatments and 113 patients were under the treatment of adjuvant treatment including azathioprine, mycophenolate mofetil and dapsone. Eighty patients received a minimum of a two-cure rituximab treatment during last year, and 15 patients a minimum of a three-cure IVIG treatment in the last year. Only 4 of the 151 patients had a Covid-19 infection history where all of them experienced a mild disease without hospitalization.

CONCLUSION: There is no consensus as for the immunosuppresive and biological treatments for autoimmune bullous diseases during the covid-19 pandemic.

Keywords: Azathioprin, bullous pemphigoid, bullous skin disorders, corticosteroids, immunosuppression

OP-23 [Dermoscopy]

The Nailfold Dermoscopy Findings of Patients w,th Atypical Hemolytic Uremic Syndrome

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INTRODUCTION & OBJECTIVES: Atypical HUS (aHUS) develops due to genetic disorders of the alternative complement pathway and results in microangiopathy. Therefore, simple and non-invasive tests are needed to evaluate the activity of the disease by assessing the microvascular structure. Nailfold Video Capillaroscopy (NVC) is a reliable method which the microvascular structure can be examined non-invasively with high-magnification (x200). However, this technique is not easily accessible. The dermoscope (x10) is an easily portable equipment used to visualise nailfold capillaries. In this study, we aimed to evaluate the microvascular changings by comparing the findings of nailfold capillary dermoscopy in aHUS patients with a healthy control group.

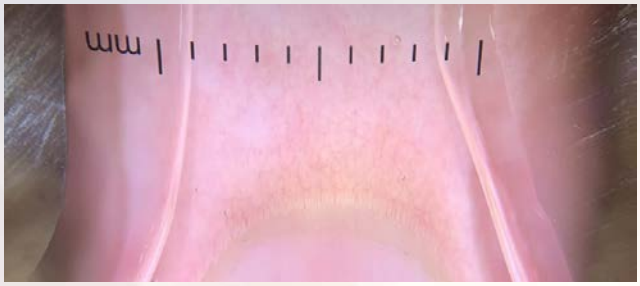
MATERIALS & METHODS: 7 aHUS patients and 7 healthy children were included in study. Patients' demographic datas were recorded andevery finger of both hands was examined with paying a greater attention on fourth and fifth finger of non-dominant hand. For both patient and control group; clarity of image, capillary density, capillary enlargement, haemorrhages, abnormal capillary shapes were examined and recorded for area of focus (the most prominent dermoscopic areas) and widefield view. To identify patients with abnormal capillary examination findings, we adapted the definitions suggested by Radic et al. and categorized as "Non-interpretable", "Normal Pattern", "Scleroderma Pattern" or "Non-specific".

RESULTS: The demographic data of the patients are shown in Table 1. All children in control group classified as "Normal" in AOF and WV. Dermoscopic findings of control group are shown in Table 2. In patient group, 6 patients (85,7%) were classified as "Non-Specific" and one patient (14,2%) was classified as "Scleroderma" pattern. Dermoscopic findings of patient group are shown in Table 3.

CONCLUSION: In this study, we found abnormalities in nailfold capillaries were higher in patients with aHUS. When we evaluate 4 CFH mutation positive patient, which triggers microvascular damaging and associated with poor prognosis; one of them is non-interpretable, all of them had decreased capillary density (100%) and 2 of them had disorganised capillary architecture (50%). 2 of 7 patients (28,6%) with the earliest age of onset in our study (0,6 years both), which is also associated with poor prognosis, had enlarged capillaries in AOF. All of our patients were normotensive while their nailfold dermoscopy was performed so we could not evaluate hypertension-capillary abnormality correlation. To the best of our knowledge, this is the first study about nailfold capillary findings in aHUS patients. Although our sample size is small, our patients were under remission and dermoscopy is not a gold standard technique to examine nailfold capillaries; nailfold capillary abnormalities were significantly higher compared to the control group. Further extensive studies should be considered to confirm the findings of the present study.

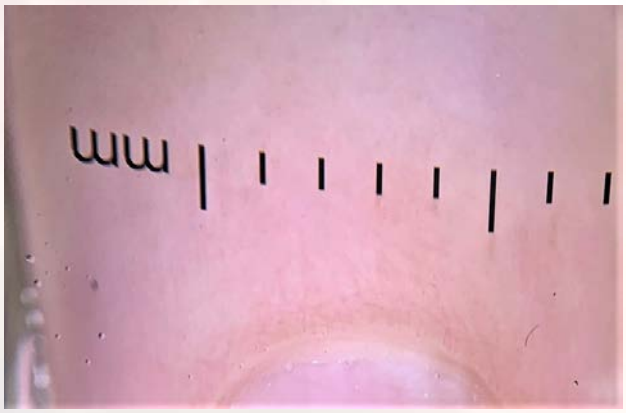
Keywords: atypical hemoliytic uremic syndrome, nailfold dermoscopy, capillaroscopy, microangiopathy

Figure 1



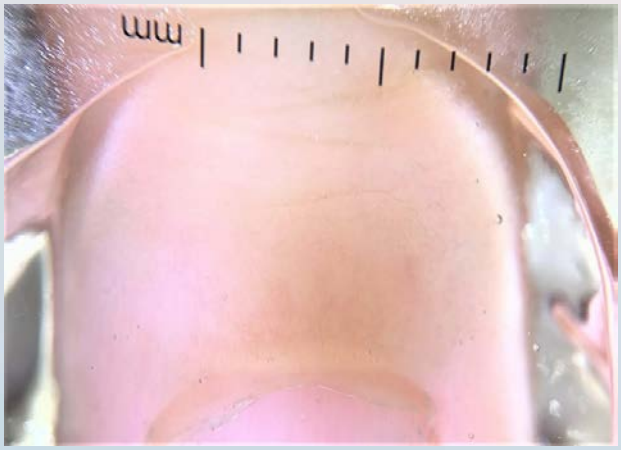
Normal nailfold capillary dermoscopic findings in control group, "Normal Pattern"

Figure 2



Decreased capillary density and disorganised capillaries in Patient 4, "Non-spesific"

Figure 3

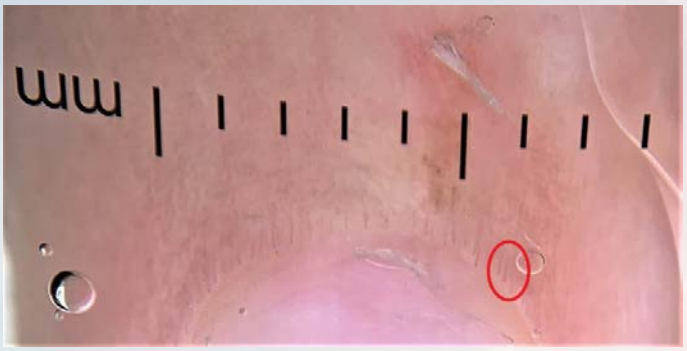


Decreased capillary densitiy in Patient 1 "Non-spesific"

Figure 4

Severe decrease in capillary density and capillary enlargement in Patient 2, "Scleroderma Pattern"

Figure 5



Non-convex capillary detected (red circle) in area of field in Patient 6

Table 1

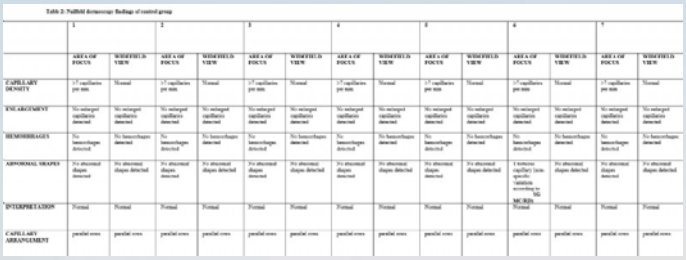
Table 1 Demographical, clinical findings and treatment modalities of seven patients with aHUS

Parameters	1	2	3	4	5	6	7
Age	$22^{5/12}$	$2^{6/12}$	$7^{5/12}$	$6^{11/12}$	$4^{11/12}$	$5^{3/12}$	$8^{8/12}$
Age at onset	$17^{5/12}$	0.6	0.9	$2^{6/12}$	0.6	$2^{2/12}$	$7^{3/12}$
Sex	Female	Female	Male	Male	Male	Female	Female
Consanguinity	No	No	No	Yes	Yes	No	No
Family history of aHUS	No	No	No	No	No	No	No
Presenting symptoms	Bloody diarrhea	Bloody diarrhea, vomiting, pallor	Diarrhea without blood, vomiting, pallor	Diarrhea without blood, vomiting, edema	Diarrhea without blood, vomiting,	Bloody diarrhea, edema	Bloody diarrhea
Oliguria/Anuria	-	Oliguria (for 48 hr)	Anuria (for 24 hr)	Anuria (for 24 hr)	Anuria (for 48 hr)	Anuria (for 24 hr)	-
HT at diagnosis	+	-	-	-	+	-	+
HT during follow up	-	-	-	-	-	-	-
Neurologic involvement	+	-	-	-	-	-	-
Pulmonary involvement	-	-	-	+	-	-	-
Cardiac involvement	-	-	-	-	-	-	-
Gastrointestinal involvement	-	-	-	-	-	-	+
ICU stay (days)	21	5	27	20	27	9	2
Hospitalization (days)	64	17	35	29	37	21	28
Number of HD/PD (days)	-	10	18	20	10	10	9
Number of PE (days)	4	-	-	-	-	-	1
Follow-up duration (months)	52	15	69	46	44	27	10
Genetic screening	CFH mut(+) pGlu936Asp hetero.	NA	CFH mut(+) pGlu936Asp hetero.	CFH mut(+) pGlu936Asp hetero.	CFH mut(+) pGlu936Asp hetero.	No mut.	NA

aHUS atypical haemolytic uremic syndrome, HT hypertension, ICU intensive care units, HD haemodialysis, PD peritoneal dialysis, PE Plasma Exchange, PI plasma infusion, NA not available, mut mutation, CFH complement factor H

Demographical, clinical findings and treatment modalities of seven patients with aHUS

Table 2



Nailfold dermoscopy findings of control group

Table 3

Nailfold dermoscopy findings of patient group

OP-24 [Corrective, Aesthetic and Cosmetic Dermatology]

An Investigation Of The Effects Of Polydioxanone Thread, Hyaluronic Acid Filler And Botulinum Toxin-A Materials On The Rat Skin, Connective Tissue And Photoaging

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OBJECTIVE: In this in vivo study, we evaluated the single or combined effects of polydioxanone (PDO) thread, hyaluronic acid (HA) filler and botulinum toxin type-A (BTX-A) practices on the rat skin and subcutaneous tissue. We also investigated how the results of these three treatments were affected during photodamage and photoaging caused by UV exposure.

MATERIALS-METHODS: The dorsal skin of 20 rats included in the study was divided into 5 areas and marked. PDO thread, HA filler and BTX-A were applied alone or in combination in the other 4 areas outside the area reserved as the control area. The rats were divided into 2 groups and the second group was exposed to UVA and UVB for 12 weeks, while the first group was exempted from this exposure. Biopsy samples were taken from the application areas of the rats in both groups at the 4th and 12th weeks. Histopathologically tissue thickness,

qualitative levels and orientation of collagen fibers and elastin in dermis, neocollagenesis and neoelastogenesis, foreign body granulomas, fibrosis, capsule-like structure formation, histiocyte and giant cell formation, fibroblast counts, inflammatory cells, vascularization, solar elastosis and tissue edema were evaluated comparatively. In molecular analysis, type I collagen (Col1A1), type III collagen (Col3A1), matrix metalloproteinase 2 (MMP-2), matrix metalloproteinase 9 (MMP-9), NF-κB, and IL-6 gene expression levels were determined by the real-time polymerase chain reaction (RT-qPCR).

RESULTS: In histopathological examination, solar elastosis was significantly higher in the UV group. The qualitative level and organization of collagen in all application areas were found to be higher than the control area. It was found that the amount of collagen decreased more irregularly in the UV group than in the non-UV group. Significant increases in inflammation and vascularity were observed in the application areas compared to the control area. Capsule-like structure formation, giant cells and foreign body granuloma were also detected histopathologically in the application areas. In molecular analysis changing the expressions of following genes: Col1A1, Col3A1, MMP2, MMP9, NFkB and IL-6 at week 4 and 12 in all areas were summarized in tables.

CONCLUSION: Single or combined applications of PDO thread and HA filler or combined with BTX have a protective and healing effect on the skin and subcutaneous tissue against chronological and photoaging. Especially until the first 4 weeks, PDO thread+HA filler combination is the application that increases type I collagen synthesis the most, followed by HA filler, PDO thread+HA filler+BTX and PDO thread applications. On the 12th week and after, the most effective application was detected HA filler on collagen production. HA filler was followed by the combination of PDO thread+HA filler+BTX. Other applications do not seem to have a stimulating effect on type I collagen and type III collagen synthesis during this period.

Keywords: Polydioxanone thread: Botulinum Toxins, Type A: Dermal Fillers: Rats, Wistar: Skin Aging: Photoaging

OP-25 [Dermatological Practice Management]

Autologous Blood Injection for Treatment of Corticosteroid Atrophy

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[2]Department of Dermatology and Venereology, Nazilli State Hospital, Aydın, Turkey

OBJECTIVES: Intramuscular corticosteroid injections are frequently used for a variety of conditions in dermatology practice. Unfortunately, many complications are associated with systemic and local administration of corticosteroids. Cutaneous adverse effects after intramuscular corticosteroid administration include dermal and/or subcutaneous atrophy, hyperpigmentation, hypopigmentation/depigmentation and alopecia. Localized subcutaneous lipoatrophy is among the most common adverse effects that can lead to permanent disfigurement. There are several treatment options for this condition such as intradermal saline injections, autologous fat grafting, poly-L-lactic acid injections and surgical excision with varying success rates. Autologous blood injection (ABI) is immediate injection of the patients' own blood into the affected tissue with the intention of stimulating the body's own tissue-healing mechanisms through cellular and humoral mediators. Herein, we would like to report successful treatment of localized steroid atrophy in a 17-year-old patient with ABI. To the best of our knowledge, this is the first report evaluating the effectiveness of ABI in localized subcutaneous lipoatrophy.

METHODS: This is a case report that presented a successful treatment of localized steroid atrophy with ABI.

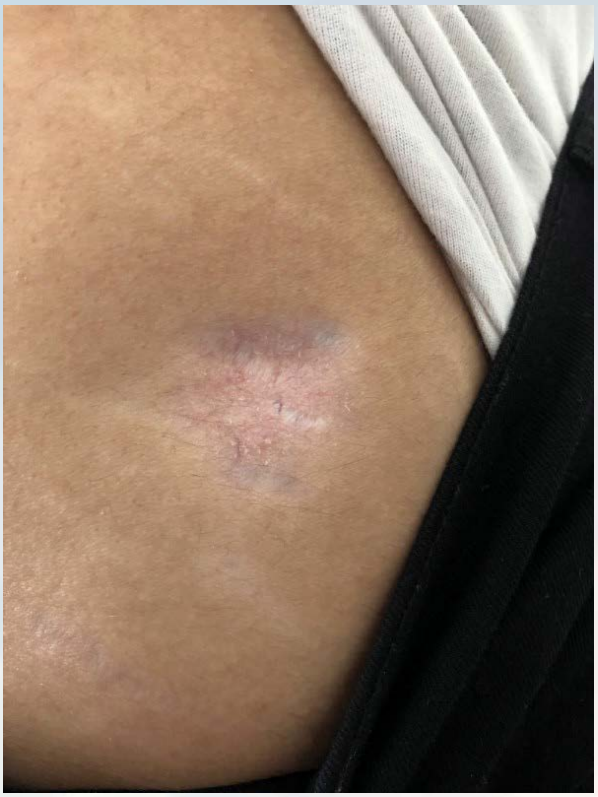
RESULTS: A 17-year-old female patient presented with severe allergic contact dermatitis on her both hands. In addition to topical steroid oinment and moisturizing agents, 40 mg intramuscular triamcinolone acetonide was prescribed to the patient for a rapid recovery. Lesions due to allergic contact dermatitis improved dramatically but within weeks, skin thinnig, depigmentation and subcutaneous fat atrophy were observed in the left gluteal region where is the site of corticosteroid injection (Figure 1). With the patient's history and clinical features, a diagnosis of localized subcutaneous lipoatrophy was made and follow-up of the lesion was planned considering that it would improve over time. The changes subsided after 6 months and there were no signs of spontaneous improvement, therefore ABI treatment was initiated. 4 cc autologous blood was injected into the dermis and subcutaneous fat tissue. One month later after ABI, there was moderate improvement so ABI was performed for the second time (Figure 2a-2b). At 2 months, there was significant improvement (Figure 3). The size and depth of the atrophy was markedly improved and depigmentation was resolved. The patient was satisfied with the result of the ABI.

CONCLUSIONS: Various treatment options are already available in the treatment of localized steroid atrophy with varying success rates. This report shows that ABI is also a simple,

effective and safe procedure for correction of corticosteroid induced cutaneous and subcutaneous atrophy with satisfying results.

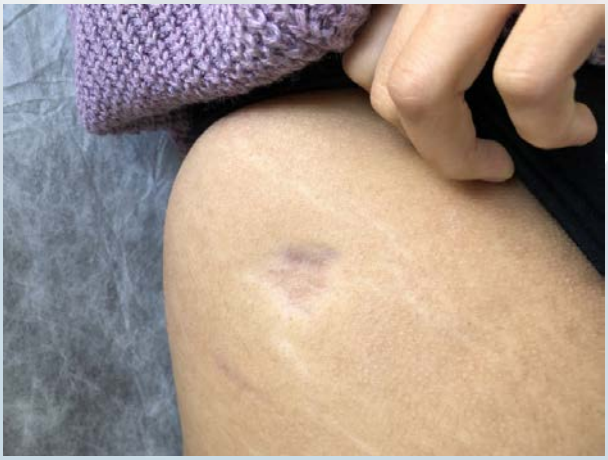
Keywords: autologous blood injection, corticosteroid atrophy, steroid

Figure 1



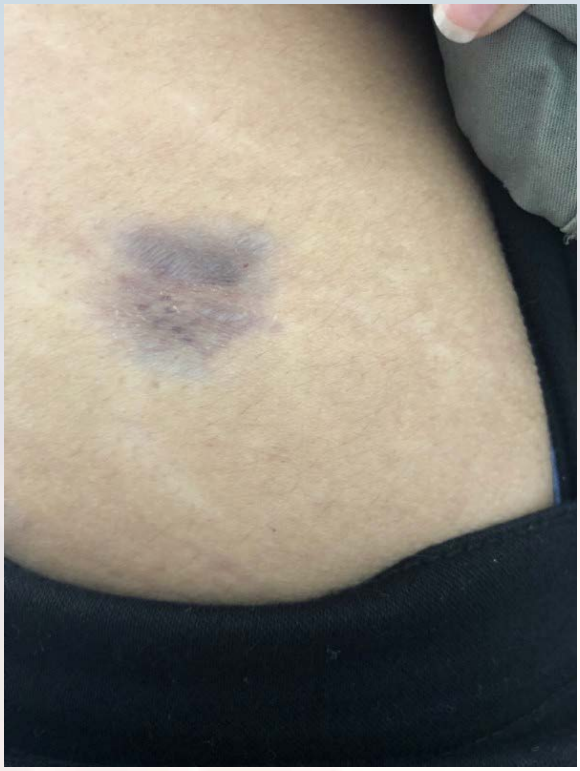
Skin thinnig, depigmentation and subcutaneous fat atrophy in the left gluteal region

Figure 2a



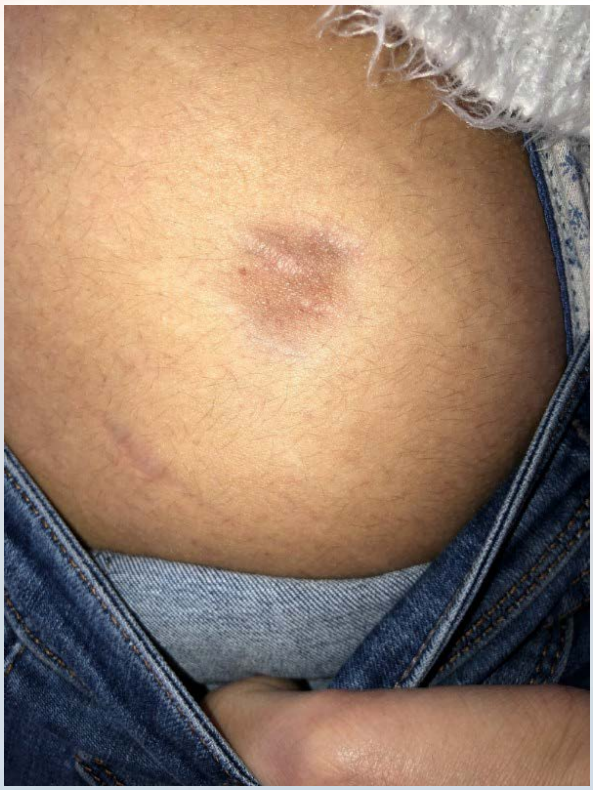
Moderate improvement after first autologous blood injection

Figure 2b



Purple coloration of the lesion due to second autologous blood injection

Figure 3



Significant improvement in the size and depth of the atrophy and depigmentation

OP-26 [Psoriasis]

Palmoplantar Pustulosis - Clinical Characteristics and Associated Diseases in a Single Tertiary Center

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INTRODUCTION and OBJECTIVES: Palmoplantar pustulosis (PPP) is a chronic inflammatory disease characterized by sterile, macroscopically visible pustules affecting the palms and/or soles. PPP has a significant negative impact on patients' quality of life as it occurs on functional areas of the body. The aim of this study was to investigate the clinical characteristics, triggering factors and comorbidities of patients with PPP.

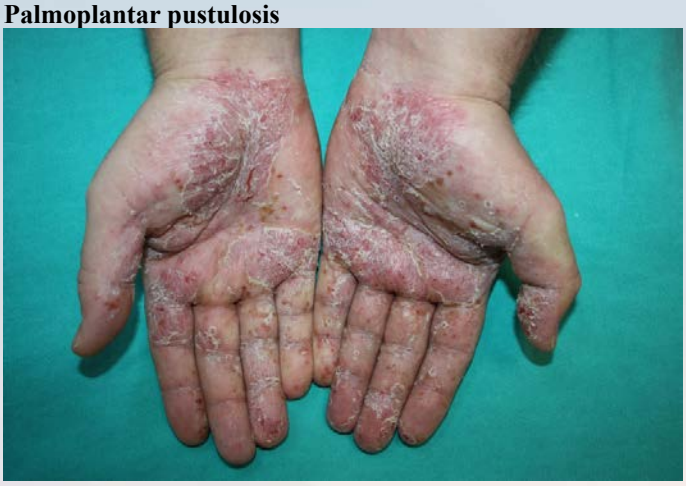
METHODS: We conducted a retrospective review of the patients with PPP at Trakya University Department of Dermatology between January 1, 2018 and January 31, 2021.

RESULTS: A total of 22 patients with PPP consisting of 7 (31.8%) male and 15 (68.2%) female were included in the study. The mean age at onset was 45.3 years. The vast majority of patients (95.5%) were current or ex-smokers. PPP usually started at only palmar (36.4%) or plantar area (40.9%) but then spread to the both localizations (90.9%). Most of the patients (63.7%) were overweight or obese and 40.9% had metabolic syndrome. Almost two third of patients (63.7%) had at least one comorbidity. Dyslipidemia and hypertension were the most frequent comorbidities. Half of the patients had psoriatic arthritis (PsA) (50.0%) whereas 68.2% had nail involvement. Four patients (18.2%) had a paradoxical PPP associated with TNF-alfa inhibitors. Almost a quarter of patients (22.7%) had co-existing psoriasis vulgaris (PsV). Smoking (95.5%) was found to be the most common triggering factor followed by psychological stress (63.6%). There were no significant differences regarding clinical features between genders.

CONCLUSIONS: Many patients with PPP had co-existing psoriatic disease (nail psoriasis, PsV and PsA) and other comorbidities (obesity, metabolic syndrome, cardiovascular disease) similar with patients with PsV. Smoking and stress were found to be considerable potential triggering factors. TNF-alfa inhibitors was the causative agents for paradoxical PPP in some patients. Determining the associated diseases and potential triggers is important for the appropriate management of patients with PPP.

Keywords: palmoplantar pustulosis,characteristic, comorbidity, psoriasis vulgaris

Palmoplantar pustulosis



A clinical picture of severe palmoplantar pustulosis

Characteristics of patients with palmoplantar pustulosis.

	All Patients (n =22)	Male (n =7)	Female (n =15)	p value
Age ± SD, mean years	45.36 ± 11.18	42.57 ± 10.35	46.67 ± 11.66	0.437
Age at disease onset ± SD, mean, years	43.36 ± 10.16	41.57 ± 9.27	44.20 ± 10.76	0.585
Disease onset, n (%)				
Early onset (≤ 40)	8 (36.4)	3 (42.9)	5 (33.3)	1.000
Late onset (>40)	14 (63.6)	4 (57.1)	10 (66.7)	
Localization at disease onset, n (%)				
Palmar area	8 (36.4)	2 (28.6)	6 (40.0)	0.645
Plantar area	9 (40.9)	2 (28.6)	7 (46.7)	
Palmar and plantar areas	5 (22.7)	3 (42.9)	2 (13.3)	
Current localization, n (%)				
No lesion	1 (4.5)	0 (0)	1 (6.7)	0.291
Palmar area	0 (0)	0 (0)	0 (0)	
Plantar area	1 (4.5)	0 (0)	1 (6.7)	
Palmar and plantar areas	20 (90.9)	7 (100)	13 (86.7)	
Smoking status, n (%)				
Never	1 (4.5)	0 (0)	1 (6.7)	0.710
Former	4 (18.2)	2 (28.6)	2 (13.3)	
Current	17 (77.3)	5 (71.4)	12 (80.0)	

Number of smoking pack years, median (25th-75th)	20 (15-30)	25 (15-35)	19 (7-30)	0.514
BMI ± SD, mean	27.07 ± 3.87	29.31 ± 3.22	26.03 ± 3.79	0.063
Nail involvement, n (%)	15 (68.2)	6 (85.7)	9 (60.0)	0.350
PsA, n (%)	11 (50.0)	3 (42.9)	8 (53.3)	1.000
Co-existing PsV, n (%)	5 (22.7)	2 (28.6)	3 (20.0)	1.000
Family history of PsV, n (%)	5 (22.7)	3 (42.9)	2 (13.3)	0.274
Potential triggering factors				
Smoking	21 (95.5)	7 (100)	14 (93.3)	1.000
Psychological stress	14 (63.6)	3 (42.9)	11 (73.3)	.343
Seasonal changes	5 (22.7)	1 (14.3)	4 (26.7)	1.000

OP-27 [Lasers]

The effectiveness of Combination of Er:YAG Laser and Tazorotene is Superior to Er:YAG Laser Alone for The Treatment of Photodamaged Hands

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OBJECTIVE: Carbon dioxide (CO2) and erbium-doped yttrium aluminum garnet (Er: YAG) lasers are the most commonly used rejuvenation modalities in daily practice. The capability of superficial skin ablation with the advantage of minimal thermal damage of Er: YAG (2940 nm) laser makes it one of the most preferred procedure for rejuvenation. Tazarotene is a third-generation synthetic retinoid derivative that has been approved by FDA for photoaging. Since the absorption of topical products through the epidermis is limited physiologically, to overcome the epidermal barrier, laser-assisted drug delivery has become more popular with the advantages of accessibility and rapid onset of topical products. This study aimed to evaluate the efficacy of combining Er: YAG laser and tazarotene on hand rejuvenation in comparison with Er: YAG laser alone.

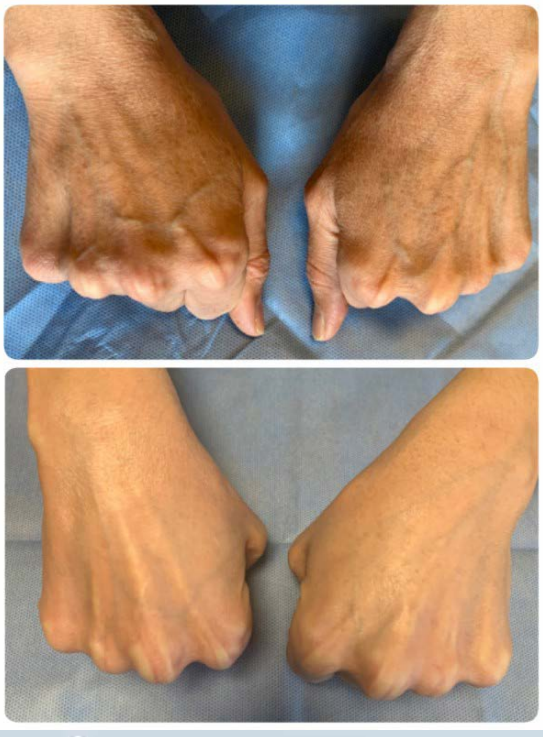
PATIENTS AND METHOD: Data were retrospectively collected from female patients' medical records who were treated in our clinic between January and March 2020 for the signs of hand aging. Among 23 patients 7 were excluded for various reasons including incompliance to the treatment and personal reasons. A total of 16 patients' medical records were evaluated for the study. Patients' mean age was 52,3±0.7. All patients had received Er: YAG laser on both hands with 2-week intervals for 5 sessions. Er-Yag laser was used in fractional mode with short pulse (SP: 250-350μs) 3joule/cm² energy, 10 Hz and 5mm spot size. In the combination group; Er-Yag laser was followed by topical tazarotene application immediately after the laser procedure and those patients were recommended to apply tazarotene topically at nights for 10 weeks. Patients in the 'only laser' group received no additional topical treatment. One month after the final treatment 2 dermatologists who were blinded from clinical data evaluated the pre-and post-treatment photographs retrospectively according to Global Aesthetic Improvement Scale 4 (GAIS 4) point scoring system as 0:worsen, 1: no difference, 2: mild, 3:moderate, 4:good.

RESULTS: The improvement scores of the patients in the combination group were listed as follows: 4 of 8 patients showed 'good' improvement, 3 patients 'moderate' and 1 of them 'mild'. While only 6 and 2 of 8 patients in the laser group had 'moderate' and 'mild' scores respectively. No 'good' response was detected in any patient in the laser group alone. The difference in improvement scores between the 2 groups was found statistically significant. (p= 0,041)

CONCLUSION: Results of this study suggest that both combination of Er: YAG laser and tazarotene and only Er: YAG laser procedure with the regimen used in this study are found effective for the improvement of aging signs on hands. In line with the results of our study, we recommend combining Er: YAG laser with tazarotene because it provides higher improvement scores in the treatment of hand aging.

Keywords: skin aging, Er-YAG Lasers, tazarotene

Figure 1



Before and after photographs of a patient from laser and tazarotene combination group

OP-28 [Miscellaneous

Human 3D Skin Models

Neslihan Fişek Izci

Tissue engineering is used to fabricate 3-dimensional (3D) artificial scaffolds to create a microenvironment that mimics human tissue. Bioprinting uses biomaterials, cells, and/or bioink to fabricate prospective scaffolds to mirror the structural, compositional, and functional aspects of the skin (1). The relevance for in vitro three-dimensional (3D) tissue culture of skin has been present for almost a century. From using skin biopsies in organ culture, to vascularized organotypic full-thickness reconstructed human skin equivalents, in vitro tissue regeneration of 3D skin has reached a golden era (2). The 3D Skin Model is a highly physiological, three-dimensional cellular system of keratinocytes, fibroblasts, and melanocytes for in vitro studies, suggesting an excellent tool to examine aspects of epithelial function and disease, particularly those related to skin biology and toxicology (3). Threedimensional (3D) skin equivalents have been established as a valuable tool in dermatological research because they contain a fully differentiated epidermal barrier that reflects the morphological and molecular characteristics of normal human epidermis (4). Herein, we will summarize 3D skin bioprinting techniques, applications and approaches.

Keywords: bioprinting, 3D, human skin

OP-29 [Acne and Related Disorders, Hidradenitis Suppurativa]

A retrospective analysis of topical and systemic treatments before isotretinoin therapy in patients with acne

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INTRODUCTİON & OBJECTIVES: Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit that can cause significant anxiety in affected patients. Standard acne treatments include both topical and systemic agents. Isotretinoin is widely recognised as a very effective treatment for severe acne. Due to the development of resistance to antibiotic treatments, there are growing concerns about reducing the duration of antibiotic use. To the best of our knowledge there are not many studies about treatment duration among patients with acne. In this study, our aim is to investigate the duration of topical and systemic treatments, that were previously used in patients, with acne who are currently receiving oral isotretinoin therapy.

MATERIALS & METHODS: Patients with moderate to severe acne who received systemic isotretinoin treatment in dermatology outpatient clinic, were retrospectively analyzed. The demographic findings of the patients and their medical characteristics including previous treatment protocols were recorded. Patients with a lack of sufficient data were excluded.

RESULTS: A total of 43 patients (33 females and 10 males) were included in the study. The mean age of initiation of systemic isotretinoin was 25,3 years in female patients and 19,9 years in male patients (p=0.001). The combination of benzoyl peroxide and erythromycin was the most commonly prescribed topical treatment, comprising 43,6% of the prescriptions. Doxycycline was the most commonly prescribed systemic antibiotic with a number of 13 patients. In this study, the average duration of topical and systemic treatment was 6,3 and 2,4 months respectively. The duration of topical treatment was 0-3 months in 22 patients (53.7%), 6-9 months in 9 patients (22%), and more than 1 year in 10 patients (24,4%). The duration of systemic treatment was 0-3 months in 13 patients (81,3%) and 6-9 months in 3 patients (%18,8).

CONCLUSIONS: To minimize antibiotic resistance, long-term therapy with antibiotics is not recommended. Recent guidelines suggest that it should be limited to 3 to 6 months. The mean duration of systemic antibiotic use in this study was found shorter than previous studies findings. In our study, systemic antibiotics was used for 6 months or less, in accordance with most consensus proposals. Expert guidelines recommend using topical retinoids as effective maintenance therapy. In our study, the average duration of topical therapy before isotretinoin treatment was 6.3 months. We observed that the combination of benzoyl peroxide and antibiotics was used more frequently than topical retinoid. Early recognition of patients who show no improvement with appropriate topical therapies and long-term oral antibiotics is necessary to prevent the potential long-term sequela.

Keywords: acne, systemic antibiotics, topical antibiotics, topical retinoid, isotretinoin

OP-30 [Acne and Related Disorders, Hidradenitis Suppurativa]

Dietary and Acne in Teenagers

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BACKGROUND: The positive relationship between acne and fatty dairy products and high glycemic index food has been implicated recently in the literature.

OBJECTIVES: This study aimed to investigate the link between diet and acne in teenagers. We tested the hypothesis that teenagers with acne consume more dairy than those without acne.

METHODS: A case-control study was conducted among 246 participants (123 acne, 123 control), aging 13 to 21 years, with or without acne. The diagnosis of acne was determined by a dermatologist using the Global Acne Assessment Scale. Participants then completed a dietary-acne questionnaire, and

food and nutrient intake were compared between groups with or without acne.

RESULTS: More dairy product intake was reported in the acne group (P =.01) than those with no acne. No significant difference was found for glycemic diet intake or body mass index. No difference was found between the patients with more facial and body lesions in the acne group.

Limitations: Limitations include self-report of diet by a questionnaire and the complex etiopathogenesis of acne

CONCLUSIONS: Consumption of dairy products was positively associated with acne

Keywords: acne, diet, diary, glycemic, teenager

OP-31 [Inflammatory Skin Diseases]

An Erythema Annular Centrifigum Case due to inactivated SARS-CoV-2 vaccine (CoronaVac); a case report and literature review

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INTRODUCTION & OBJECTIVES: In this presentation, it is aimed to present an erythema annular centrifigum complication developed 3 days after coronavac vaccine and, review of the skin complications that may develop due to the vaccines.

MATERIALS & METHODS: A 24-year-old woman presented with a history of erythematous annular plaques in the face and whole body that progress from the center to the periphery since 7 days before admission. The medical history was positive for covid 19 vaccination before the beginnig of symptoms. There was no history of any other disease or drug use in his medical history. There were no features in his family history. In the histopathological examination of the skin lesions with hematoxylin and eosin staining, a mild inflammation consisting of polymorphonuclear leukocytes and sporadic eosinophils in the perivascular area was observed in the superficial dermis. Taking into account clinical findings and the history of COVID-19 vaccination, the suspicion of COVID-19 was proposed.

RESULTS: The patient was treated with potent topical corticosteroids.

CONCLUSIONS: Skin complications due to coronavirus vaccines are very rare in the current published literature. Although these complications can often be treated with simple interventions, It should be borne in mind that they may be an alarm sign for vital complications

Keywords: Erythema Annular Centrifigum,

Type IV hypersensitivity reaction, inactivated SARS-CoV-2 vaccine (CoronaVac)

OP-32 [Dermatological Practice Management]

Comparison of dermatology consultations requested from pandemic wards and non-pandemic wards

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Basaksehir Cam and Sakura City Hospital Dermatology

INTRODUCTION: During the SARS-Cov-2 pandemic period, the number of patients admitted outpatient clinics and their profiles have changed. Also changes were observed in dermatology consultations requested from inpatient clinics. In addition, it was noted that the diagnoses determined in the requested Dermatology consultations differ between pandemic wards and patients hospitalized in non-pandemic wards. The aim of the study is to evaluate these observed changes and differences between pandemic and non- pandemic wards.

MATERIALS-METHODS: This study was conducted in the dermatology clinic of Istanbul Basaksehir Cam and Sakura City Hospital between 1 October-31 December 2020, during the second wave of the pandemic. The pandemic and non-pandemic inpatient dermatology consult database was reviewed and compared retrospectively.

RESULTS: A total of 414 patients were evaluated during this period. The mean age of the patients was 44.3 (0-90 years). 90.5% (375) of the consultations were requested from non-pandemic wards and 9.5% (39) from pandemic wards. Among consultations requested from non-pandemic wards, 286 (69%) from internal subspecialities, 68 (16,4%) from surgical subspecialities, 21 (5,1%) from intensive care unit. Diagnoses detected in all consultations were cutaneous infections 37,6%, followed by inflammatory skin disorders 17,3%, wound and ulcers 14,7%, drug reactions 12.5%, pruritus 6.2%, vasculitis/vasculopathy 4.8%, urticaria 3.4% and others 3.5%. Among the diagnoses of pandemic wards consultations, the most frequently detected ones were ulcers 34.7%, drug reactions 32.6%, vasculitis / vasculopathy 18.7%. The order of frequency of consultations requested from non-pandemic services were 39.3% for cutaneous infections, 18.9% for inflammatory skin disorders, 12.2% for ulcers, and 10.6% for drug reactions. In this process, Dermatology consultations requested from pandemic wards were found at a lower rate (9.5%) compared to the literature. This situation has been associated with the fact that our hospital is a 3rd stage large metropolitan hospital with inpatient capacity of 2800 and has been associated with the continuation of intensive patient follow-up in non-pandemic wards during this period. This difference in diagnostic distribution of requested consultations from pandemic wards was thought to be related to the high selectivity, like for cases considered to be highly complicated.

CONCLUSION: The SARS-Cov2 pandemic has also caused changes in Dermatology consultations during this period. In the SARS-Cov2 pandemic, differences were detected in the rate and diagnosis of requested Dermatology consultations between pandemic wards and non-pandemic wards. These differences

may vary according to the capacity of the hospital, the continuity of non-pandemic patient follow-up and the selectivity of consultations requested from pandemic services. The causes of these differences needs to be supported by prospective multi-center studies.

Keywords: Dermatology consultations, pandemic wards, non-pandemic wards, SARS-Cov-2

OP-33 [Biologics, Immunotherapy, Molecularly Targeted Therapy]

Quantiferon-TB Gold Test Conversion in Psoriasis Patients on Biologic Therapy: A Retrospective Study

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INTRODUCTION & OBJECTIVES: Biologics are commonly used in dermatological practice, especially in psoriasis. Testing for latent tuberculosis infection (LTBI) is mandatory at the beginning and during biologic treatment, as they may lead to reactivation.

MATERIALS & METHODS: This is a retrospective study with data obtained from our psoriasis patient database. Psoriasis patients on biologic drugs, having at least two consecutive Quantiferon-TB-Gold test (QFT) results one year apart were included in the study. Patients only evaluated through tuberculin skin test (PPD) were excluded. In patients with PPD also available, cut-off value for PPD positivity was 10 mm. QFT outcomes after one year treatment were defined according to baseline and follow-up QFT RESULTS: seroconversion if from negative to positive, seroreversion if from positive to negative, persistently seronegative or persistently seropositive.

RESULTS: Thirty-nine patients, of whom 21 (53.85%) were male were included in the study. Mean age was 45.67 (24-85) and mean disease duration was 16.19 years (5-74). Mean follow-up duration was 39.1 months (14-108). Patient distribution according to different biological medications were as follows: Adalimumab 6 (15.38%), Certolizumab 8 (20.51%), Ixekizumab 8 (20.51%), Infliximab 1 (2.56%), Secukinumab 8 (20.51%) and Ustekinumab 8 (20.51%). The number of patients with a negative QFT at the beginning of the treatment was 27 (69.23%) and the rest were positive. 21 patients also had PPD results, 14 (66.67%) of them were 10 mm or above. Only 8 (38.1%) of these patients also had QFT positivity. QFT and PPD were concurrently negative in 6 (28.58%) of patients. After one year of treatment, 31 (79.49%) of patients had negative and 8 (20.51%) had positive QFT results. Only 2 (5.13%) patients showed seroconversion. These patients were on ixekizumab and secukinumab. Six (15.38) exhibited seroreversion, three of which were on certolizumab, one on adalimumab and two on ustekinumab. For persistent seronegativity and seropositivity, the numbers were 25 (64.1) and 6 (15.38) respectively. No cases of active TB were detected.

CONCLUSIONS: Annual testing for LTBI reactivation is required for patients on biologics. Two tests commonly used for this purpose, PPD and QFT have low concordance ratios, and QFT is generally accepted as more specific, therefore more strongly recommended. Our cohort had a low rate of seroconversion of QFT, although we live in a country with a relatively high TB disease burden. Interestingly, a higher ratio of patients exhibited seroreversion, which may have been caused by isoniazide prophylaxis. Our cohort was too small to compare seroconversion rates seen under different therapeutics. Notably, the two seroconversions in our cohort happened during treatment with anti-IL17 agents, although these agents have previously been favored in latent TB infection.

Keywords: biologics, quantiferon, tuberculosis, psoriasis

OP-34 [Biologics, Immunotherapy, Molecularly Targeted Therapy]

The efficacy of ustekinumab treatment in patients with moderate-to-severe plaque psoriasis

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INTRODUCTION: Psoriasis is a chronic inflammatory skin disease and the TNFα–IL23–Th17 axis plays an important role especially in plaque psoriasis. Ustekinumab is a human IgG1k monoclonal antibody and acts by binding to the p40, the common subunit of IL-12 and IL- 23. In this study, we aimed to evaluate the efficacy of ustekinumab in patients with plaque psoriasis followed up in our clinic.

MATERIALS & METHODS: Age, gender, previous systemic and biological treatment, additional diseases, nail involvement, duration of treatment, Psoriasis Area and Severity Index (PASI) values of patients who received ustekinumab treatment were recorded.

RESULTS: Fourteen patients (10 males and 4 females) were included in the study. A total of 5 patients had comorbidity and one of them had psoriatic arthritis. One patient was using ustekinumab at a dose of 90 mg and one patient was using the drug every 8 weeks. Of 14 patients,13 patients had PASI 50 response at the 16th week of the treatment, 9 patients had PASI 90 response at the one year of the treatment.

CONCLUSIONS: In our study, ustekinumab treatment well tolerated and no serious adverse effects were observed in any of the patients. We think that ustekinumab is effective and safe in the treatment of moderate and severe plaque psoriasis. In patients who only partially respond to the initial regimen with ustekinumab, the dose may be increased to 90mg or administered every 8 weeks to achieve a complete response.

Keywords: biological agent, psoriasis, ustekinumab

OP-35 [Dermatological Practice Management]

The role of dermatologists during early COVID-19 pandemic in Turkey: Implications of the results of a nation-wide online survey for Turkish health care system

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INTRODUCTION & OBJECTIVES: The coronavirus disease 2019 (COVID-19) has led to a re-organization of health services throughout many countries. In this study, we aimed to get an overview of the role of the dermatologists during COVID-19 pandemic in Turkey. We aimed to interpret the results according to current Turkish health care policies.

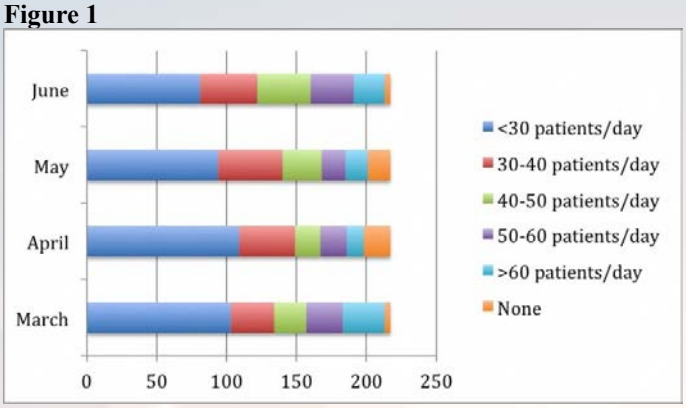
MATERIALS & METHODS: Dermatologists across Turkey were asked to fill in an online 11-item questionnaire survey, investigating their duty/duties (dermatology outpatient and inpatient clinics, pandemic outpatient and inpatient clinics, emergency etc.) month by month during March-June 2020. The study was approved by both the local review board and Turkish Ministry of Health.

RESULTS: A total of 217 responses were obtained. Considering there were 2351 actively working dermatologists in Turkey during the study period, results of our survey with 217 participants has a 95% confidence interval and a margin error of 6.3%. Dermatologists of all ages, from residents to senior dermatologists, participated in the survey (age range: 27-70). Vast majority of the participants were working in governmental hospitals including research and training hospitals (28.1%) and public hospitals (25.3%). Although respondents were from nearly all cities of Turkey, dermatologists from three biggest cities of Turkey dominated (34.6%, 10.1% and 6% for Istanbul, Ankara and Izmir, respectively). Academic degrees of participants were specialist (66.4%), resident (18.9%), associate professor (8.3%) and professor (6.5%). Vast majority (91% to 98%) of the participants reported that they performed dermatology outpatient visits. Each month, at least half of dermatologists reported examining more than 30 patients per day. While 41.5 to 56.2% of participants were redeployed to pandemic inpatient clinics, 12.9 to 29% were mobilized to pandemic outpatient clinics. Across four months, the percentage of participants that were mobilized to COVID inpatient clinics and outpatient clinics showed statistically significant changes. These changes were in accordance with the rate of COVID cases in Turkey. Each month, at least 90% of the residents that participated in the questionnaire reported they were recruited to pandemic inpatient clinics.

CONCLUSIONS: Our findings indicate that nearly all participants continued the dermatology outpatient visits during early pandemic. In addition, a significant percentage of dermatologists were redeployed to COVID-19 wards in Turkey, especially the residents. As the impact of COVID-19 pandemic is ongoing in Turkey, this data should be taken into consideration in order to rapidly implement new measures in Turkish health policies such as a referral system for dermatology outpatient visits to equitably distribute dermatology services, widespread use of telemedicine and virtual educations of residents.

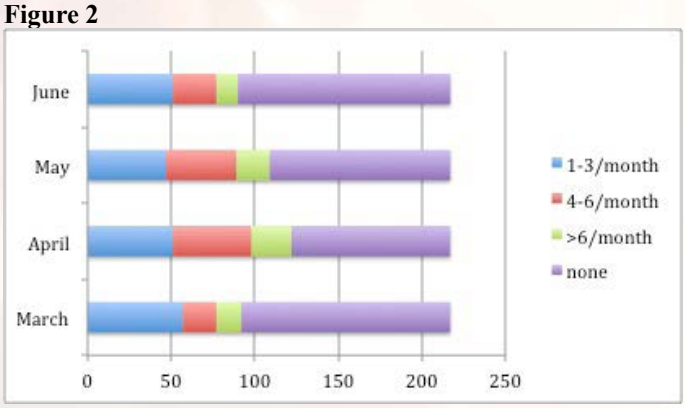
Keywords: clinical practice, coronavirus, dermatology, health policy, pandemic, redeployment

Figure 1



Monthly distribution of participants working in dermatology outpatient clinics and number of daily visits performed

Figure 2



Monthly distribution of participants involved in pandemic inpatient care and number of monthly shifts

OP-36 [Infectious Diseases, Parasitic Diseases, Infestations]

COVID-19 and Human Papillomavirus: Paradoxical immunity

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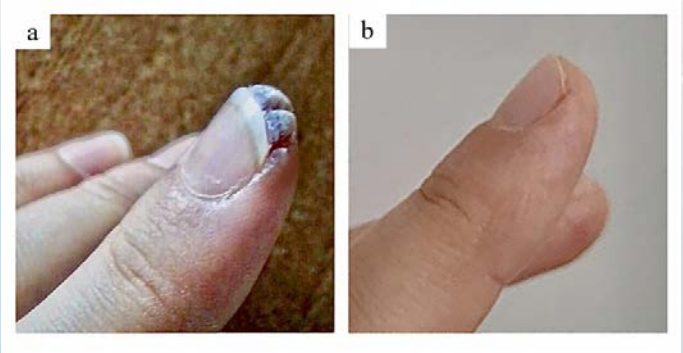
Coronavirus disease 2019 (COVID-19) is a multisystemic disease that can cause progressive lung failure, organ dysfunction and coagulation disorder associated with high mortality and morbidity. COVID-19 is known to either primarily cause skin symptoms or increase existing skin diseases. Human papillomavirus (HPV) is a DNA virus that can cause benign and malignant neoplasms. Mucocutaneous verruca vulgaris are common benign lesions of HPV. Here, we report a case of verruca vulgaris regressed after COVID-19.

Keywords: COVID-19, Human Papillomavirus, Paradoxical immunity

Figure 1.



a. Periungual verruca vulgaris before COVID-19, b. Lesions that spontaneously regress after COVID-19.

OP-37 [Epidemiology]

Evaluation of dermatology consultations requested from the patients hospitalized in COVID-19 wards

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INTRODUCTION & OBJECTIVES: Coronavirus 2019 disease (COVID-19) has affected the whole world since December 2019, and the health system has been inevitably affected by this pandemic. COVID-19 causes pneumonia that presents with fever, cough, shortness of breath, and myalgia. However, skin involvement has also been reported. The aim of this study is to evaluate the dermatology consultation notes of patients with Covid-19 pneumonia at covid wards.

MATERIALS & METHODS: Patients hospitalized in covid wards at Bursa City Hospital between March 16, 2020, and February 15, 2021, were included in the study. Patients were diagnosed with Covid pneumonia with either the positiveness of polymerase chain reaction test or compatible computed tomography findings as described by the World Health Organization. Dermatology consultation notes of the patients over 11 months were retrospectively analyzed.

RESULTS: There were 94 patients; 53 (56.3%) of the those were male, and 41 (43.6%) were female. The average age of male patients was 56.7, and female patients were 55.9 years old. The diagnoses made at consultations were drug eruption, 18%; dermatitis, 17%; pruritus, 9%; urticaria, 7%; herpes zoster, 7%; superficial fungal diseases, 6%; cellulite, 5%; decubitis ulcer, 5%, and others, 26%.

CONCLUSIONS: The covid-19 disease can be associated with various dermatological findings. The drugs used during the treatment of covid pneumonia and long-lasting hospital stays may also cause rashes and a variety of dermatological disorders by affecting the immunity and skin barrier. Understanding these diseases and a multidisciplinary approach including dermatology is very important in the management of Covid-19 disease.

Keywords: inpatient, dermatology, Covid-19

OP-38 [Infectious Diseases, Parasitic Diseases, Infestations]

Evaluation of the frequency and economic impact of patients with scabies in a cross-sectional study

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INTRODUCTION & OBJECTIVES: Scabies has been reported with increasing frequency in recent years. It has become a serious health problem due to widespread nocturnal itching, sleep disturbance, and a tendency to secondary skin infections. Also, it can affect a large number of patients due to human-to-human transmission. With the scabies epidemic in our country, the data are gradually increasing. The aim of this study is to present the economic and social dimension of the epidemic by giving the number of individuals affected, the frequency of treatment, and the number of physician visits in infants, children, and adults.

MATERIALS & METHODS: Within the study, only one person from the same family was evaluated among the patients diagnosed with scabies who applied to the dermatology outpatient clinic of Başakşehir Çam and Sakura City Hospital. The patients were questioned about the family member who started itching first in the family, the duration of the disease onset, the number of affected individuals in the family, the number of physician visits of the patients, the number of treatments applied, and the treatments applied.

RESULTS: Thirty adults, 30 children, 30 infant patients were evaluated in the study. There were 32 female and 58 male patients (64.4%). The average age is 12.32 years; Male gender predominance was present in all infant, child, and adult groups. In the family, babies were the most common carriers of scabies, and children took second place. The first person in the family where the symptom started was rarely seen as the father. When the individuals with itching and rash in the family were questioned, 384 patients were recorded. The disease's duration was 315 months (average 4.5 months), the average number of physician visits was 3.9, and the average number of repeated treatments was 4.1.

CONCLUSIONS: Scabies continues as an important health problem in our country. It is observed that infants and children are the most affected and carriers of the disease. We can say that there are four times more affected patients in the community than the number of patients identified in our study. Scabies patients create significant psychological and economic losses. We think that cooperation with dermatology, family physicians, pediatricians, and emergency physicians may be effective in the control of the epidemic in terms of the epidemic outbreak.

Keywords: scabies, infants, outbreak

OP-39 [Systemic Treatment]

Retrospective Evaluation of Side Effects After Using Finasteride at a Hair Transplant Center

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INTRODUCTION & OBJECTIVES: Finasteride is a 5-α reductase inhibitor and it is widely used in the management of benign prostatic hyperplasia and androgenic alopecia (AGA). Although these agents improve the quality of life in men suffering from these conditions, they are associated with some adverse effects. The aim of this study was to analyze the side effects of finasteride treatment used in men with AGA.

MATERIALS & METHODS: We enrolled 59 male patients who administered to our hair transplantation center between October 2019 and October 2020 and used finasteride for AGA. We recorded their demographic data, duration and dosage of finasteride usage, smoking status and side effects they experienced during usage or cessation of the drug.

RESULTS: The age of the patients were 39.06±6.79 years. Patients started finasteride use in the age range of 24–52 years (34.23±6.67 years). Finasteride was used in a range of 6-240 months (38.5±47.5 months). 52 patients assumed finasteride at dosage of 1 mg/day, 5 patients 1.25mg/day and 2 patients 2.5 mg/day. 14/59 (23.7%) patients reported side effects related with finasteride and 9/14 (64.2%) pateints reported more than one side effects (Table1). Loss of libido was the most common side effect among our patients (9 patients), erectile dysfunction was the second most common side effect (8 patients). Depression was the least seen side effect (2 patients). Two patients taking 2,5mg/day finasterid and five patients taking 1,25 mg/day finasterid had side effects while seven of 52 patients taking 1mg/day finasterid had side effects. Side effects persisted for over 4.1±2.7 months after finasteride discontinuation.

CONCLUSIONS:: Finasteride, decreases serum and scalp dihydrotestosterone by inhibiting conversion of testosterone to DHT. Although finasterid has side effects, all is temporary and disappear after cessation of the treatment. Our study shows that the side effects of finasterid is dose dependent and patients should be warned to take low dosage of finasterid. New studies that evaluates the effect and side effects of intermittent finasterid treatment should be done.

Keywords: finasteride, alopecia, side effect

Demographic characteristics, Side effects of finasteride sexual and non-sexual symptoms

Characteristic or symptom	Patients, N = 59 Mean ± SD or n (%)
Age, years	39.06±6.79
Age at starting finasteride assumption, years	34.2±6.6
Duration of finasteride use, months	38.5±47.5
Dosage used, mg/day	1.13±0.58
Duration of side effects after cessasion of drug, months	4.1±2.7
Erectile dysfunction	8
Decreased libido	9
Premature ejaculation	5
Gynecomastia	4
Depression	2

OP-40 [Inflammatory Skin Diseases]

Sweet Syndrome: The Natural Course of Blau Syndrome or a Paradoxal Reaction to Adalimumab?

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[3]Manisa Celal Bayar University, Faculty of Medicine, Department of Pathology

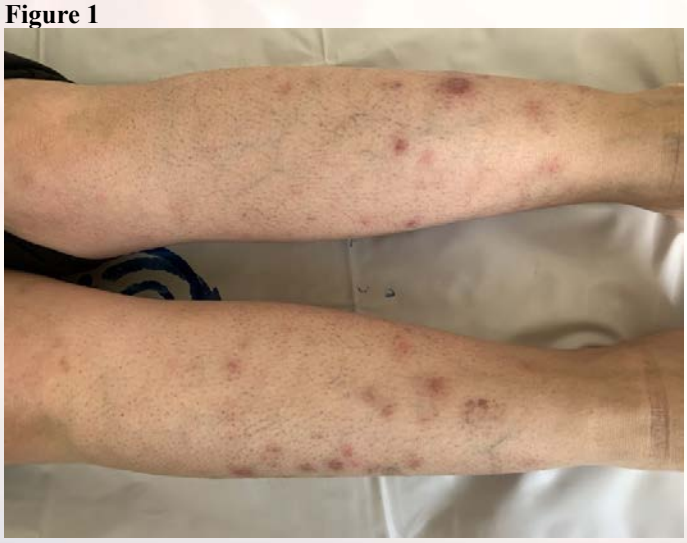
INTRODUCTION & OBJECTIVES: Blau syndrome is an autosomal dominant inherited granulomatous autoinflammatory disease which is caused by mutations in NOD2/CARD15 gene. Clinical presentation is characterized by skin eruption, granulomatous arthritis/synovitis and uveitis triad which show noncaseous granulomas under histopathological examination. Sweet's syndrome is an inflammatory and reactive dermatosis which presents with pyrexia, neutrophilia, painful erytomatous papules, nodules and plaques; in addition extensive infiltration of neutrophils into dermis histologically. It can be idiopathic, malignancy-associated or drug-induced. In this report, Sweet's syndrome is discussed etiologically in a patient with Blau syndrome.

MATERIALS & METHODS: A Sweet's syndrome case with also had Blau syndrome was presented. RESULTS: A 30-year old female patient had multiple tender erythematous nodules on the lower extremities that developed after second adalimumab injection (Day 0: 80 mg Adalimumab sc, Day 7: 40 mg Adalimumab sc) was consulted. In her medical history, she was followed by Blau syndrome with recurrent uveitis, severe joint deformities and granulomatous dermatitis. In her family history, her mother and two of her sisters were diagnosed with uveitis and granulomatous dermatitis. A punch biopsy is performed. In histopathological examination, severe neutrophilic inflammation is detected in dermis and subcutaneous tissue. She was diagnosed with Sweet's syndrome and given 0,5 mg/kg oral methylprednisolone. Adalimumab can not be stopped because of recalcitrant uveitis even to other anti-tumor necrosis factor (TNF) alpha agents.

CONCLUSIONS: To the best of its knowledge, idiopathic Sweet's syndrome could be triggered by inflammatory disorders. Anti TNF alpha agents such as adalimumab have been used successfully on many occasions to treat disorders with neutrophilic dysfunction, including Sweet's syndrome. On the other side, four adalimumab-induced Sweet's syndrome cases were reported so far, suggesting that anti TNF-alpha agents may paradoxically potentiate neutrophilic dysfunction in predisposed patients. The occurrence of Sweet syndrome can be integrated into the natural course of the Blau syndrome as an autoinflammatory disease, but the imputability of adalimumab is at issue. Follow-up is in progress.

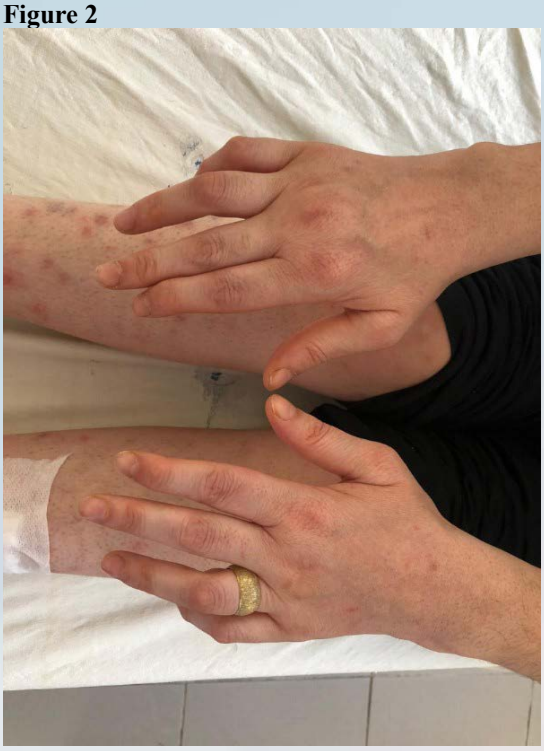
Keywords: blau syndrome, Sweet's syndrome, adalimumab

Figure 1



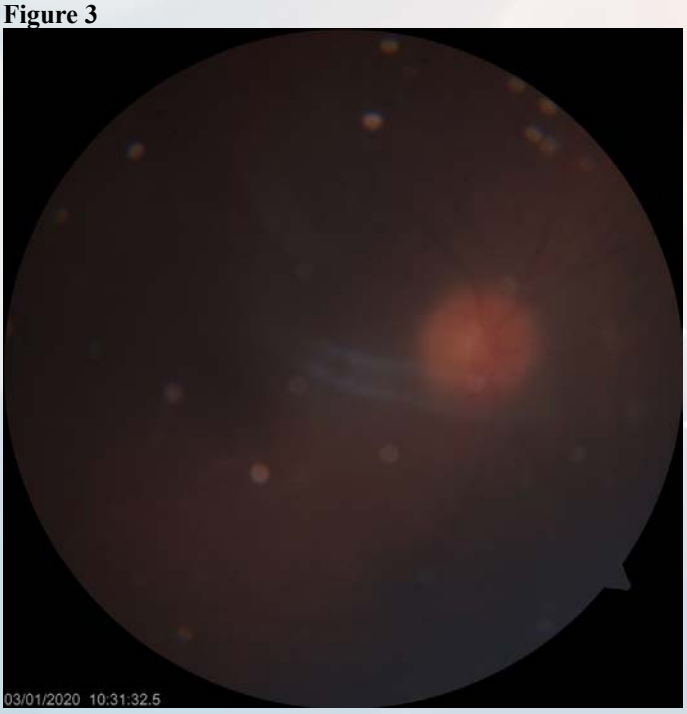
Erythematous nodules in lower extremities

Figure 2



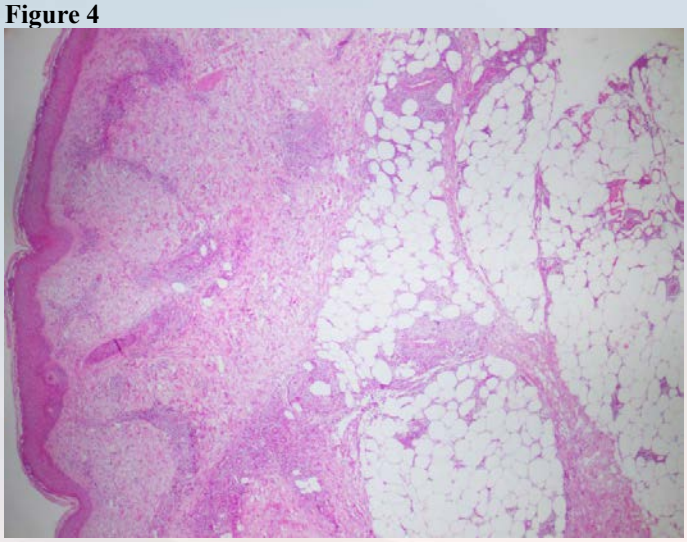
Camptodactily

Figure 3



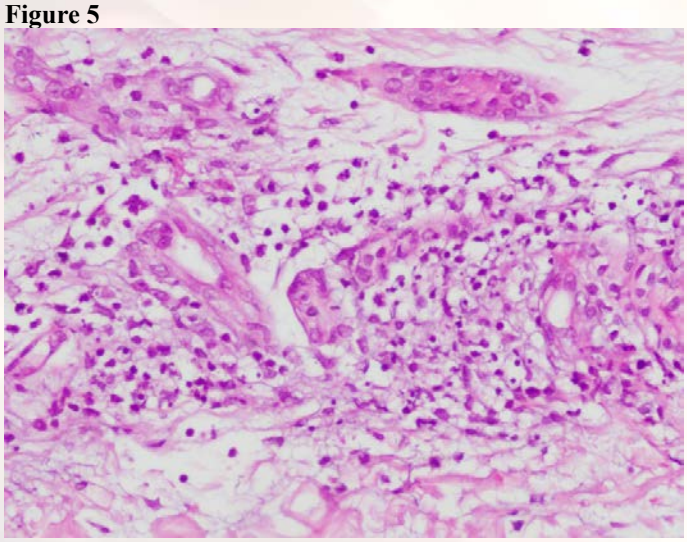
Vitreal condensation and panuveitis

Figure 4



Neutrophil predominant mixed inflammatory infiltration in dermis and subcutaneous fat tissue (HE, x20)

Figure 5



Dermal perivascular dense neutrophilic infiltration (HE,x200)

OP-41 [Inflammatory Skin Diseases]

C-reactive protein to albumin ratio: Is a prognostic factor for the Behçet Diseases?

Bülent Nuri Kalaycı, Rabia Aydogan

C-reactive protein to albumin ratio: Is a prognostic factor for the Behçet Diseases?

INTRODUCTION: Behçet's disease is recurrent oral and genital ulcers, ocular and cutaneous lesions, and a multisystemic inflammation involving various organs and systems. Although some hypotheses have been created, including genetic, infection, immune complexes, and environmental factors, the cause and pathogenesis of Behçet's disease have not yet been fully explained. Diagnosis of Behçet's disease is based on clinical parameters. Laboratory tests can help to diagnose the disease and during the follow-up period. In this study, it was aimed to evaluate whether inflammatory markers such as CRP / Alb ratio, Neutrophil / Lymphocyte ratio, MPV are significant for the disease in patients diagnosed with Behçet's disease in outpatient clinic conditions.

METHODS: We retrospectively examined the demographic and clinical data of 28 patients with Behçet's Disease, and similar age 28 control groups. We calculated NLR, CAR, and MPV values with the SPSS v25 program.

RESULTS: There were 28 patients, including 16 men (80%). In the control group, there were 24 females (66.7%), 4 males (20%). The mean age of the patient group was 38.8 (St: 12.2). Mean Platelet Volume (MPV), p value:0.08 (mean: 0.54, St:0.30), CRP/ALB rate (CAR) p:0.63(Mean: 0.008, St:0.17), Neutrophil/Lymphocyte Ratio(NLR) p value:0.08(Mean:2.51, St:1.19)

CONCLUSION: In Behçet's disease, tests such as C reactive protein (CRP), sedimentation (ESR), thrombocyte (Plt), mean thrombocyte volume (MPV), neutrophil count, and albumin are easily used routinely in the follow-up of the disease and complications. The relationship between MPV and complications such as recurrent aphthous stomatitis, thrombosis, and ocular involvement in Behçet's disease. High risk of MPV and thrombosis is correlated with low-grade inflammatory conditions, cardiovascular-cerebrovascular disorders. In our study, the MPV ratio was not significant in the Behçet's disease group compared to the controls. Neutrophil (N) and lymphocyte(L) count can be obtained from the complete white blood count part. In Behçet's disease, a higher N / L ratio was found in the control and inactive Behçet groups. In our study, the N / L ratio was not significantly higher than the control group. CRP is an acute-phase reactant (AFR) synthesized mainly by hepatocytes under the control of proinflammatory cytokines. Albumin is a negative acute phase reactant.The CRP / Alb ratio (CAR) is a new inflammatory marker. CAR has been shown to have a prognostic value in lung cancer, with a significant correlation with overall survival. In a retrospective study involving patients with rheumatoid arthritis, CAR was found to be higher than controls and positively correlated with DAS28-ESH. Recently, CAR value was evaluated as a prognostic factor in psoriasis patients and correlated with disease severity. CAR was not significant compared to the control group in our study. The reason for this may be the small sample size of the patient and control groups.

Keywords: CAR, CRP,Albumin, Behçet Diseases

POSTER PRESENTATIONS

PP-01 [Corrective, Aesthetic and Cosmetic Dermatology]

Treatment of Keratosis Pilaris Rubra with 577-nm Pro-yellow Laser

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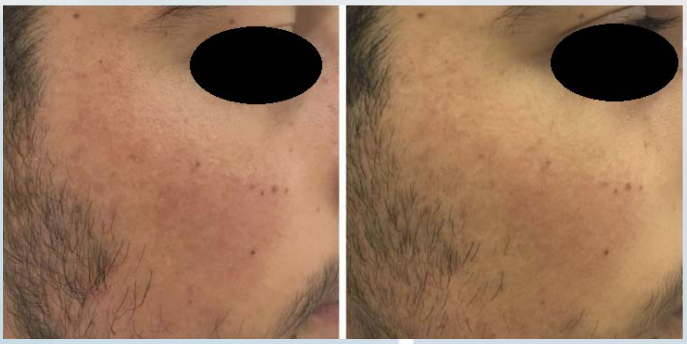
Keratosis pilaris rubra (KPR) is a rare group of idiopathic hereditary disorders of keratinization, and it is considered as variants of keratosis pilaris. Keratosis pilaris rubra is an aesthetically distressed situation, and especially vascular erythema is the most common complaint. In the literature, pro-yellow laser therapy has never been used before in keratosis pilaris rubra.

In our study, four patients with keratosis pilaris rubra treated with pro-yellow laser in Necmettin Erbakan University Meram Faculty of Medicine Cosmetology Unit between December 2017 and March 2019 were evaluated. Objectifying a clearance of erythema > 75% was clinically evident in three patients, in the fourth patient, erythema regressed approximately 50 %. There has been no recurrence of the lesions after a minimum six months follow-up.

As a result, the pro-yellow laser is a well option for the treatment of keratosis pilaris rubra. Additionally, we think that the well tolerance to treatment and a low incidence of serious side effects make it a very reliable therapy. Further clinical studies are needed to improve our findings.

Keywords: Keratosis pilaris rubra, laser treatment, pro-yellow, 577-nm laser, vascular laser

Figure 1



The significant reduction in erythema of the lesion

PP-02 [Phototherapy, Photodynamic Therapy]

Treatment Results of Mycosis Fungoides with continuously 200 mJ / cm2 Narrow-band UVB: Case Series

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Narrow-band UVB (NB-UVB) therapy remains the gold standard in early stage mycosis fungoides (MF) therapy. There is insufficient data in the literature about how to continue the treatment in patients who cannot increase the dose due to erythema.

In this study, the files of seven patients who were clinically and histologically diagnosed as having MF between September 2010 and April 2020 and whose initial dose did not show erythema at 200 mJ/cm2 and could not tolerate the increase in dosage were retrospectively evaluated. In our study, a complete response (CR) was seen in four patients (57.1%), and a partial response (PR) was observed in three patients (42.9%). The mean number of treatment sessions was 358.6 ± 222.6. The mean cumulative ultraviolet (UV) dose was 71.7 ± 44.9 J/cm2. The mean duration of remission was 15.7 ± 10.5 months. The recurrence rate was 57.1%.

As a result, although long treatment times are required in the treatment of NB-UVB in such patients, treatment and recurrence rates were not found to be very different from the literature. Based on our findings, it may be recommended that NB-UVB treatment cannot tolerate the increase in dose, and that patients who develop erythema continue with minimal doses. We think that further prospective controlled studies are needed in this regard.

Keywords: Mycosis fungoides, phototherapy, narrow-band UVB, 200 mJ/cm2

Table 1

Patient No	Age, gender	Skin phototype	TNM Stage	Clinical response	Number of sessions	Remissionduration (months)
1	45, F	III	IB	PR	120	12
2	85, F	III	IA	CR	310	8
3	36, F	IV	IA	CR	160	24
4	64, M	III	IB	CR	520	8
5	72, M	IV	IB	CR	650	36
6	75, F	III	IA	PR	590	10
7	55, F	IV	IB	PR	160	12

The clinical features of patients (PR: Partial Response, CR: Complete Response, M: Male, F: Female)

PP-03 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

Superior vena cava syndrome: a case report

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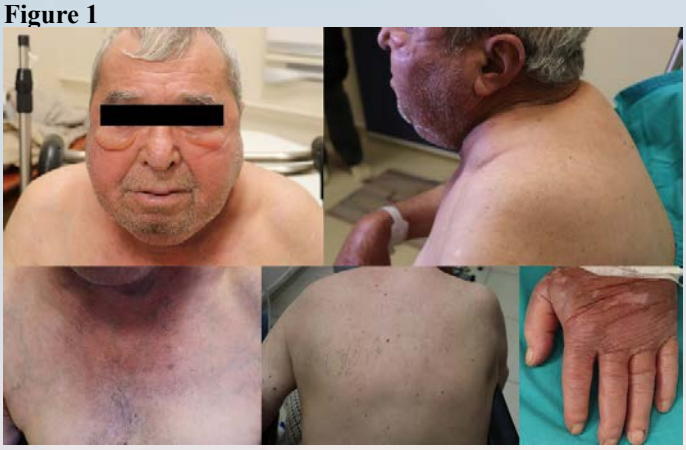
INTRODUCTION: Superior vena cava syndrome (SVCS) is a medical condition that consists of a collection of symptoms and signs resulting from the obstruction of the superior vena cava (SVC). The most common underlying cause is bronchogenic carcinoma. Common presenting complaints of patients with SVCS include dyspnea, cough, face or upper neck swelling, upper extremity swelling, dilated chest veins, chest/shoulder pain, hoarseness, flushing/plethora, syncope/presyncope and headaches. Timely diagnosis of SVCS and treatment of the underlying disease are critical. Here we report a case of SVCS caused by small cell lung cancer.

CASE: A 73-year-old male patient was admitted to our outpatient clinic with the complaint of swelling around his eyes for 3 weeks. He also complained of shortness of breath, difficulty in swallowing, cough, flushing, headache and hoarseness. In dermatological examination, in addition to bilateral infraorbital edema, widespread edema in the neck region and on the back of both hands, erythema on the face and neck region, and dilated vessels on the chest and back were present (Figure 1). There was bilateral rhonchi in the lungs in other system examinations. Hemogram and biochemical tests were normal. He had a history of chronic obstructive pulmonary disease, diabetes mellitus, benign prostatic hyperplasia and 30 pack-year smoking. In his family history, one of his uncles had died of lung cancer. Chest radiography showed a large mass in the right hilar region and bilateral perihilar lymphadenopathies. Thereupon, the patient was consulted to the chest diseases department. Neck ultrasound and computed thorax tomography were requested from the patient. While edema was detected in the skin and subcutaneous tissues in the neck ultrasound, computed thorax tomography revealed an 8 cm diameter mass compressing the SVC in the upper right lobe of the lung. The patient subsequently underwent a bronchoscopic biopsy and the biopsy was consistent with small cell lung cancer. With these findings, the patient was diagnosed with SVCS and was referred to the thoracic surgery department.

CONCLUSION: Here, we present a patient who applied to our outpatient clinic due to angioedema and was subsequently diagnosed with SVCS. Patients with SVCS may develop life-threatening complications such as laryngeal or cerebral edema and may sometimes be referred to the outpatient clinic with skin findings. We believe that early detection of the characteristic skin manifestations by dermatologists is crucial for improving the prognosis of patients with SVCS.

Keywords: Superior vena cava syndrome, angioedema, dilated cutaneous vessels, lung cancer

Figure 1



The clinical pictures of the patient

PP-04 [Acne and Related Disorders, Hidradenitis Suppurativa]

Nodular Cystic Acne Treated with Systemic Dapsone: Case series

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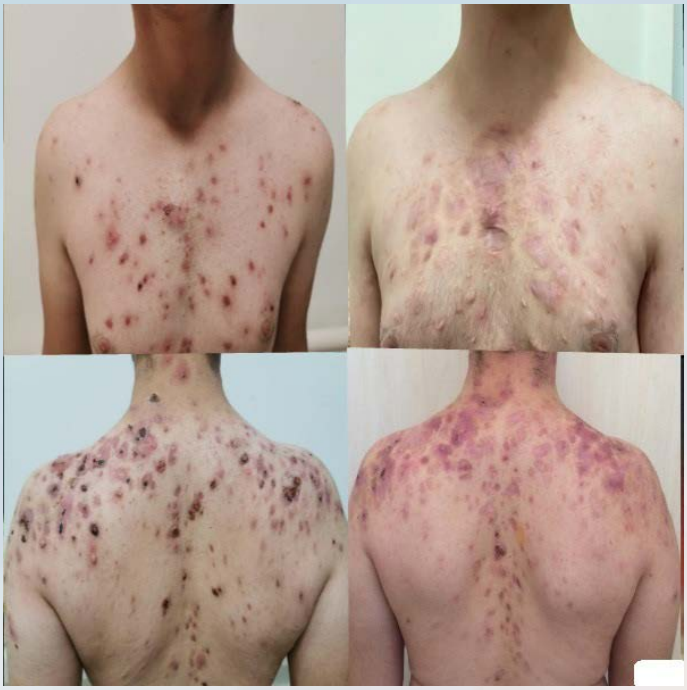
Dapsone (4,4'-diamino diphenyl sulfone) is an aniline derivative treatment agent derived from synthetic sulfones that have both anti-bacterial and anti-inflammatory effects. It was first used in the treatment of leprosy in 1940. It was later used in the treatment of dermatitis herpetiformis and non-infectious inflammatory dermatoses.

Acne vulgaris (AV) is a chronic inflammatory disease of the pilo-sebaceous unit. It is characterized by open and closed comedones, inflammatory papules, pustules, nodules and cysts, which can cause scar formation and altered pigmentation. Abnormal follicular keratinization, increased sebum production, propionibacterium acnes colonization and inflammation are blamed for AV pathogenesis.

We planned dapsone treatment in four patients in whom systemic isotretionine was initiated due to severe nodular cystic AV, but could not be continued due to elevated liver enzymes. We present four AV cases who respond well to systemic dapsone (Figure 1) to draw attention to dapsone as a treatment option in resistant AV.

Keywords: Dapsone, isotretinoin, nodulocytic acne

Figure 1



Clinical appearances before and after treatment

PP-05 [Psoriasis]

Successful treatment of severe pustular psoriasis with adalimumab after treatment failure of infliximab and secukinumab

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[2]Clinic of Dermatology, Konya Ereğli State Hospital, Konya, Turkey
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Generalized pustular psoriasis (GPP) is a rare, severe and potentially life-threatening inflammatory skin disease that is characterized by recurrent, acute onset, generalized pustular eruptions on inflamed or erythematous skin.

Biological agents such as an interleukin (IL)-12 and IL-23 blocker (ustekinumab), tumour necrosing factor (TNF)-α blockers (infliximab, adalimumab, etanercept, e.g.) and IL-17 inhibitors (e.g., ixekizumab, secukinumab) have revolutionized the treatment of psoriasis and pustular psoriasis. However concerns remain about drug options for the patients who have drug-resistant GPP. Again, there are deficiencies in the literature regarding which drug to choose after resistance development. In our case, the success of this treatment change, which was not reported in the literature before, in pustular psoriasis, a rare disease, was remarkable.

Herein, we report a case of severe GPP resistant to conventional and biological agents (including secukinumab and infliximab), however successfully treated with adalimumab.

Keywords: Psoriasis, anti-tnf agents, biologics, adalimumab, infliximab, secukinumab

PP-06 [Cutaneous Oncology]

Cutaneous Nodules as an Initial Manifestation of Neuroendocrine Carcinoma with Unknown Primary Site: A Case Report

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[2]Department of Pathology, Gazi University, Ankara, Turkey

Neuroendocrine tumors are heterogenous group of neoplasms arising from cells of neuroendocrine origin. They have a wide spectrum of clinical behavior and malignant potential. Cutaneous metastases of these tumors have been reported very rarely. We report a patient diagnosed with metastatic neuroendocrine carcinoma after a biopsy was performed from his skin nodules. Cutaneous nodules were one of the first manifestations of his internal malignancy and helped us to diagnose and manage the patient.

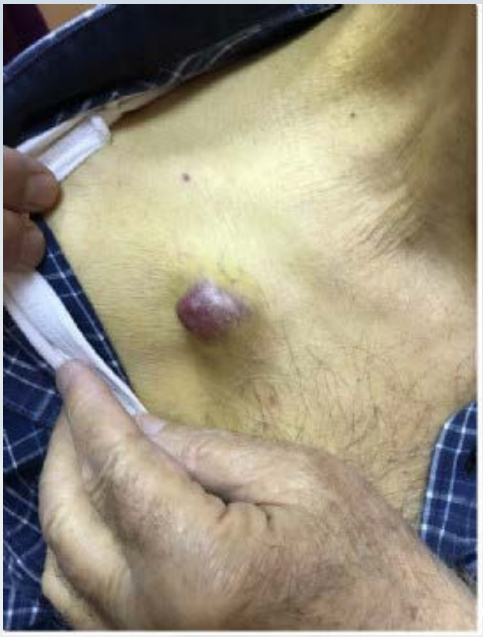
A 72-year old man visited our clinic with multiple nodules on his trunk. He had a history of jaundice, malaise and weight loss for 3 weeks. His cutaneous nodules first appeared on right subclavicular area, followed by 4 new nodules on trunk within 1 week. Nodules were rapidly enlarging, but he did not describe any symptoms. He was brought to emergency department with intractable jaundice and constitutional symptoms a few days ago. Hepatobiliary ultrasonography was performed. In the head of pancreas; 2.5-cm sized, hypoechoic mass containing cystic, necrotic areas was observed.

The patient was directed to oncology department and malignancy work-up has been started. He was consulted to our dermatology department for diagnosis of cutaneous nodules. In the dermatologic examination; painless, firm, dome-shaped, red-purplish five discrete nodules were present on right subclavicular area, abdomen and right lateral site of thorax. (Figure 1 and 2) A biopsy was taken from the lesions, monomorphic, atypical small cells with round, hyperchromatic nuclei were seen in subcutaneous tissue with hematoxylin&eosin staining. (Figure 3) Tumor cells were stained positive with chromogranin, synaptophysin, CD56 and TTF-1 (Figure 4 and 5); but negative with CK7, CK20, CD45, CDX2. Immunohistochemical staining features of cells were compatible with metastatic neuroendocrine carcinoma. Ki-67 proliferation index was studied and more than %95 proliferative activity was reported. (Figure 6) Further diagnostic tests were initiated to detect the primary tumor. In his thoracoabdominal computed tomography (CT); 12x10 cm sized, lobulated mass containing cystic and necrotic areas was observed in the right lung parenchyma. The mass was obliterating right main bronchus and invading right middle and inferior lobe arteries. Tumoral masses were also observed in head and neck of pancreas and adrenal glands in

CT. Thoracentesis was performed, but atypical cells were not observed. Endoscopic retrograde cholangiopancreatography (ERCP) procedure was performed by gastroenterologists. During ERCP, a biopsy was taken from ampulla of Vater; but neuroendocrine tumor or a tumor with epithelial origin could not be detected histopathologically. The exact location of primary tumor was still being investigated; etoposide/cisplatin chemotherapy has been started for metastatic neuroendocrine tumor.

Keywords: Neuroendocrine tumor, cutaneous metastasis, cancer of unknown primary

Figure 1

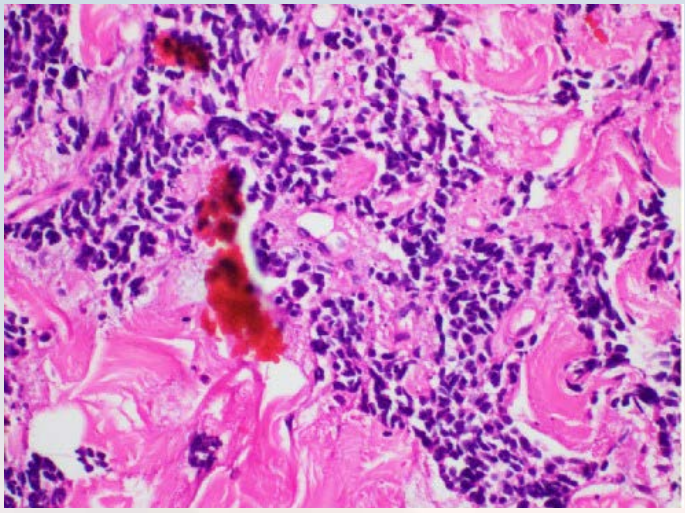


A firm, painless, 3x2-cm sized, purple nodule on the right subclavicular area

Figure 2

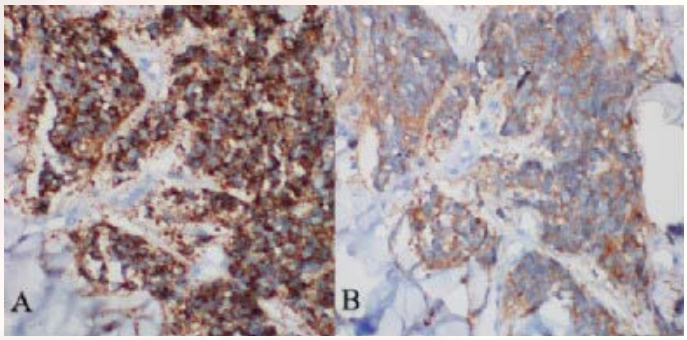
A painless, smooth-contoured, round-shaped, 2x2-cm sized red-purple nodule on the right lateral site of thorax

Figure 3



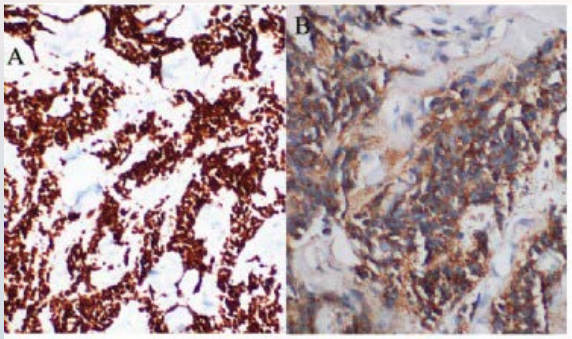
Monomorphic, atypical small cells with round, hyperchromatic nuclei in subcutaneous tissue are seen in hematoxylin&eosin staining.

Figure 4



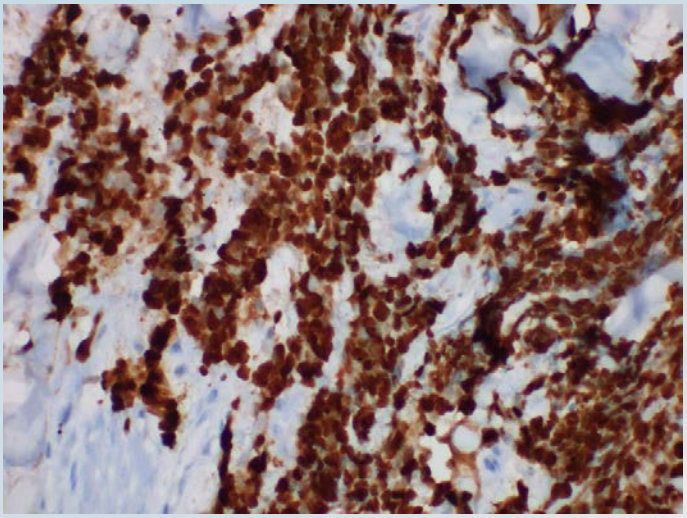
Immunohistochemical features of tumor cells. Tumor cells are immunoreactive with (A) chromogranin and (B) synaptophysin.

Figure 5



Immunohistochemical features of tumor cells. Tumor cells are immunoreactive with (A) TTF-1 (SP141 clone) and (B) CD56.

Figure 6



Tumor cells are stained diffusely positive with Ki-67.

PP-07 [Adverse Drug Reactions, TEN]

Flagellate hyperpigmentation as a unique complication caused by either local or systemic bleomycin administration: Two case reports

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INTRODUCTION & OBJECTIVES: Bleomycin is used either systemically for the treatment of some malignancies or intralesional for the treatment of warts and vascular malformations. Flagellate hyperpigmentation is a rare and unique side effect of bleomycin. The lesions are mostly found on the back and flanks, preceding pruritic linear erythematous lesions fade over time into hyperpigmentation.

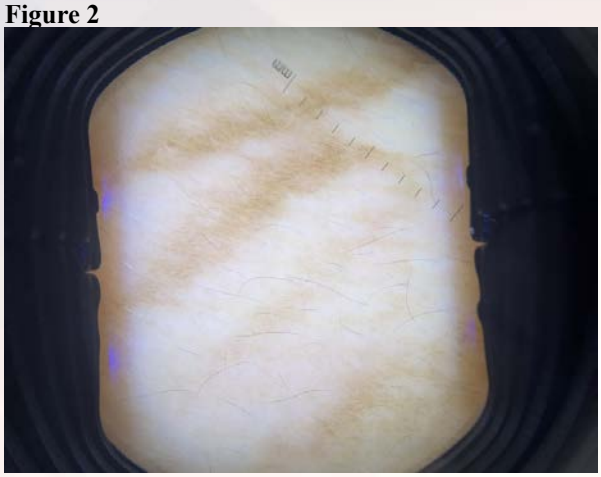
MATERIALS & METHODS: Two flagellate hyperpigmentation cases followed by either intralesional or systemic exposure to bleomycin are presented.

RESULTS: Case 1. A 23-year old female patient had multiple linear brown macules on the lomber region and on the lower extremities that developed after one session of intralesional bleomycin (30 mg) injection for the venous malformation on her left palm. Dermoscopic examination revealed ill-defined diffuse hyperpigmentation. Orthokeratosis, mild acanthosis and dermal perivascular inflammatory cell infiltration were seen in histopathological examination. Case 2. A 31-year old male patient had multiple linear brown macules on his chest and upper back. He was treated with one cycle of BEP protocol (bleomycin, etoposid and cis-platin) for 21 days with the diagnosis of testicular mixed germ cell tumor. Bleomycin was given 30 mg per week with a total dose of 90 mg. Ill-defined diffuse hyperpigmentation was seen on dermoscopic examination.

CONCLUSIONS: Flagellate hyperpigmentation was previously thought as a dose-dependent reaction with cumulative doses greater than 100 U, however local and low dose administrations may also lead the same reaction. Case 1 that we report here is the second case in the literature that developed after one session of intralesional bleomycin (30 U) administration for venous malformation. Although harmless, pigmentation may be a cosmetic concern for some patients. Clinicians should be aware of this rare side effect of bleomycin that is independent of dose and route of administration.

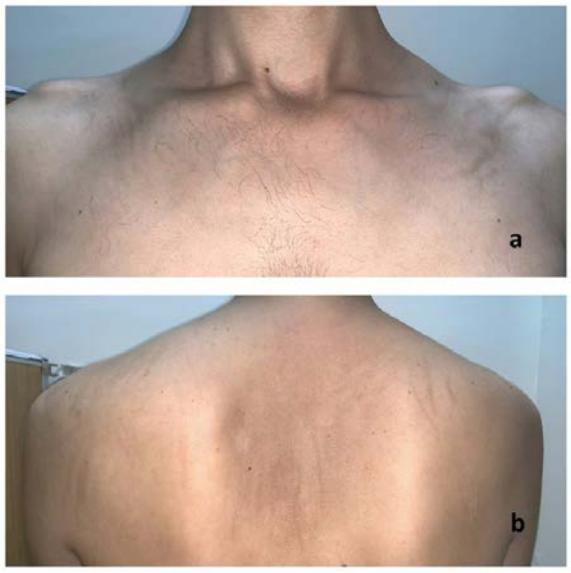
Keywords: flagellate hyperpigmentation, bleomycine, acquired hyperigmentation, drup eruption

Figure 2



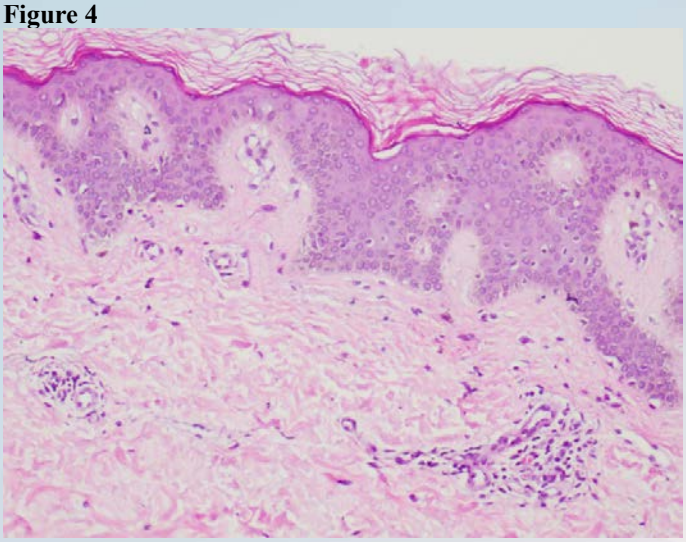
Ill-defined diffuse linear hyperpigmentation on dermoscopy (x10) of Case 1.

Figure 3



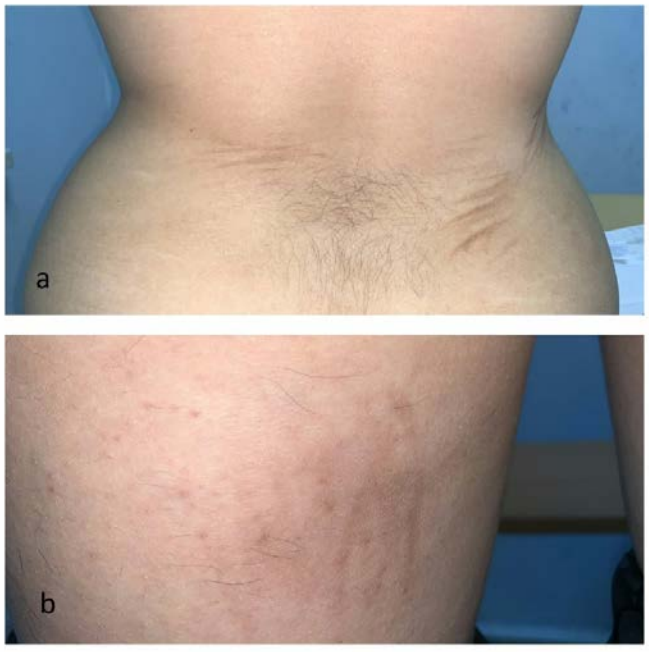
Brown, linear brown macules on the patient's chest (a) and back (b) of Case 2.

Figure 4



Superficial orthokeratosis, mild acanthosis and dermal perivascular inflammatory cell infiltration (H&E, x100)

Figure1



Brown, linear brown macules on the patient's back (a) and femoral region (b) of Case 1.

PP-08 [Adverse Drug Reactions, TEN]

Neutrophil-to-lymphocyte Ratio Is A Prognostic Predictor In Emergency Department Patients With Cutaneous Adverse Drug Reaction

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INTRODUCTION & OBJECTIVES: The skin is the most frequently affected organ by adverse drug reactions.While the most common drug reactions with benign course are maculopapular or urticarial rashes,severe cutaneous adverse drug reactions are AGEP, DRESS, Stevens-Johnson syndrome (SJS), TEN aren't good. Neutrophil-to-lymphocyte ratio (NLR) is a simple parameter that indicates the systemic inflammatory state of patients, a good marker to predict prognosis and mortality in many diseases. There is limited data on the prognostic value of NLR in patients with cutaneous adverse drug reactions. We aimed to evaluate the prognostic value of NLR in emergency department (ED) patients with cutaneous adverse drug reactions

MATERIAL & METHODS: In this retrospective study,patients who admitted to the ED and requested consultation from the Department of Dermatology with the diagnosis of cutaneous adverse drug reaction between 2014 and2020 were included.The ethical committee approved the study.Age(18>),gender,existing comorbid diseases,drug history thought to trigger the rash, dermatological examination findings,eruption distribution areas,type of drug reaction, hospitalization information of the patients were recorded.Patients with known hematological diseases,received chemotherapy in the last week before ED admission,patients who had missing complete blood count were excluded from the study.The NLRs of patients were calculated using the recorded neutrophil and lymphocyte counts.For primary outcome(hospitalization), the patients were divided into two groups: hospitalized and discharged from the ED. For the secondary outcome(type of drug reactions), the patients were grouped five groups.The hematological parameters were compared between the patient groups.

RESULTS: A total of 135 patients were included in the study.The median age of patients was 50 (36-64),63(46.7%) of them were male.79.3% of the patients had a history of taking a single drug,the leading drugs that triggered the reaction in those patients taking single drug were antibiotics(31.9%),analgesics(24.4%).The most common comorbiditiy was hypertension (15.6%).71.9% of the patients had acral,73.3% of the extremity,28.9% of the oral mucosa involvement.The most common diagnoses were maculopapular(32.6%), anaphylaxis/angioedema/urticarial(31.1%),EM/SJS/TEN (13.3%). 79 (58.5%) of 135 patients were hospitalized.Hospitalized and discharged from the ED patients compared, oral mucosal involvement was significantly higher in hospitalized patients(39.2% vs.14.3%, p=0.002).The median NLR of hospitalized patients was

significantly higher than discharged patients from the ED(6.13 vs.3.69,p=0.006).The median NLR of the patients with the EM/SJS/TEN was significantly higher than maculopapular and fixed drug eruptions(p=0.022,p=0.015).

CONCLUSION: NLR can be used prognostic parameter for the patients who admitted to th ED with severe cutanous adverse eruptions.It can be use to decide hospitalization of patients with clinical symptoms

Keywords: Adverse Drug Eruption, Neutrophil-to-lymphocyte ratio, Emergency, Dermatology

PP-09 [Inflammatory Skin Diseases]

An AGEP Case Due to COVİD-19 or Favipravir

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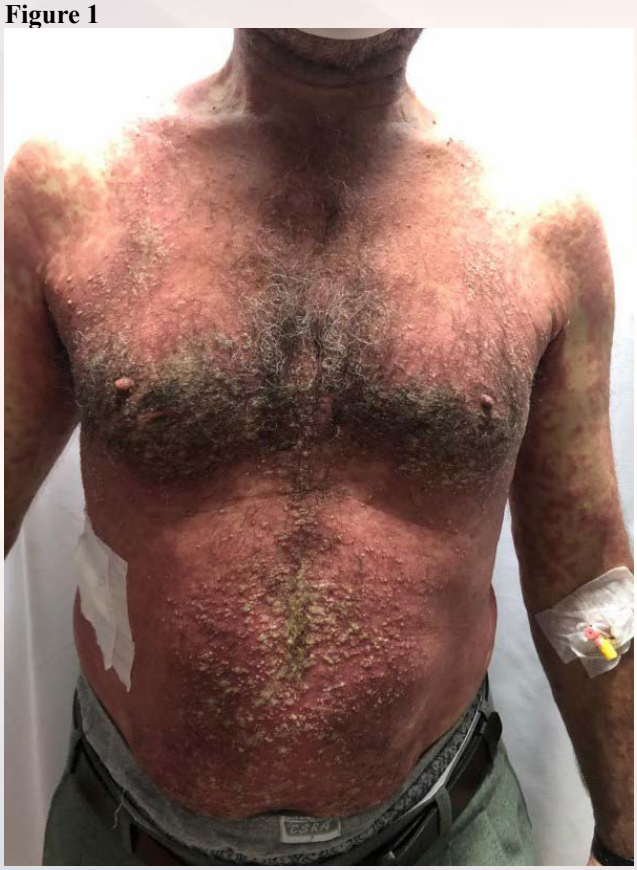
INTRODUCTION & OBJECTIVES: The new coronavirus (SARS-CoV-2), the cause of the 2019 corona virus disease (COVID-19),is very infectious and is the primary cause of the current pandemic.Many systemic symptoms affecting the upper airways, lungs, and gastrointestinal tract have been associated with COVID-19.Urticarial, erythematous-papular/vesicular lesions usually present on central body,and chilblains/perniosis on acral sites are the reported COVID-19 associated dermatological manifestations.These skin lesions have been reported before or during the active COVID-19 infection. Several drugs have been used empirically for the treatment of COVID-19. Some of the described cutaneous eruptions in COVID-19 could also be related to these drugs. There are few reports about treatment-related mucocutaneous drug reactions of COVID-19.AGEP is characterized by the acute onset of generalized non-follicular sterile pustules. AGEP is mainly caused by drugs in most cases, there have been few reports of AGEP associated with viral infections.Here we present a patient with AGEP triggered by COVİD19 or favipravir.

CASE: A 54-year-old man referred to our clinic with widespread pustular lesions.1 month before He was COVİD19. At that time, he was treated with oral favipravir,enoxoparin.He had no history of other diseases or using any other medications. He abruptly developed extremely pruritic pustular lesions 2 weeks after recovering from COVID-19. The pustular lesions first appeared on his face and neck and then spread to his trunk and other parts of body(Figure 1).In labaratory test we observed leucocytosis:13.940,SGOT:57,SGPT142.3,CRP:109 except this he was in good general health.Blood,urinary cultures, chest graphy,abdominal USG were normal. On histopathological examination of skin lesions subcorneal pustul and papillary edema, papillary edama and mild spongiosis in the epidermis, eritrosit extravasaciation nearby subcorneal pustul,epitelyal neutrophils,a few eosinophils were observed (Figure2).With these findings we diagnosed the patient AGEP..We treated patient with metil prednisolone 40 mg/day,antihistamines,emprically ceftriaxone,topical moderate steroid,eau borique %2 cold dress and moisturizers.All of the eruption regressed in one week and labarotory tests were regressed.

CONCLUSION: Hydroxychloroquine is a treatment choice for COVİD 19 an ıt has potential side effects, such as (AGEP). Tthere are few AGEP reports due to favipravir. SARSCoV2 might predispose at least some patients to develop severe atypical AGEP like cutaneous pustular eruption as a late-onset skin manifestation associated with COVID-19 due to its possible effect on the immune system and may also prone the patients to develop late-onset atypical and bizarre drug-induced skin reactions.

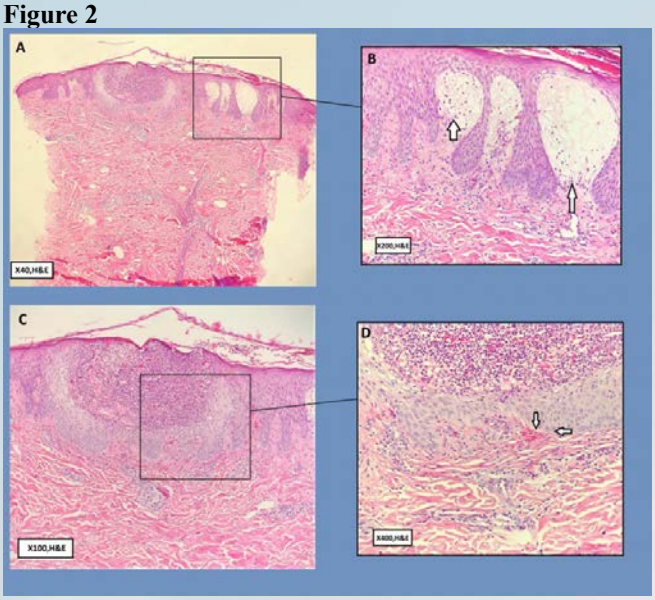
Keywords: COVİD-19,AGEP,Favipravir

Figure 1



Pustular lesions on an erythematous base and placed on his trunk other parts of body

Figure 2



Resim: A) X40,H&E;Subcorneal pustul and papillary edema B) X200,H&E; papillary edama and mild spongiosis in the epidermis C) X100,H&E;Subcorneal pustul D) X400,H&E;Eritrosit extravasaciation nearby subcorneal pustul,epitelyal neutrophils,a few eosinophils

PP-10 [Autoimmune Bullous Diseases]

Mask-İnduced Koebner Phenomenon: Persistent Pemphigus Vegetans On The Nose

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Pemphigus vegetans is a variant of pemphigus vulgaris; a group of autoimmune blistering disordes characterized by acantholysis. Pemphigus vegetans is typically characterized by vegetating plaques mostly affecting intertriginous areas, scalp and face. Koebner phenomenon, namely isomorphic response, which is defined as the development of new skin lesions of a pre-existing skin disease following trauma is infrequently described in pemphigus.

Herein, we present a case of 56 year old man with pemphigus vegetans who developed new lesions on his nose following the continuous mask wearing due to coronavirus disease-2019 (COVID-19) pandemic. The patient had a history of 3 years pemfigus vegetans. The disease activity had been under control by different choices of therapies that included methylprednisolone 60 mg/day and rituximab. Last infusion of rituximab was administered on 17 February 2020 and methylprednisolone dose was gradually reduced and cessated, The patient had no lesions afterwards. However, a short while after the COVID-19 pandemic and the necessity to wear a mask, the patient referred to our dermatology outpatient clinic with new lesions on his nasal dorsum where the mask irritated the most. At first examination, he had vegetating erythematous plaque on his nasal dorsum with crusts and he had no other skin lesion on another part of his body. He was administered oral tetracycline and niacin with topical clobetasol propionate and called for examination two months later. But, there was no improvement of the skin lesion in the second examination. Furthermore, the lesion was enlarged and there were thick, adherent crusts on it. Therefore, previous treatments were discontinued and oral methylprednisolone 16 mg/day and topical mupirocin was administered by reminding the measures to be taken for COVID-19. At the third examination which was one month later, due to persistence of the lesion, oral methylprednisolone dose was increased to 32 mg/day and azathioprine 100 mg/day was added with topical clobetasol propionate and fusidic acid. Two weeks later, the lesion showed a little improvement. Thus, azathioprine 100 mg/day and topical treatments were continued and oral methylprednisolone dose was gradually reduced to 8 mg/day. COVID-19 pandemic has affected individuals lives in many ways not only with the disease itself but also with the necessities that came with it such as continuous wearing of masks. Even though Koebner phenomenon is rare in pemphigus, it was seen in this patient in consequence of regular mask use.

Keywords: pemphigus, koebner, covid-19

PP-11 [Inflammatory Skin Diseases]

A Rare Condition: Caucasian Patient with Pityriasis Rotunda

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INTRODUCTION & OBJECTIVES: Pityriasis rotunda is a rare acquired condition and a keratinization disorder which presents with perfectly sharped, scaly, brownish, round patches usually occur on the buttocks, thighs, trunk, upper and lower extremities. The etiology of pityriasis rotunda is not certain but it thought to be a variant of ichthyosis vulgaris and diagnosis is usually based on clinical examination. Pityriasis rotunda is commonly seen in black race with no sex predilection. There are two types of pityriasis rotunda has defined. Type 1 is the most common type, seen mostly in black race, patients older than age 60, less than 30 lesions and mostly associated with malignancies (especially with solid organ malignancies), systemic diseases (most commonly liver disease, female genital tract diseases and malnutrition), and chronic infections (most commonly tuberculosis). Type 2 is rare in addition commonly seen in ages younger than 40. It usually presents with more than 30 lesions and can be familial in some cases. Type 2 is not associated with internal diseases or malignancies. In this report, we represent a rare case of pityriasis rotunda in a Caucasian patient.

MATERIALS & METHODS: Nineteen year-old male patient had non other systemic disorders with pityriasis rotunda is presented.

RESULTS: Nineteen year-old male patient presented with two weeks history of brownish, scaly round patches on his thigh. He had no history of any medical conditions or drug use. He did not have relevant family medical history or any previous skin disease. Dermatological examination revealed 36 hyperpigmented well-defined perfectly circular patches 5 to 20 mm in diameter on left thigh. Dermoscopic examination showed an erythematous hyperpigmented macules surrounded with peripheral scaling. Mycological examination was negative for fungal infections. Skin biopsy was performed. Histopathology of lesion had superficial hyperkeratosis, perifollicular parakeratosis, diminished granular cell layer, epidermal acanthosis and perivascular inflammatory cell infiltration in dermis. The patient is diagnosed with pityriasis rotunda and topical oinment with 10% urea is given.

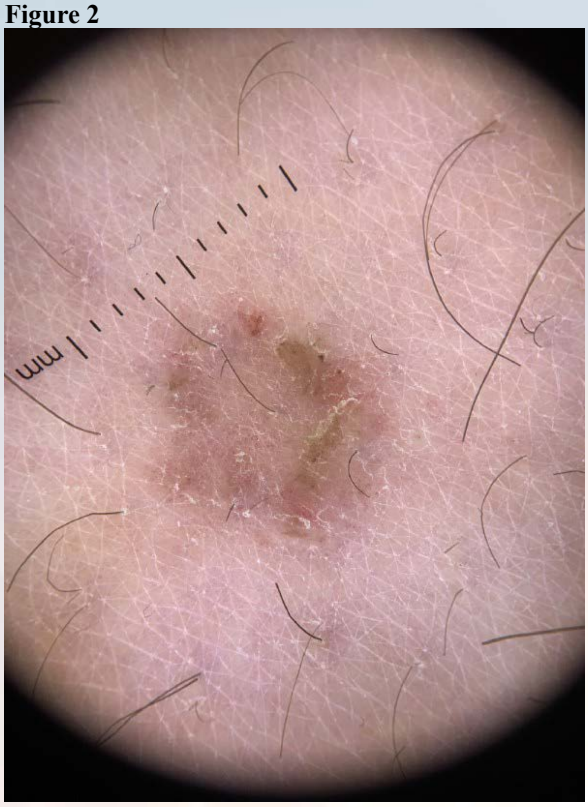
CONCLUSIONS: Pityriasis rotunda is a rare skin disorder may be difficult to diagnose. It seems further rare in white race and could be a diagnostic dilemma. In differential diagnosis hereditary or acquired ichthyosis, nummular dermatitis, mycosis fungoides, tinea corporis, erythrasma, leprosy and pityriasis alba can be assumed. For work-up, examining scales with using potassium hydroxide,Wood's lamp examination and performing a skin biopsy is required for definitive diagnosis and exclude other diseases mentioned in differentials. If history and physical examination is suggestive for any systemic disease or malignancy, laboratory test should be extended. The prognosis for pityriasis rotunda is good and lesions are not associated with morbidity and mortality by oneself.

Keywords: pityriasis rotunda, caucasion, dermatopathology

Figure 1

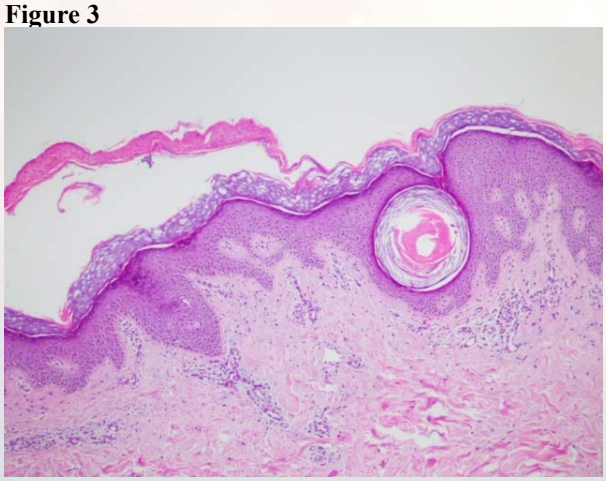
Hyperpgimented, peripherally scaled macules on lower extremity

Figure 2



Dermoscopic examination shows central hyperpigmentation with pinpoint vessels surrounded by scales and crusts

Figure 3



Superficial hyperkeratosis, parakeratosis located in periphery of a hair follicle, mild acanthosis, loss of granular layer in some areas. Some hair follicles are dilated and plugged. Dermal perivascular chronic inflammatory cell infiltration is noted.

PP-12 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

Rheumatoid Nodule: Is It Due To Medication Or Disease

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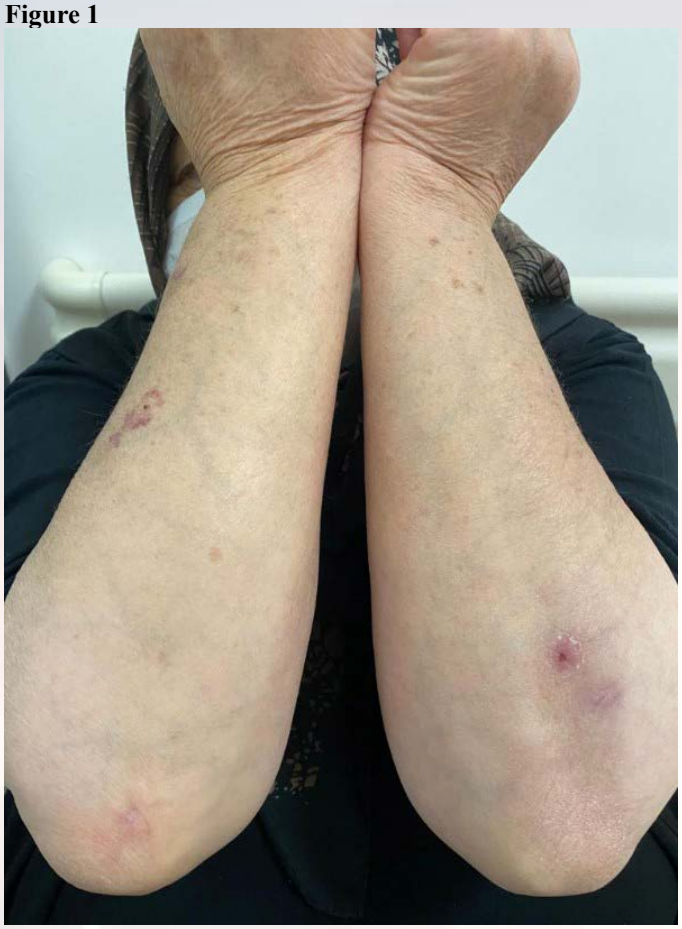
INTRODUCTION: Rheumatoid nodules(RNs) are the most common extra-articular manifestation of rheumatoid arthritis. Rheumatoid factor(RF) is positive in most patients with rheumatoid nodules. Nodules are nontender and seen on extensor surfaces such as the olecranon and dorsal part of the hand, and areas of pressure or repetitive trauma. Nodules can be seen in lungs, pleura, pericardium, tendons, synovial, bones. The differential diagnosis of rheumatoid nodules contains chronic gouty tophi, rheumatic fever nodules, the subcutaneous nodules found in SLE, nodular or keloidal scleroderma, and the nodules seen in necrobiosis lipoidica and granuloma annulare. A 63 year-old femalepatient was admitted to our polyclinic having had the nodules 2 cm and they are firm, nontender, moveable in subcutaneous space. It was learned that the patient had been treated for rheumatoid arthritis. To the best of our knowledge, RNs is important as a clue to dermatologists in the early diagnosis of Rheumatoid Arthritis(RA).

METHODS AND RESULTS: A 63-year-old female patient was admitted to our polyclinic having presented with a firm, non-tender, inflamed, red swelling.1 month of redness in both elbows and İnflammatory dİscharge ın the left elbow. She had RA and hypertensıon use methotrexate, methylprednisolone, hydroxychloroquine. In the dermatological examination, a firm, nontender, moveable nodules on the olecranon(Figure 1).Histopathologically; Fibrin deposition and necrobiosis is often seen in center of nodule surrounded by well developed palisading of CD68(+) histiocytes, vascular granulation tissue, lymphocytes were observed (Figure 2a,b,c).Differential diagnosis were panniculitis,pilomatriccoma,sarcoidosis,lupus tumidus,mycosis fungoides-like panniculitis.The patient was diagnosed RNs with clinical and histopathological findings. Topical clobetasol is planned until the biopsy is completed.We recommended RA treatment and nodule excision to the patient.

DISCUSSION: Classical RNs occur in about 20- 25% of seropositive RA patients and are the most common extra-articular manifestation of RA. Rheumatoid nodules are painful and can cause infection.Rheumatoid nodules are an indication that extra-articular symptoms will be more severe. Most RNs are localized for the elbows and fingers. It has been observed that drugs such as methotrexate, azathioprine, cyclosporine A increase the risk of developing rheumatoid nodules. In our case, rheumatoid nodule occurred five years after the disease. It is not possible to reveal whether the rheumatoid nodule is due to extraarticular activation of the disease or to DMARDs. The rheumatoid nodule is self-limited and controlled with nonsteroidal anti-inflammatory drugs.The effectiveness of hydroxychloroquine and anti-RA drugs has been demonstrated. Excision is considered if joint movement is restricted. In our study, we wanted to emphasize that rheumatoid nodules should be considered in the differential diagnosis of diseases with cutaneous nodules.

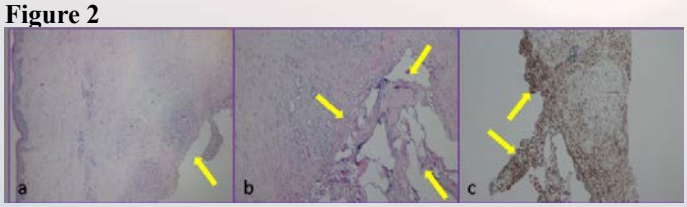
Keywords: Rheumatoid Arthritis, Rheumatoid Nodule, Cutaneous nodules

Figure 1



firm, nontender, moveable nodules on the olecranons

Figure 2



a) x20 H&E Rheumatoid nodules in deep reticular dermis.
b) x 40 H&E. Rheumatoid nodules in deep reticular dermis
c) X40 CD-68. Histiocytic marker. Positive in palisading of histiocytes.

PP-14 [Autoimmune Connective Tissue Disorders]

A case of dermatomyositis associated with breast cancer

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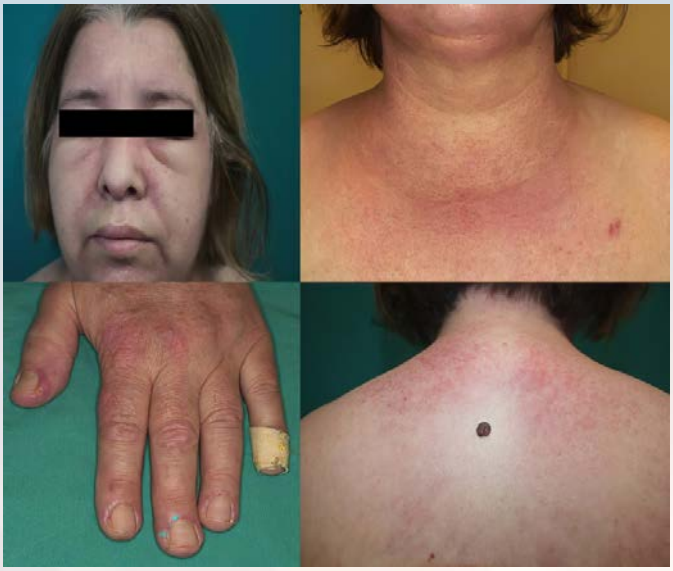
INTRODUCTION: Dermatomyositis (DM) is an idiopathic inflammatory myopathy characterized by proximal muscle weakness, rash, and other systemic manifestations. It is associated with malignancy in 3% to 60% of cases. Cancers that are more strongly associated with DM are lung, ovarian, pancreatic, gastric, colorectal cancers and non-Hodgkin's lymphoma. Breast cancer, the most frequent malignancy diagnosed in women, may rarely be associated with DM. Here we report a cases of DM associated with breast cancer.

CASE: A 50-year-old woman was admitted to our clinic with complaints of swelling around the eyes and gradually increasing weakness in her arms. Her complaints had been present for a month and she had applied to the emergency room several times. In dermatological examination, bilateral periorbital edema, erythema on the face, upper back, and the chest "V" region, violaceous plaques on the dorsal metacarpophalangeal and proximal interphalangeal joints, periungual erythema and cuticular overgrowth were present (Figure 1). Other system examination revealed mild weakness in the proximal upper extremities and a 2x2 cm palpable firm mass over the right breast. Laboratory investigations showed sedimentation rate: 60 mm/hr, C-reactive protein:48 mg/L, creatin kinase: 1980, ANA 1:160 (+). Skin biopsy taken from the chest was consistent with interface dermatitis. Elongated capillaries and hemorrhagic spots were observed on the dermoscopic examination of the periungual tissue (Figure 2). Electromyography showed myopathic changes in both proximal superior limbs. Breast ultrasonography revealed a 2x2,5-cm, irregularly-shaped nodule in the right breast. A needle biopsy was performed and pathological diagnosis was ductal carcinoma. With these findings, the patient was diagnosed with DM associated with breast cancer and was referred to medical oncology and general surgery department for treatment.

CONCLUSION: DM is an idiopathic inflammatory myopathy that is characterized by distinct skin lesions. Patients with DM have a high incidence of malignancy. All patients newly diagnosed with DM should be evaluated for the possibility of an underlying malignancy. A comprehensive history and physical examination along with the appropriate investigations should be done.

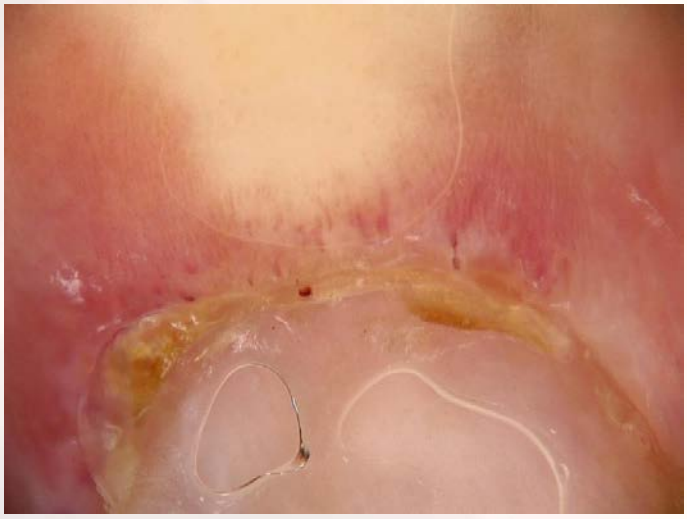
Keywords: dermatomyositis, breast cancer, paraneoplastic syndrome

Figure 1



The clinical pictures of the patient

Figure 2



Dermoscopy of the periungual tissue showed elongated capillaries and hemorrhagic spots

PP-15 [Cutaneous Oncology]

Sister mary joseph nodule: a case report

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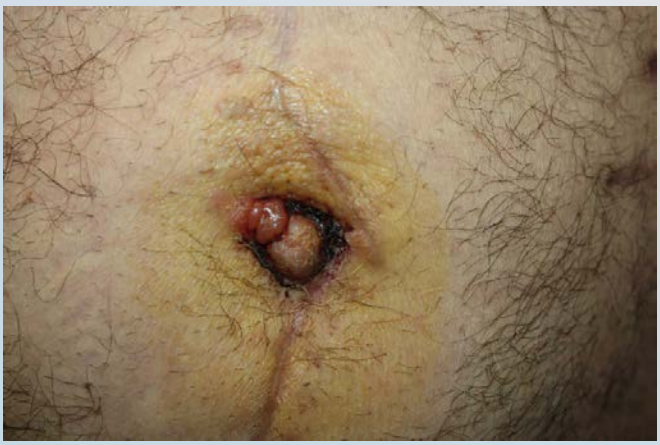
INTRODUCTION: Sister Mary Joseph Nodule (SMJN) is a metastatic umbilical lesion secondary to a primary malignancy of any viscera, stomach and colon. In approximately 50% of cases, the SMJN is associated with gastrointestinal malignancies. It is not only shows the presence of visceral malignancy but also reveals the poor prognosis of these malignancies. Here, we present a 53-year-old male patient who presented with an umbilical nodule and was subsequently diagnosed with SMJN (umbilical metastasis) associated with gastric signet ring cell-type adenocarcinoma.

CASE: A 53-year-old male patient was referred to dermatology outpatient clinic for evaluation of an umbilical lesion. It was learned that he had a total gastrectomy 5 years ago due to stomach cancer and then had received chemotherapy. Dermatology examination revealed a painless, firm nodule with a diameter of 1.5 cm in the umbilicus (Figure 1). The lesion had first appeared a month ago and had enlarged gradually. Laboratory examination showed a normocytic anemia (Hb: 10 g/dl, Htc: 28.7%). All other blood chemistry tests were within in the normal range. His mother's father had died of gastric cancer. A skin biopsy was performed from the umbilical nodule and histopathology was compatible with signet ring cell-type adenocarcinoma (Figure 2). The patient was referred to the oncology department for further management.

CONCLUSION: We find it appropriate to present a case of SMJN associated with gastric signet ring cell-type adenocarcinoma because of its rarity.

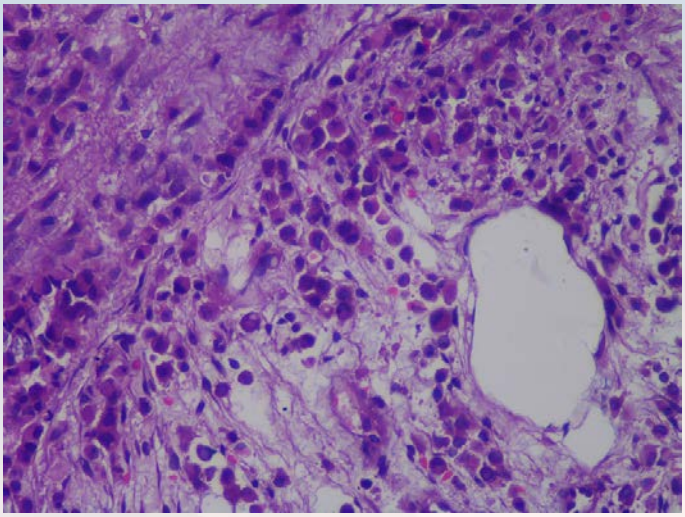
Keywords: sister mary joseph nodule, gastric cancer, signet ring cell carcinoma, cutaneous metastasis

Figure 1



The umbilical nodule

Figure 2



Histopathology revealed signet ring and plasmacytoid cells.

PP-16 [Nail Disorders/Diseases]

Periungual basal cell carcinoma: a case report

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INTRODUCTION: Basal cell carcinoma (BCC) is the most common skin cancer and is commonly localized on sun-exposed areas such as head, neck and hands. Here we report a case of BCC occuring in the periungual region which has been described rarely in the literature.

MATERIAL AND METHODS: A 90-year-old man presented with a nonhealing wound on the thumb for 6 years. The patient had worked as a construction worker in the past and he had a history of hitting his hand with a hammer several times. Dermatological examination revealed a 10 x 10 mm in size erythematous hemorrhagic ulcerated asymptomatic nodule on the periungual region of left thumb. His medical history included prostatectomy, bladder stone and an eye region tumor of which the name is unknown by the patient, excised 30 years ago. He had no known history of arsenic and X-rays exposure, and his family history was unremarkable for BCC. Our preliminary diagnosis was squamous cell carcinoma. A punch biopsy was performed and resulted as BCC. Standard excision was performed. Surgical wound was left secondary healing. Cosmetic and functional result was excellent.

DISCUSSION / CONCLUSION: BCC occurs on the hand only 0.37-2% of all cases. Nail unit BCC has only been reported in approximately 30 cases in the literature. The average age of the cases is about 65 year. The fact that BCC is extremely rare in the nail unit although it is an area exposed to sunlight, has been explained as that other etiological factors such as trauma, arsenic and radiation exposure may have a role in the development of

the disease. The lesions can be seen as onycholysis, longitudinal melanonychia and periungual ulcerations. Periungual BCC may be often confused with other diseases such as chronic paronychia, herpes simplex, pyogenic granuloma, eczema, dermatophyte or bacterial infections, squamous cell carcinoma, amelanotic melanoma. In the treatment of the lesions, the most widely used method with low relapse rate is Mohs micrographic surgery and the next one is standard excision. Other treatments are the use of topical imiquimod, radiation therapy, topical 5-fluorouracil, intralesional interferon, electrodesiccation, curettage and cyrosurgery. Our patient had a history of trauma which can be the etiological factor of his lesion. Our case presented clinically with ulceration like other periungual BBCs reported in the literature. BCC was not among our prediagnoses due to its atypical localization and clinical characteristics. After histopathological diagnosis, standard excision was performed with clear surgical margins. An excellent result was obtained with secondary healing. BCC should be kept in mind in the differential diagnosis of ulcerated lesions located around the nail. Such lesions should not be treated empirically without a histopathological diagnosis. Early diagnosis and appropriate treatment of lesions are important in preserving the function of the fingers of patients.

Keywords: basal cell carcinoma, nail unit, unusual site

PP-17 [Cutaneous Oncology]

Generalized Mucocutaneous Involvement of Kaposi Sarcoma in a HIV-Positive Patient

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Kaposi sarcoma(KS) is usually a slow growing angioproliferative spindle cell tumor derived from enndothelial and immune cells infected by Human herpes virus (HHV)-8.Kaposi sarcoma was classified into 4 different types according to etiology including the AIDS-related (epidemic), iatrogenic (immunosuppressant therapy related). Although all types of KS have in common infection with HHV-8, each has a distinct clinical course.

Herein we want to present a 57-year old patient presented to our out-patient clinic with the chief complaint of dysphagia and weight loss due to large tumours covering the gingiva, buccal mucosa and the hard palate, physical examination revealed multiple violaceous tumours on his face and neck, he had remarkably large tumours located on his upper and lower eyelids, large plaques covering his body and upper extremities, his trunk and large nodular lesions on the face, upper and lower eyelids and the neck. In the buccal mucosa he had multiple large tumours biggest measuring up to 3*1,5cm in size. The patient's history previously revealed the tumours appearing 2 years before the patients presentation, but the patient didn't seek any medical care. Viral serology, biopsy and PET-CT scan was performed for diagnosis and staging. The viral serology resulted in positive anti-HIV and HIV RNA confirming. CBCs revealed a CD4+ count of 232/mm3 confirming the diagnosis of AIDS. Biopsies taken from the tumors showed an increase of spindle cells accompanied by cells with mild to complete nuclear atypia, classic sieve-like pattern and HHV-8 positivity. Meanwhile the PET-CT scan revealed disseminated pulmonary and gastrointestinal involvement. The patient was followed up in the intensive care unit and immediately treated with HAART and single agent chemotherapy (liposomal doxorubicin).

The presentation of KS ranges from minimal mucocutaneous disease to extensive organ involvement. A surge in KS cases was noted just prior to the identification of the AIDS epidemic in the early 1980s. AIDS-related KS is the most common KS presentation in the United States. Estimates indicate that the risk of KS in people living with HIV from 2009-2012 was 500-fold higher than for the US general population. KS accounts for 12% of cancers in people living with HIV, with 765 to 910 new cases per year in the US. The AIDS related Kaposi sarcoma is known to have a more aggressive course and patients diagnosed in late stages are related to high mortality and morbidity. We want to present this case to remind the importance of the early diagnosis and treatment of HIV related Kaposi sarcoma with its aggressive and poor course.In these patients all mucosal surfaces should be examined.

Keywords: dermatology, dermato-oncology, HHV-8, HIV, Kaposi sarcoma

Figure 1

PP-18 [Inherited Skin Diseases]

A Rare Case of Pachyonychia Congenita in a 19-month-old boy

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I. INTRODUCTION

Pachyonychia congenita (PC) is one of the rare autosomal dominant disorders of keratinisation caused by a mutation in the genes encoding keratin. Mutant keratin gene is also defining phenotypic features of the disease. Affected areas included nail bed, oral mucosa, teeth pilosebaceus unit and palmoplantar skin. The main presentation of the disease is including toenail dystrophy, focal keratoderma and plantar pain but also presents with hyperhidrosis, oral leukokeratosis, follicular hyperkeratosis, hoarseness, and palmoplantar keratoderma. Here, we present a case of Pachyonychia congenita who applied mainly with nail findings and diagnosed both physical examination and genetic testing.

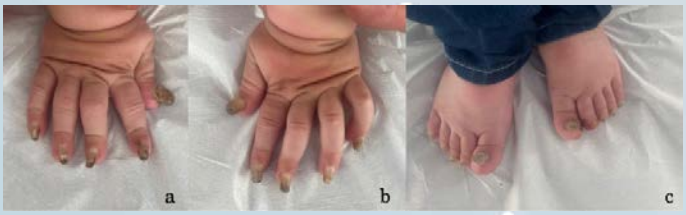
2. CASE REPORT

A 19 month--old boy was referred to our department because of the onset and progression of nail deformity and difficult to trim. (Figure 1) Nail deformity had been since birth. He had no family history. In pyhsical examination, he had hyperkeratotic and discolorated nails all of the digits. He had also follicular hyperkeratotic papules both on his knees, anguler cheilitis and pink-to-red, patch with irregular borders located on the occipital area thought as nevus flammeus. (Figure 2-3) With these findings we thought it was the one of the keratinisation disorders with sporadic mutation. The diagnosis of Pachyonychia congenita was made in consideration of the clinical examination and genetic tests. He consultated to otorhinolaryngology for laryngeal involvement and genetic department about to type the mutation. Application of emollient with urea was recommended considering the age of the patient.

The aim of this case report to underline the importance of the dermatological examination. Patient presenting with nail findings should have a detailed physical examination and pachyonychia congenita should be kept in mind in differantial diagnosis.

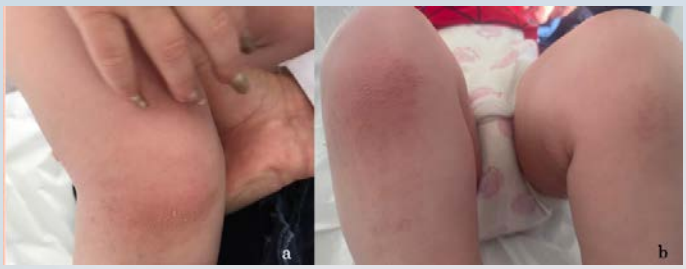
Keywords: pachyonychia congenita, nail dystrophy, genodermatoses, keratinisation disorders.

Figure 1



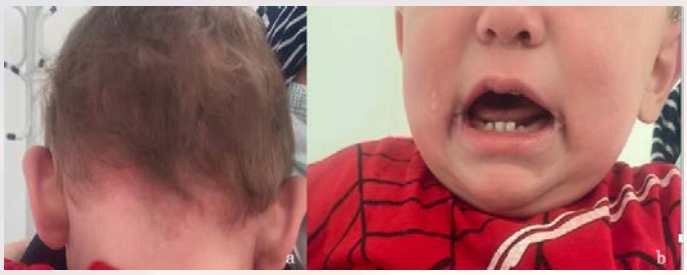
Hypertrophic nail distrophy on both hands (a) and foot (b) digits.

Figure 2



bilateral hyperkeratotic follicular papules on knees

Figure 3



Nevus flammeus (a) and anguler cheilits (b)

PP-19 [Dermatopathology]

A case of discoid lupus erythematosus: Widespread erythematous involvement of the face

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A 57-year-old female patient was admitted to the dermatology outpatient department with the complaint of crusting and redness on her nose, cheeks and forehead that started 3 months ago. In her medical history she had NSAID medication for joint pain. Dermatological examination revealed the erythematous, scaly plaques over the face, nose and accompanied by scarring and hypopigmentation.

Histopathologic findings show mild hyperkeratosis with follicular plugging, atrophic epidermis, thickening and tortuosity of the basement membrane, hydropic degeneration of basal cells, dermal perifollicular and periappendicular lymphocytic inflammatory infiltrate, intersititial mucin deposition, edema, extravasation of erythrocytes and lymphoplasmacytic infiltrates surround ecrine coils in the deep dermis. İnterstitial mucin deposits are present in the adjacent stroma among collogen bundles. Diagnosis: Discoid lupus erythematosus(DLE)

DISCUSSION: DLE is a dermatosis that is localized in 80% of patients and occurs mainly on sun-exposed areas of the skin, such as the scalp, face, and ears. In 20% of cases it occurs on the extremities and upper trunk (1) The lesions are typically scaly, erythematous macules or papules and are found on sun-exposed skin areas, including the face, scalp and neck. A case report eyelid lesions occur in only 6% of cutaneous LE cases,and isolated eyelid involvement is an extremely unusual

presentation; case typifies the frequent delay in diagnosing DLE due to its nonspecific clinical presentation in unusual anatomical sites.(2) Due to its autoimmune etiology, women are affected more than men, and it can affect any age group, although it is more common in individuals between the ages of 20 and 40 (3). DLE is a common type of cutaneous lupus that is chronic and is typically associated with atrophy and scarring of the skin. The primary discoid lesion is a discrete erythematous papule or plaque with adherent scaling, follicular plugging, atrophic scarring, central hypopigmentation, and hyperpigmented borders. Direct immunofluorescence (DIF) of lesions shows granular deposits of immunoglobulin G at the dermal-epidermal junction. DIF should be used as a confirmative, not as a necessary criterion for DLE diagnosis (4,5).

Keywords: Discoid lupus erythematosus,mucin,immunoglobulin G

PP-20 [Adverse Drug Reactions, TEN]

Nicolau Syndrome Following Subcutaneous Glatiramer Acetate Injection

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INTRODUCTION: Nicolau syndrome (embolia cutis medicamentosa) is a rare iatrogenic complication of injectable medications usually after intramuscular injection that can lead to skin necrosis. Herein we report a case of a 34-year-old woman with a history of tenderness, local heat sensation, and redness on umbilical region who was diagnosed with Nicolau syndrome following subcutaneous glatiramer acetate injection.

CASE PRESENTATION: A 34-year-old woman presented with painful discoloration over her abdominal skin. She had been on treatment with subcutaneous glatiramer acetate injections thrice weekly for multiple sclerosis for 18 months. Shortly after the last injection, she described tenderness, local heat sensation, and redness around the injection site. On the second day, the lesion had expanded with some purple blotches. When the patient was admitted to our centre on the third day, we observed a large, tender, and erythematous patch with bizarre livedoid purpuric areas on the left side of the umbilical region (Figure 1). Laboratory analyses revealed complete blood count, liver and renal function tests, inflammatory markers, and coagulation parameters were within normal limits except elevated serum creatine kinase level (714 U/L; normal range: 24-170). Superficial ultrasonography showed dermal oedema without any collection of fluid. After performing a skin biopsy, topical betamethasone valerate cream and mucopolysaccharide polysulfate cream twice daily were recommended. Histopathological examination of the lesion showed marked epidermal ischemia, necrotic keratinocytes, fibrin deposits within multiple capillaries, and no remarkable inflammation (Figure 2). Clinical and histopathological findings were consistent with Nicalou syndrome (embolia cutis medicamentosa). After 15 days of treatment, the lesion completely regressed with only minimal hypopigmented irregular scarring (Figure 3). Besides, serum creatine kinase level reduced to normal limits (76 U/L).

CONCLUSION: Nicolau syndrome is a rare drug adverse reaction that may emerge out following subcutaneous glatiramer acetate injection although the patient is on a long-lasting treatment.

Keywords: Nicalou syndrome, embolia cutis medicamentosa, glatiramer acetate, intramuscular injection

PP-21 [Angiology, Haemangiomas, Vascular Malformations, Vasculitis]

Cavernous hemangioma of the foot: A case report

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INTRODUCTION: Cavernous hemangiomas are benign vascular tumors. Cavernous hemangioma. It is most often seen at birth or infancy. The incidence of these tumors in the extremities varies from 4.9% to 28.5%. The pathogenesis of cavernous hemangiomas is not certain yet. Pregnancy, infection, and trauma are associated with their formation and development. Microscopically, cavernous hemangiomas are masses of dilated, thin-walled vessels or sinuses, lined with endothelium and surrounded by a fibrous connective tissue stroma. We present a 17-years old male with cavernous hemangioma of the foot

CASE: 17- years old male patient referred to our clinic for multiple painless nodule his foot present for 4 years and no other pathological symptoms. He had no previous history of any medical illness. In his dermatological examination, there are multiple viyolese conglemerated nodules. There is no anomaly on the blood sample. An incisional biopsy from lesions were performed. The histopathological examination was reported as cavernous hemangioma.

DISCUSSION: Several classification systems have been described for hemangiomas ranging from four to nine categories, which are based on depth, clinical appearance, histology, and location. In general, there are capillary hemangiomas, cavernous hemangiomas, combined or mixed types, and diffuse or systemic hemangiomas. The occurrence of cavernous hemangiomas involving the foot is rare.

Keywords: Cavernous hemangioma, Foot, Vascular Tumor

PP-22 [Adverse Drug Reactions, TEN]

A case of erythema multiforme major in a patient with COVID 19: The role of corticosteroid treatment

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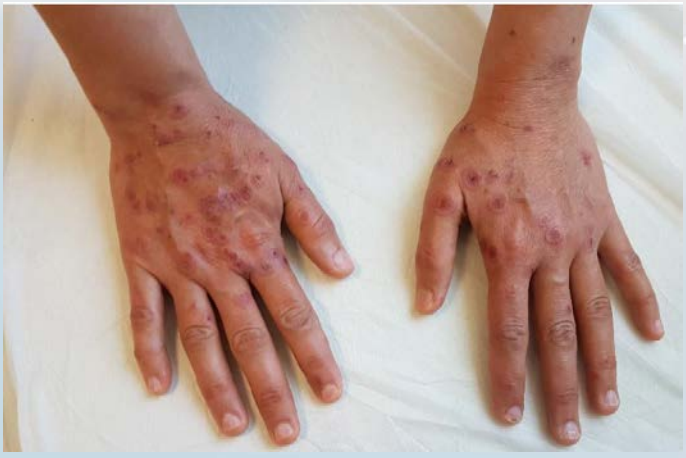
In December 2019, the cases of pneumonia of unknown etiology were reported in Wuhan city Hubei province of China. Severe acute respiratory syndrome coronavirus 2 (SARS - CoV - 2) pathogen, a novel coronavirus, was detected from the lower respiratory tract samples of infected patients, and this virus-caused respiratory tract infection was termed Coronavirus Disease 2019 (COVID - 19). The disease has been reported to show different types of cutaneous findings including urticarial, maculopapular, erythema multiforme-like, varicella-like, purpuric, livedoid, and thrombotic-ischemic lesions. Given the high mortality rate of the disease, prompt and accurate identification of the relevant skin manifestations may play a significant role in the early diagnosis and appropriate management of the entity.Here, we will present an erythema multiforme major developing in a 37-year-old female patient with COVID-19.

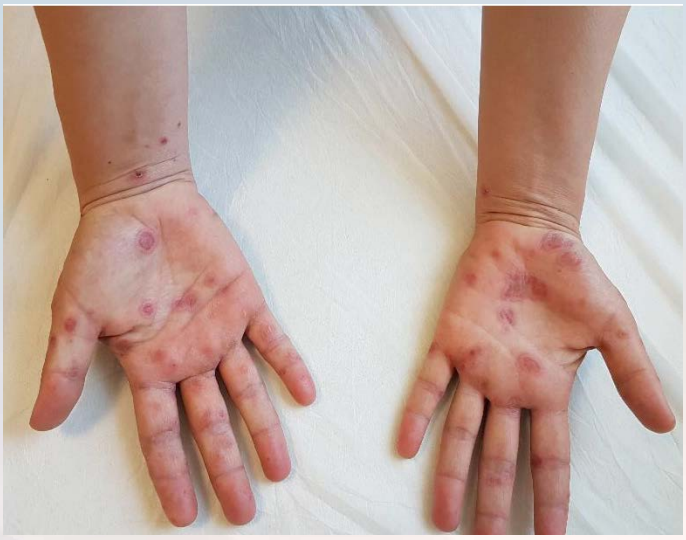
Keywords: COVID-19, Erythema multiforme major, Corticosteroid

Figure 1.



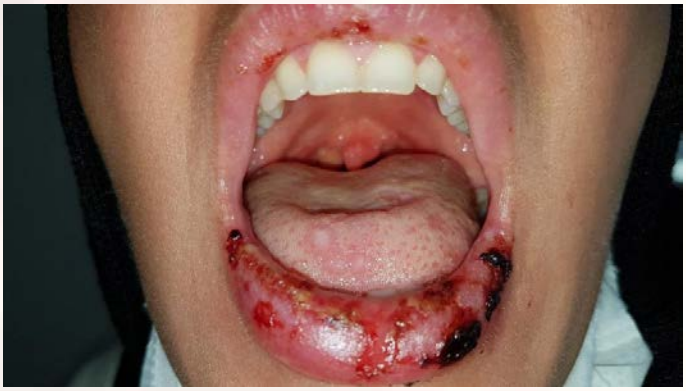
Erythematous targetoid lesions distributed over the dorsal sides of the hands.

Figure 2.



Erythematous targetoid lesions distributed over the palmar surfaces.

Figure 3.



Ulcerated lesions involved the lower lip and tongue

PP-23 [Dermatology and Internal Medicine, including Skin Manifestations of Systemic Diseases]

Superficial thrombophlebitis in a patient with COVID 19: Heparin treatment after evaluation of D – Dimer

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Coronavirus Disease 2019 (COVID-19) is a respiratory tract disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which first appeared on December 1, 2019 in Wuhan, China. The pandemic was declared by World Health Organization on March 11, 2020. The role of obstructive vasculopathy has been an essential topic of discussion in the pathogenesis of COVID-19. Endothelial damage and autoimmune mechanisms have been reported to contribute to the development of microvascular thrombosis and occlusion. Furthermore, severe COVID-19 cases have been shown to be complicated by disseminated intravascular coagulation. Here, we present a case of superficial thrombophlebitis that developed in a patient with COVID-19

Keywords: COVID-19, Superficial thrombophlebitis, Heparin, D-Dimer

PP-24 [Inflammatory Skin Diseases]

Jessner's lymphocytic infiltration as a symptom of Immune Reconstitution Inflammatory Syndrome in an HIV-infected patient: A case report

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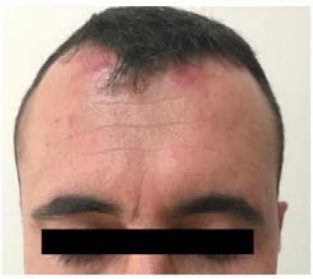
Jessner's lymphocytic infiltration is a benign, chronic, T cell infiltrative skin disease that often appears as erythematous papules or plaques on the face, neck and back. We are presenting a case which is 36-year-old male patient with HIV infection, presenting with a large number of erythematous infiltrated plaques on forehead and neck depending on immune restoration following highly active antiretroviral therapy (HAART). Inflammatory or autoimmune disease cases caused by HAART-related immune restoration are called Immune Reconstitution Inflammatory Syndrome (IRIS), and the relationship between IRIS and Jessner's lymphocytic infiltration has not been reported previously.

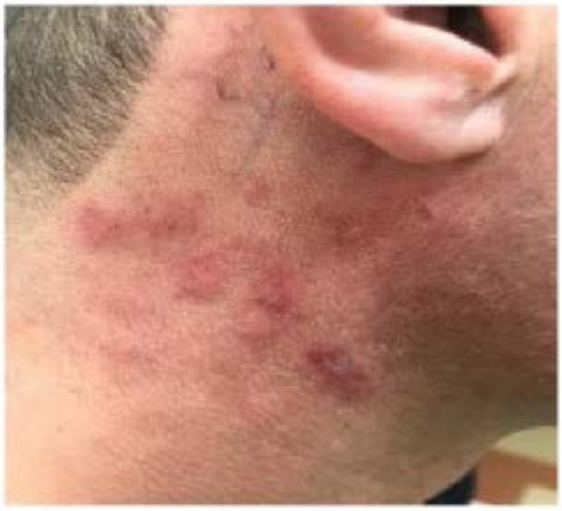
Keywords: Jessner's Lymphocytic Infiltration, Hiv, Immune Reconstitution Inflammatory Syndrome

Figure 1.



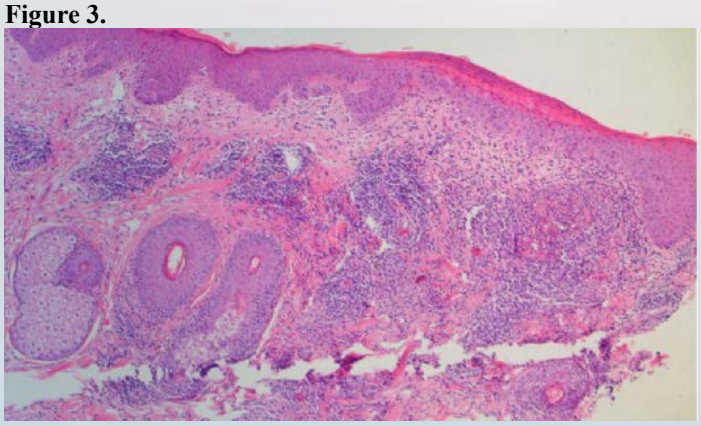
Erythematous infiltrated multiple plaques on the forehead

Figure 2.



Erythematous infiltrated multiple plaques on the neck.

Figure 3.



In the dermis, perivascular and periadnexal intensive lymphocyte infiltration (HE X 100).

PP-25 [Dermatopathology]

Refining diagnosis is the prerequisite for the correct treatment: the cytodiagnostic utility of SOX10 in the diagnosis of metastatic melanoma

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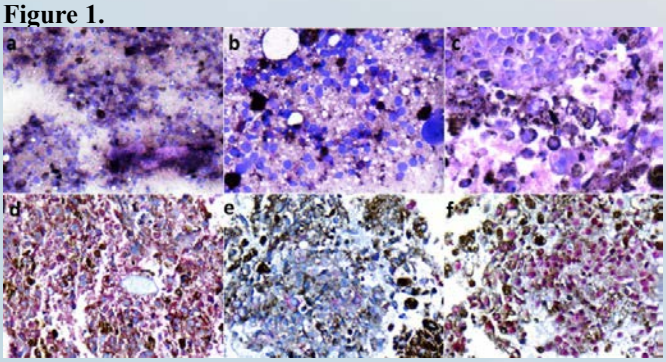
Melanoma is known to have a strong tendency to metastasize to any part of the body. It is usually not easy to made a diagnosis based only on cytological characteristics in metastatic melanoma, since melanoma can exhibit a wide variety of cytological features, imitating different types of epithelial, mesenchymal, lymphoid malignancies. Metastatic tumors may have different cytological characteristics than primary ones. Therefore, an accurate diagnosis of metastatic melanoma can be a real challenge. HMB-45, Melan-A, S-100, cytoplasmic markers for melanocytes, are frequently used immunocytochemical markers in cytology practice. However, their sensitivity has been demonstrated to be suboptimal, and their expression rates may be lower in metastatic lesions. SOX10, a nuclear marker, is considered more reliable than cytoplasmic and membranous markers. Here, we present the utility of cytodiagnostic markers such as SOX 10 in a 60-year-old male patient with metastatic melanoma.

Keywords: Metastatic melanoma, SOX10,Treatment

Figure 1.



Cytomorphological examination of the metastatic melanoma demonstrated large, pleomorphic, atypical tumor cells with brown pigments (Papanicolaou, x100; Papanicolaou, x200) (a,b), loosely cohesive, atypical epithelioid cells with multinucleation, prominent nucleoli and intranuclear inclusion (cell block; H&E stain, x200) (c), cytoplasmic HMB-45 staining in cell block (x200) (d), focal weak positivity with Melan-A (x200) (e), diffuse nuclear positivity for SOX10 (x200) (f).

PP-26 [Infectious Diseases, Parasitic Diseases, Infestations]

Eccrine chromhidrosis due to SARS-CoV-2 virus infection treated with favipiravir

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A 31-year-old otherwise healthy male was examined in dermatology outpatient clinic for abnormal palmar pigmentation for 2 days. On dermatologic examination, well-demarcated, irregularly-edged brown, hyperpigmented patches on his left palm were noted and, there was brown hyperpigmentation on the tip of the 5th finger of his right hand and on that nail bed. He had applied to the emergency department 2 weeks ago with the complaint of muscle pain and sore throat. A nasopharyngeal swab was taken for PCR (polymerase chain reaction) for SARS-CoV-2, which was positive. He had been diagnosed as COVID-19 infection without pneumonia or any other complications. He received 5 days of oral favipiravir and 10 days of subcutaneous enoxaparin treatment. Laboratory tests were normal. Wood examination was unremarkable. Exogenous pigmentation was ruled out because the patient denied the history of with any substance, dye, henna, antiseptics, etc. A 4-mm punch biopsy was taken and the patient was diagnosed as eccrine chromhidrosis and treated with topical emollient only. Five days later the lesions were markedly disappeared. A 28-year-old male admitted to the emergency department for abnormal hand pigmentation for 1 day. Due to COVID-19 infection he received the same regimen, that ended 5 days ago. Due to clinical diagnosis of eccrine chromhidrosis he was treated with topical emollient without histopathological examination. His complaints regressed completely within 3 days. Coronavirus disease is a pandemic disease caused by the SARS-CoV-2 virus, that primarily affects the respiratory tract epithelium. It has been reported that the disease is frequently seen with acral chilblain and pernio-like lesions,erythematous maculopapular rashes, viral exanthem, vesicular eruptions, urticarial eruptions and livedoid lesions. Eccrine chromhidrosis is a rare disorder characterised by the excreation of coloured sweat via the eccrine sweat glands. Although it is known that exogenous excretions of the drugs can also cause eccrine chromhidrosis, it has been shown in publications that SARS-CoV-2 spike proteins are found in eccrine cells in chilblain-like skin lesions. To the best of our knowledge there has been no previous reported cases in the literature with eccrine chromhidrosis in COVID-19 patients.

Keywords: chromhidrosis, ecrine, COVID-19, palmoplantar

PP-27 [Cutaneous Oncology]

Trichoscopic Features of Primary Cutaneous B-Cell Lymphoma

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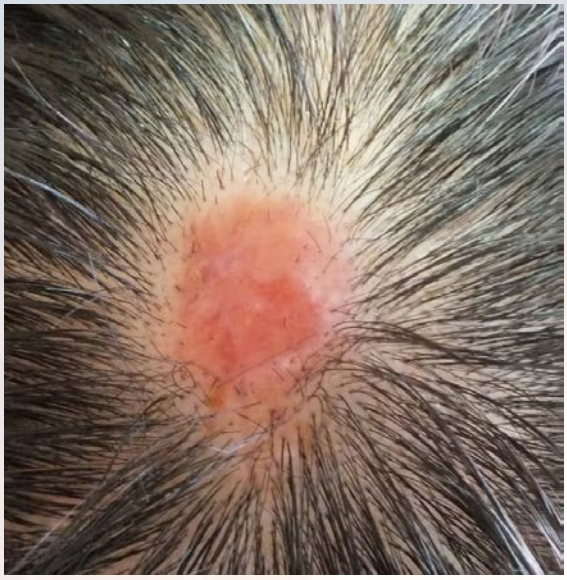
Primary Cutaneous Marginal Zone B-Cell Lymphoma (PCMZL) is very rare, malignant lymphoproliferative B-cell disorder. PCMZL mainly involves the skin and extracutaneous spread is rare. PCMZL is characterized by slowly growing infiltrated red to violaceous multifocal papules, plaques, or nodules with a predilection for trunk, arm or head. Lesions sometimes may resolve spontaneously but patients may have recurrence.

The prevalence of scalp involvement in PCMZL is unknown. To our knowledge, trichoscopic features of scalp PCMZL have not been previously reported.

A 43-year-old woman presented with a nodule on scalp for several months. Hodgkin lymphoma in the patient's sibling of family history. An incisional biopsy was performed in another center about 1 month ago, histopathological diagnosis was unknown.On physical examination, there was a endure, erythematous and painless nodule on the scalp (Fig. 1). The dermoscopic examination an organized lesion with multiple follicular plugs, that were surrounded by shiny white lines and thin, subtle arborizing and serpentine vessels on the periphery over an salmon colored background (Fig. 2). Excisional biopsy of the nodule was performed and histopathological examination showed a distinct diffuse small lymphocytic cell infiltration was detected around the perivascular and skin appendages accompanied by histiocytes, eosinophils, and a small number of multinucleer giant cells, starting from the superficial dermis to the subcutaneous adipose tissue, leaving a thin grain zone in the epidermis forehead. Neoplastic small lymphoid cells were CD19, CD20, CD23, Bcl-2-124 positive, CD10, CD30, Cyclin D1, Bcl-6, EBV negative. The patient was evaluated by the hematology department for systemic involvement. Considering the clinical and histopathological findings, the patient was diagnosed with PCMZL. In the literatures, the studies reports PCMZL cases within the head/neck area, but no clinical photographs and dermoscopy concerning specifically the scalp area were included in the manuscript. The most commonly reported dermoscopic features in other areas were branching/arborizing or serpentine vessels, scale, white lines/circles, follicular plugging, ulceration and a orange-salmon-colored background. Trichoscopic features similars to the dermoscopy of common areas of PCMZL. PCMZL presenting as solitary tumors can be confused with pseudolymphomas, amelanotic melanoma, BCC, SCC, and adnexal tumors, keloid among others. Although dermoscopic findings may improve the clinical recognition of PCMZL useful in clinical practice, these features are not sufficient for the diagnosis of PCMZL and histopathology remains mandatory. In conclusion, this report shows for the first time trichoscopic features of scalp PCMZL. The dermoscopic findings of scalp PCMZL are not specific, but these findings are important for early diagnosis of PCMZL, early detection of relapses, and rapid tumor intervention.

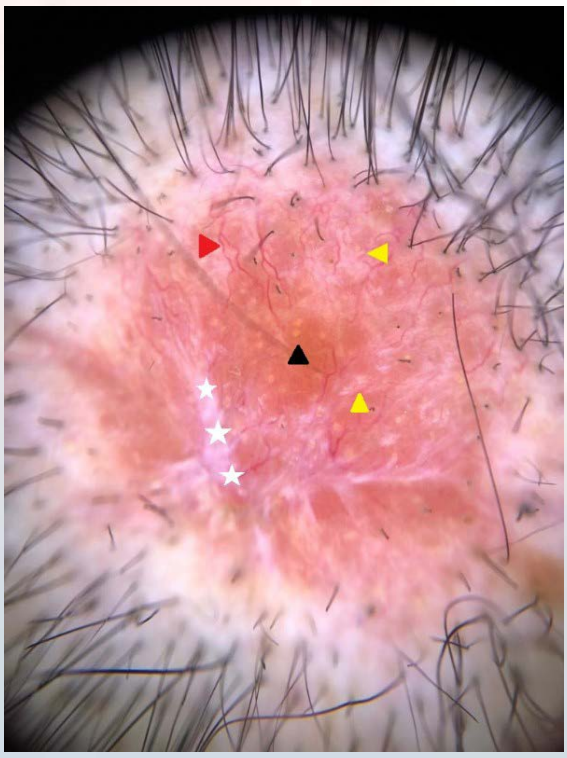
Keywords: Cutaneous, dermoscopy, lymphoma, scalp, trichoscopy

Figure 1



Asymptomatic erythematous nodule on the scalp

Figure 2



Dermoscopy of the nodule revealed an organized lesion with multiple follicular plugs (black arrow) that were surrounded by shiny white lines (yellow arrow) and thin, subtle arborizing and serpentine vessels on the periphery (red arrow) over an orange background and pink periphery (polarized light dermoscopy, original magnification ×10). The asterisk represents a previous biopsy site.

PP-28 [Dermatological Surgery]

Axillary giant lipoma opening to the skin surface: A unique presentation mimicking accessory breast

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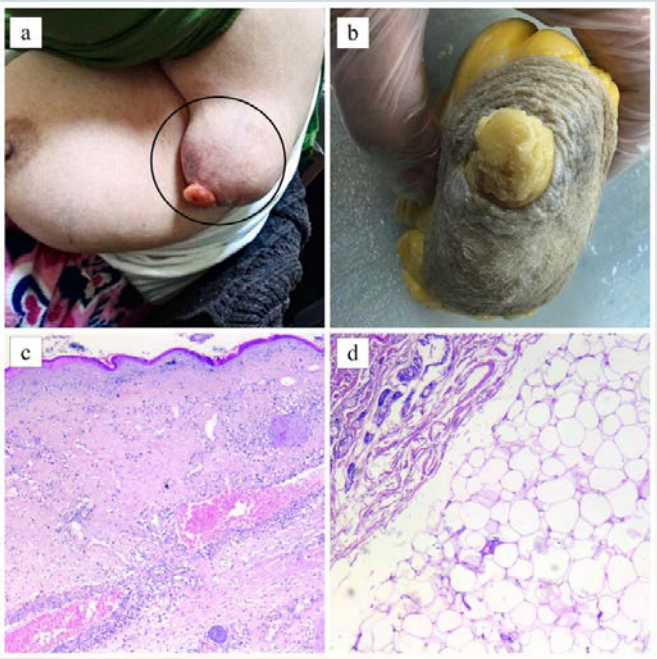
Lipomas are benign tumors of mature adipose tissue originating from subcutaneous tissue or internal organs. A total of ten patients with axillary giant lipoma has been reported in the relevant literature (Table 1). However, none of them showed spontaneous perforation. The pathogenesis of the uncontrolled growth of giant lipomas is clearly unknown. It has been suggested that rupture of the fibrous septa following trauma may cause proliferation of adipose tissue. According to another hypothesis, local inflammation related to trauma may induce differentiation of pre-adipocytes and disrupt the normal regulation of adipose tissue. We though that, in the current patient, the growth of the lesion may have been triggered by repetitive microtrauma caused by each movement of the upper limb. Prolonged pressure on the lesional area due to the patient being bedridden may have caused the overlying skin to break down and eventually rupture. Here, we present a 78-year-old female patient with a large lipoma in the left axillary region.

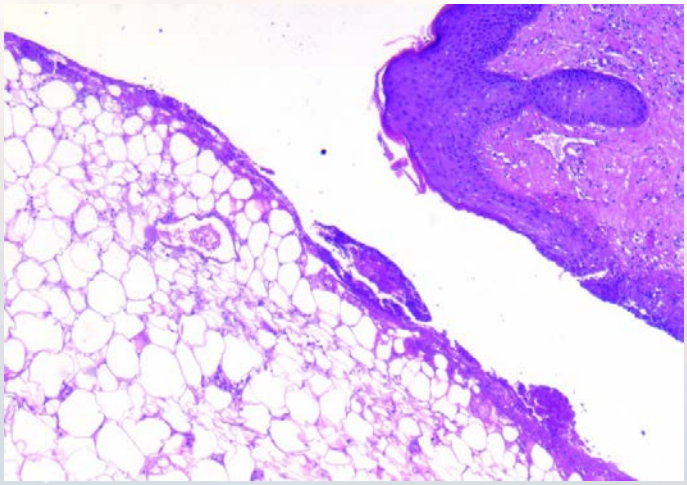
Keywords: Giant lipoma, accessory breast, histopathological examination

Figure 1.



A giant axillary mass with spontaneous rupture 11x8,5 cm in diameter, protruding from the left axillary region (a). Gross examination of the excision specimen showed an encapsulated yellow fatty tissue partially opened to the skin surface (b). H&E sections of the overlying skin showed epidermal atrophy, degenerated collagen fibers, numerous dermal dilated vascular structures and mixed inflammatory infiltration (c). H&E sections of the mass revealed mature benign adipose tissue (d).

Figure 2.



Perforated part of the lipoma with surrounding skin (H&E).

Table 1

Case	Gender	Age	Duration	Site	Treatment	Pathologic specimen size	Pathologic specimen size
1	Male	15	9 years	Left axilla	Total excision with primary closure	19x16x14 cm	None
2	Female	50	18 months	Right axilla	Total excision with primary closure	20x18x9 cm	None
3	Male	32	4 years	Right axilla	Total excision with primary closure	24x10x6 cm	Unremarkable except for dilated veins
4	Female	62	5 years	Left axilla	Total excision with primary closure	16x15x5 cm	None
5	Male	70	6 years	Right axilla	Total excision with primary closure	Unavailable	None
6	Male	47	4 months	Right axilla	Total excision with primary closure	28x24x4 cm	None
7	Female	42	2 months	Left axilla	Total excision with primary closure	10.5x8x3 cm	None
8	Male	60	5 years	Right axilla	Total excision with primary closure	15x10 cm	None
9	Male	38	9 years	Left axilla	Total excision with primary closure	32x15x6 cm	None
10	Male	18	unavailable	Left axilla	Total excision with primary closure	23x10x5 cm	None

The main features of the patients with axillary giant lipoma reported in the relevant literature

PP-29 [Autoimmune Bullous Diseases]

A case of COVID-19 in a patient with pemphigus on azathioprine: successful management with methylprednisolone

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COVID-19 is an infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that first identified December 2019. It is not considered just a respiratory disease but a multisystem disorder. Well-known risk factors for mortality and morbidity include advanced age, male gender, hypertension and immunosuppressive conditions. We present a case of COVID-19 that developed in a 36-year-old female patient who received azathioprine therapy with a diagnosis of pemphigus.

Keywords: Pemphigus, COVID-19, azathioprine, methylprednisolone

PP-30 [Autoimmune Bullous Diseases]

Case of COVID-19 in a patient with Pemphigus successfully managed with favipiravir

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Coronavirus disease 2019 (COVID-19) is a multisystemic infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has caused many social, cultural, and economic problems since declared as a pandemic by the World Health Organization and caused disruptions in health activities. The management of cutaneous diseases, including pemphigus, has also been affected from the difficulties and disruptions caused by the pandemic.Here, we present a case of COVID-19 in a patient with Pemphigus successfully managed with favipiravir.

Keywords: COVID-19, Pemphigus, Favipiravir

PP-31 [Dermoscopy]

The utility of dermatoscopy in the diagnosis of acanthosis nigricans

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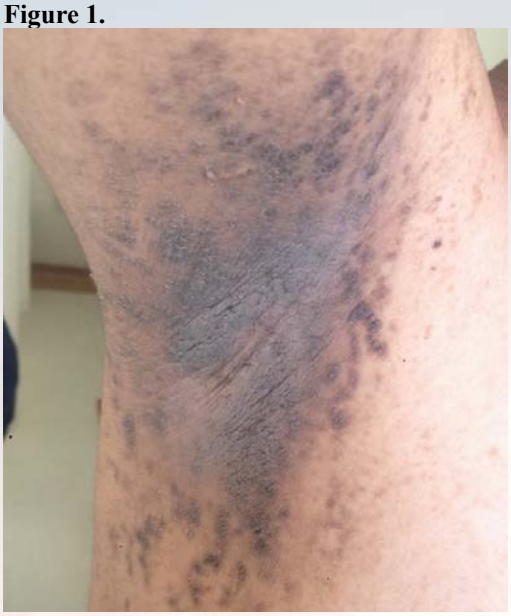
Recently, dermatoscopy has become an indispensable diagnostic tool in dermatology practice. Dermatoscopic features of many neoplastic and non-neoplastic cutaneous conditions have been well described. However, only a few studies have aimed to identify the dermatoscopic features of AN. The reported dermatoscopic features for mild to moderate AN include diffuse dark brown background, cerebriform appearance, multiple cristae, sulci, milia-like cysts hyperpigmented dots, and streaks.The pattern of multiple cristae and sulci is especially more visible in dark-skinned patients due to the contrast with unaffected dark skin. Here, we would like to briefly discuss the role of dermatoscopy as an adjunctive diagnostic tool that will facilitate the diagnosis of AN.

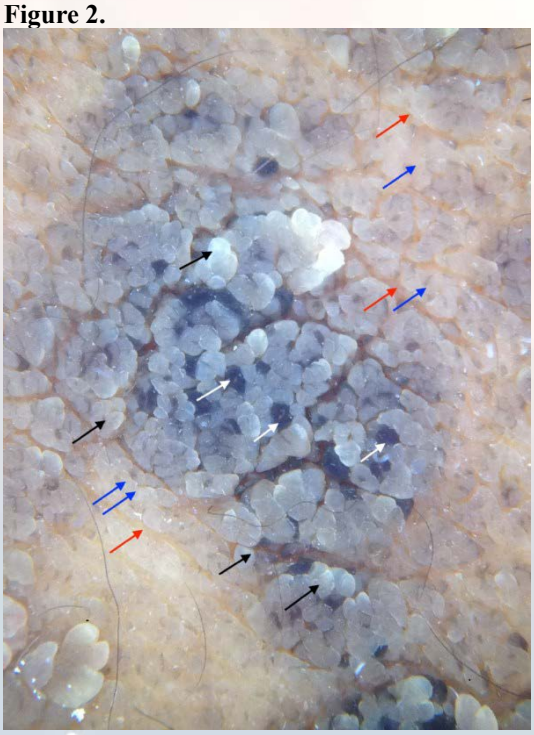
Keywords: Dermatoscopy, Acanthosis nigricans, Diagnosis

Figure 1.



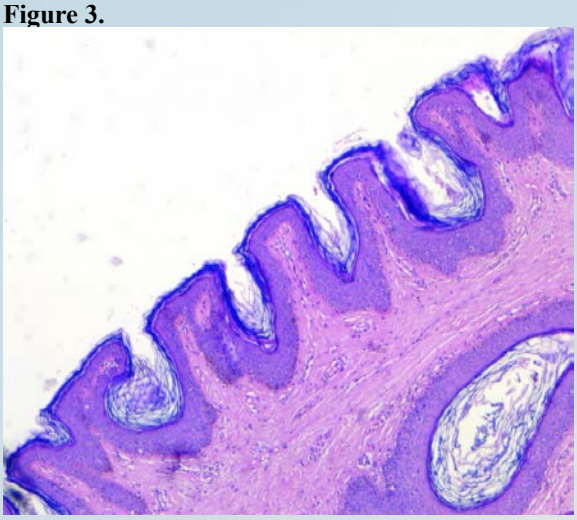
Dark, velvety papules and plaques distributed over the axillary region

Figure 2.



Dermatoscopic examination showed multiple cristae (blue arrows) and sulci (red arrows), multiple white to brown exopyhtic papillary structures (black arrows) and black blotches (white arrows).

Figure 3.



Histopathological examination showed epidermal papillomatosis, hyperkeratosis, hyperpigmentation of the basal layer, and upward finger-like projection of dermal papillae (H&E, x100)

PP-32 [Autoimmune Connective Tissue Disorders]

Dermatoscopy of subacute cutaneous lupus erythematosus

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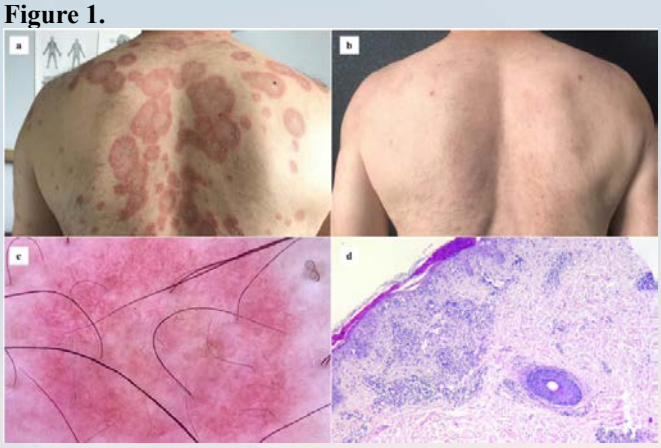
Dermatoscopic examination may provide helpful clues in differentiating SCLE from other differential diagnoses including pityriasis rosea, psoriasis, granuloma annulare, and mycosis fungoides. Pityriasis rosea generally shows peculiar peripheral collarette scales and patchy distribution of dotted vessels. Psoriasis is usually characterized by regularly distributed dotted vessels on a dull red background. Granuloma annulare displays red to yellow background with or without dotted and short linear vessels. Mycosis fungoides is characterized by spermatozoon-shaped vascular structures, short linear vessels, and orange to yellow patchy areas. Here, we present a case of subacute lupus erythematosus in a 43-year-old male patient.

Keywords: Dermatoscopy, subacute cutaneous lupus erythematosus, histopathology

Figure 1.



Confluent, scaly, and annular plaques with central clearance on the back (a). Complete clearance of the lesions following hydroxychloroquine treatment (b). Dermatoscopic examination revealed a peripheral distribution of dotted and irregular linear vessels on a reddish background (c). Histopathological examination showed basal vacuolar degeneration, and subepidermal perivascular and periadnexal lymphocytic infiltration (d).

PP-33 [Atopic Dermatitis/Eczema]

Unilateral and Flexural Pityriasis Rosea: An Atypical Presentation

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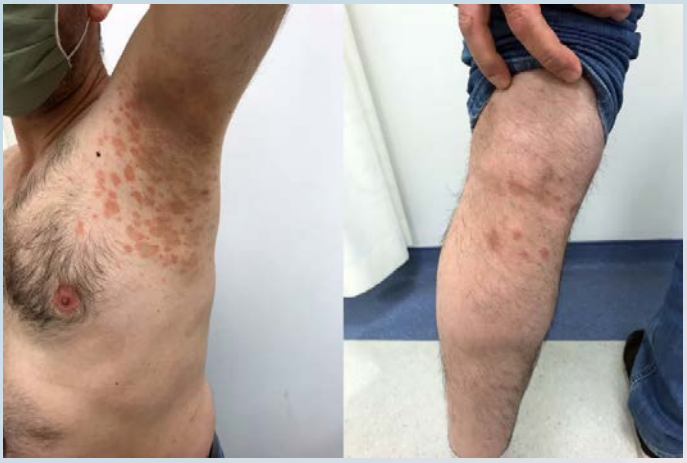
Pityriasis rosea (PR) is an acute, self-healing, papulosquamous eruption of unknown etiology. It usually presents as symmetrical, multiple, oval, scaly papules and plaques on the trunk.

A 45-years-old man was admitted to our outpatient clinic with a mild pruritic eruption which started on his left axilla 2 weeks ago. On dermatological examination there were multiple macules and patches with peripheral collarette scaling on the left axillar and popliteal fossa. The physical examination and routine laboratory tests were normal. Histopathological examination revealed parakeratosis, mild spongiosis, erythrocyte extravasation in superficial dermis and perivascular dematitis with lymphocytic infiltration. The patient was diagnosed as unilateral pityriasis rosea with flexual distribution and topical corticosteroid therapy was prescribed.

We wanted to share our patient as unilateral pityriasis rosea which also has a flexural distribution is a very rare condition.

Keywords: pityriasis rosea, unilateral, atypical, flexural

Figure 1



PP-34 [Inflammatory Skin Diseases]

Early prurigo pigmentosa: A diagnostic challenge

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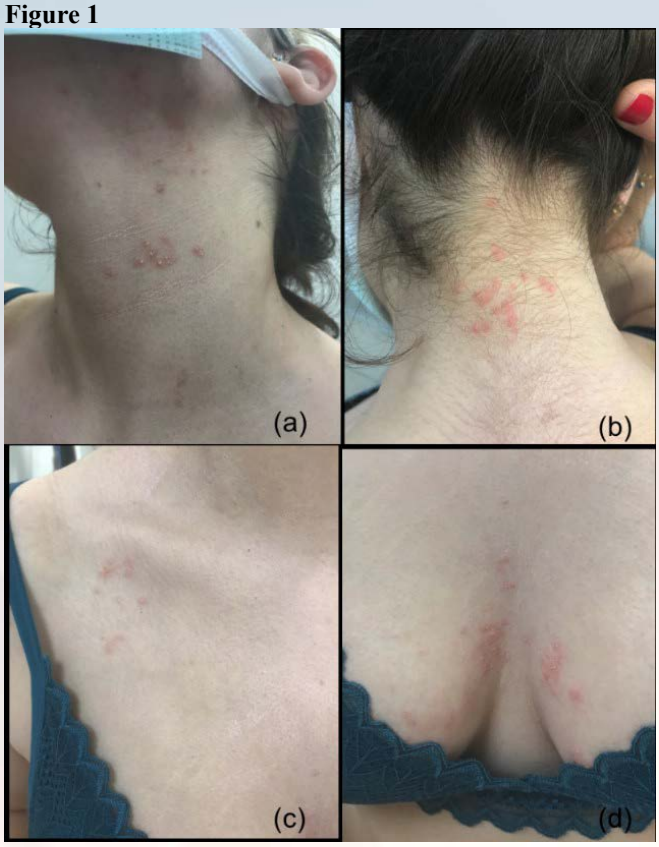
INTRODUCTION: Prurigo pigmentosa is a recurrent inflammatory skin disease with unknown etiology. Typical clinical features are reticularly arranged pruritic urticarial papules and reticular hyperpigmentation. However, early presentations may lack specific features of the disease. Here, we report a case of early prurigo pigmentosa misdiagnosed as insect bite reaction.

CASE: A 24-year-old lady presented to our outpatient clinic with a four-day history of intensely itchy eruption. She did not have any medical antecedents and denied any medication use. Dermatologic examination revealed erythematous papulovesicular lesions on the lateral neck, nape of the neck, at supraclavicular and intermammary regions (Figure 1). An insect bite reaction was suspected. The patient was prescribed topical steroid and systemic antihistamine. One week later, she presented with exacerbation of her symptoms. Papulovesicular lesions were replaced by reticularly arranged urticarial papules (Figure 2). Upon questioning, the patient reported cutting down on carbohydrates. She refused biopsy. With clinical diagnosis of prurigo pigmentosa doxycycline 100 mg BID was started. Lesions completely resolved at one week, leaving only subtle hyperpigmentation (Figure 3). At three month follow up there was no recurrence.

CONCLUSION: It is difficult to diagnose early stages of prurigo pigmentosa, especially in the lack of reticular pattern and hyperpigmentation. A change in diet should be questioned in young patients with a recent onset of pruritic eruption. As patients may refuse biopsy due to cosmetic concerns, clinicians should be familiar with typical dermatologic findings of the disease.

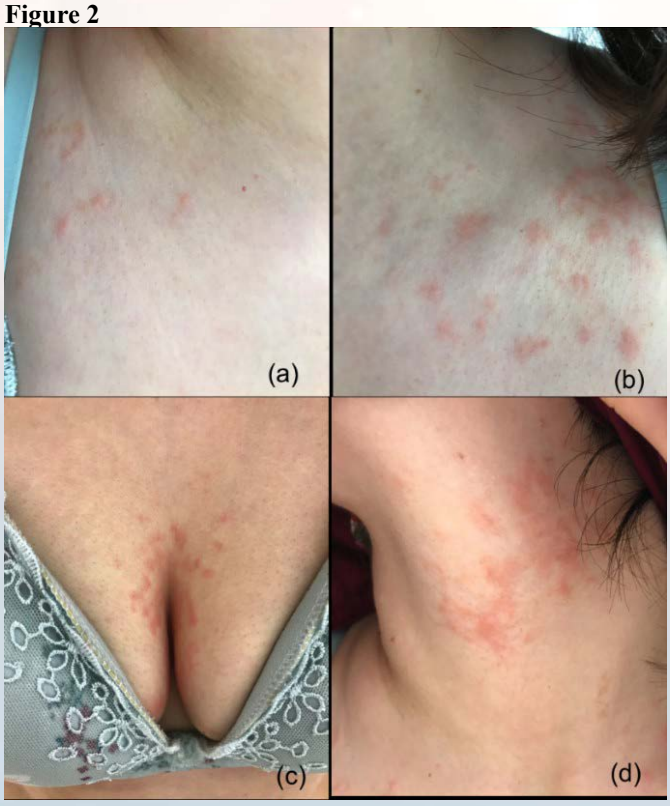
Keywords: diagnosis, diet, prurigo pigmentosa

Figure 1



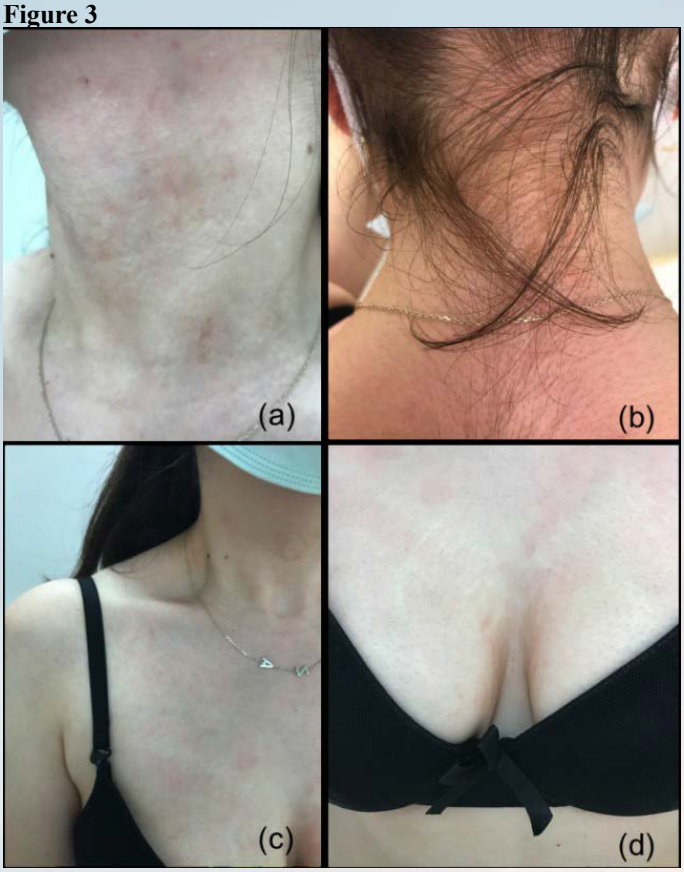
Clinical features at initial presentation with erythematous papulovesicles

Figure 2



Clinical features at 1 week with typical reticularly arranged urticarial papules

Figure 3



Complete resolution of the lesions following doxycycline therapy

PP-35 [Inflammatory Skin Diseases]

A case of infantile acropustulosis with ant-bite sign

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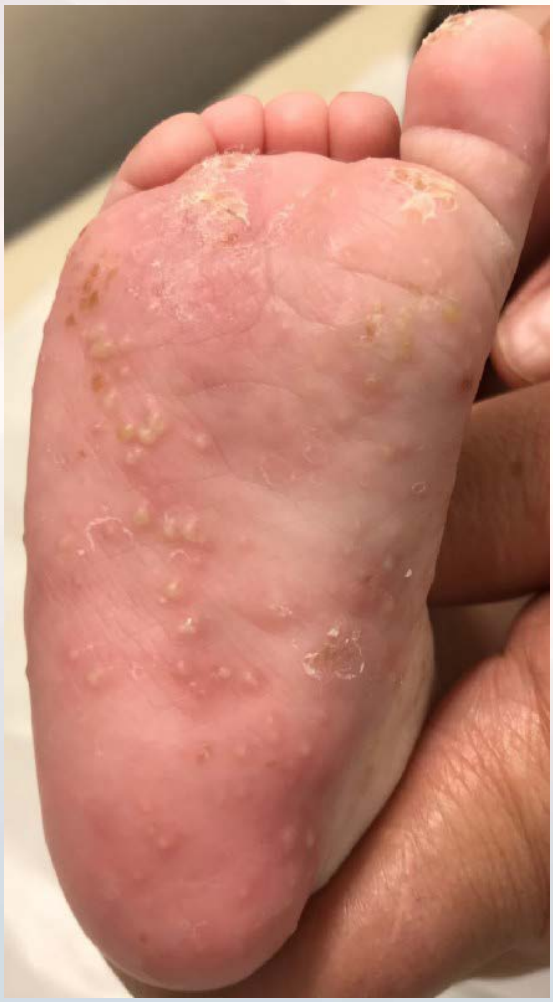
INTRODUCTION: Infantile acropustulosis is a benign, recurrent neutrophilic dermatosis of unknown etiology, predominantly affecting children aged between 1 to 3 years. The disease typically presents with episodic attacks of itchy 1 to 4mm vesicles or pustules on the soles and palms. "Ant-bite sign" without known exposure to ants has been reported as a clue to the diagnosis of infantile acropustulosis. The major differential diagnosis is active scabies infestation. Here, we report a case of infantile acropustulosis with ant-bite sign responsive to topical steroid treatment.

CASE: A 4-month-old female infant was referred to dermatology clinic for evaluation of a pruritic pustular rash on both soles. She had a history of scabies that was treated successfully when she was one-month-old. The patient was otherwise healthy. The lesions had first appeared one month earlier, lasted for two weeks and subsided spontaneously. New lesions had appeared a week ago. Topical permethrin was prescribed by the family physician due to presumed scabies infestation, without improvement. Dermatological examination revealed multiple vesicles, 2 mm in size, on the patient's both soles with ant-bite sign (Figure 1). Hyperpigmented macules and desquamation were also seen. Based on the patient's history and physical examination infantile acropustulosis was diagnosed. The lesions resolved with use of topical mometasone furoate. Milder attacks were observed in the six-month follow-up period, all of which responded to topical steroids.

CONCLUSION: Infantile acropustulosis is very frequently misdiagnosed as scabies, leading to repetitive and unnecessary use of anti-scabietic treatment. Distinguishing clinical features of the two conditions is important. An acral rather than a truncal eruption with typical ant-bite sign, lack of burrows and absence of shared pruritus are typical for infantile acropustulosis.

Keywords: acral, acropustulosis of infancy, infant, pustules, pustulosis, scabies

Figure 1



Multiple vesicles with linear arrangement along with hyperpigmented macules and desquamation

PP-36 [Inherited Skin Diseases]

Segmental Darier Disease: An Unusual Presentation

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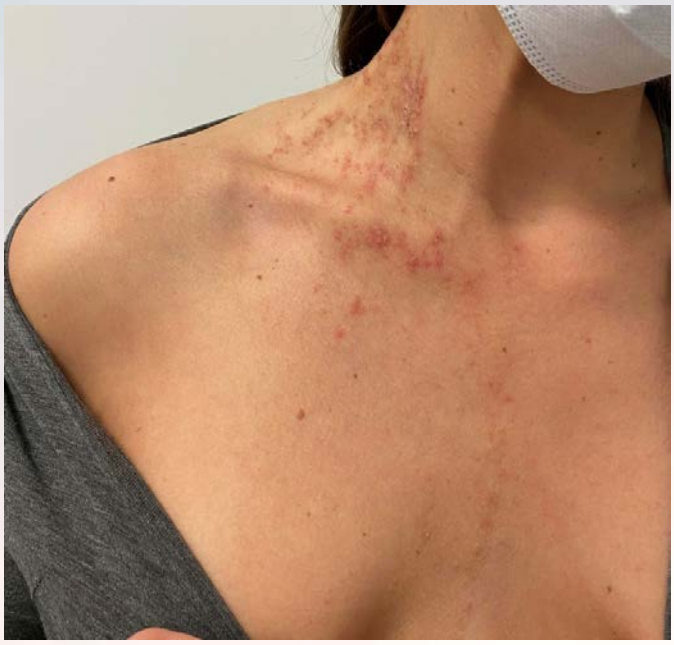
INTRODUCTION AND OBJECTIVES: Darier disease (DD) is a rare autosomal dominant disorder with variable expressivity. The clinical characteristics of the disease include multiple, red to brown, crusted, follicular and nonfollicular hyperkeratotic papules most commonly affecting the seborrheic areas of the trunk, scalp, face, and neck symmetrically. In approximately 10% of cases, DD may present with localized pattern such as unilateral, linear, segmental, and zosteriform arrangements. In this case report, we present a rare case of clinically and histopathologically confirmed segmental Darier disease.

CASE: A 41-year-old woman who attended to our dermatology outpatient clinic with a six-year history of itchy skin lesions on the right side of her neck, which were reportedly worsen in the hot climates. Physical examination showed numerous hyperkeratotic, some excoriated, erythematous papules in a blaschkoid distribution (Figure 1). Lesions were localized unilaterally, extending from neck to substernal area. Full body examination did not reveal similar lesions elsewhere; moreover, mucosal and nail examinations were normal. She did not recall any relatives with a similar condition. A punch biopsy was performed on the neck. Histology revealed focal acantholytic dyskeratosis (Figure 2). The diagnosis of segmental type 1 DD was rendered, and treatment with tazarotene gel 0.1% instituted with moderate improvement.

DISCUSSION: DD is caused by mutations in the ATP2A2 gene found on chromosome 12q23-24.1, which encodes the calcium pump Ca2+ ATPase type 2 (SERCA2), an integral part of intracellular calcium signal transduction mechanism. Impaired activity of endoplasmic reticulum disrupts junctional protein production and causes stress induced apoptosis, which latter leads to acantholysis and dyskeratosis in DD. Segmental DD is subclassified into two groups, both with a distribution of lesions along the lines of Blaschko. Type 1 segmental DD is caused by postzygotic somatic mutation in the ATP2A2 gene during embryogenesis. In type 1 DD, only affected skin harbors heterozygous ATP2A2 mutation, not the background skin. Type 2 segmental DD is characterized with generalized DD, with more prominent lesions or erosions along the lines of Blaschko. Phenotypically, type 1 segmental DD may differ from classic DD. Nail and oral mucosa lesions are usually absent in this form and, lesions do not typically involve seborrheic areas. Another proposed difference of type 1 DD is the age that lesions first present. The first manifestations of DD usually appear between ages 6 and 20; but our case and previous case reports demonstrate a late-onset disease in type 1 segmental DD. Histopathology of both forms are similar, showing acantholytic dyskeratosis. By reporting this case, we would like to point out a different manifestation of DD. DD can present with various clinical subtypes and physicians should be aware of them to avoid diagnosis delay.

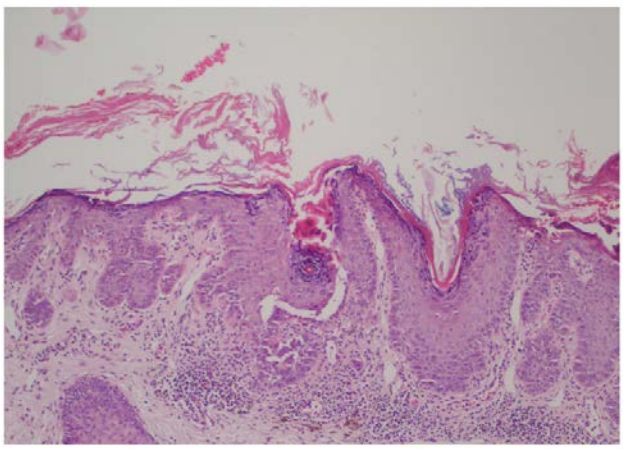
Keywords: Darier disease, segmental, unilateral

Figure 1



Erythematous keratotic papules in a unilateral blaschkoid distribution.

Figure 2



Biopsy demonstrating suprabasillar acantholytic dyskeratosis (hematoxylin and eosin stain x100).

PP-37 [Allergology and Immunology]

Real-Life Experience of Omalizumab Treatment in 134 Patients with Chronic Spontaneous Urticaria

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BACKGROUND: Omalizumab (anti-Ig E monoclonal antibody) is known to be an effective and safe treatment agent in the treatment of chronic urticaria. However, real-life data on omalizumab therapy in patients with chronic urticaria are still limited.

OBJECTIVE: In this study, we aimed to present the survival in the initial dose regimen as well as the responses to the drug dose and interval changes in patients who started 300 mg omalizumab every 4 weeks in the treatment of chronic spontaneous urticaria.

MATERIALS-METHODS: In this single-center retrospective analysis, 134 patients who started omalizumab with a diagnosis of chronic spontaneous urticaria between June 2019 and January 2021 and received at least three doses of treatment were examined. During the observation period, disease activity, duration of drug response, clinical response to dose and interval changes, duration of treatment, survival of urticaria-related concomitant medications, and time to relapse after discontinuation of treatment were analyzed.

RESULTS: Patients were grouped according to the number of doses they stayed on 300 mg omalizumab every 4 weeks. The proportions of patients receiving ≤6, 7-15 and ≥16 doses of continuous fix 300 mg/4 weeks were 41.8% (n=56), 41% (n=55) and 17.1% (n=23), respectively. 61.9% of the patients were able to discontinue concomitant antihistamines within the first 6 months of the omalizumab treatment. During the observation period, 84.3% (n=113) of patients with chronic spontaneous urticaria achieved complete remission or well-controlled disease symptoms, 12.7% (n=17) moderately controlled disease symptoms.

CONCLUSION: Omalizumab is an effective and safe treatment to control symptoms in the long term. We recommend adding omalizumab treatment without delay to CSU patients resistant to non-sedative antihistamines. When disease symptoms are controlled with 300 mg omalizumab every 4 weeks, we recommend dose reduction or extending intervals for a cost-effective approach.

Keywords: omalizumab, chronic spontaneous urticaria, real life experience

PP-38 [Angiology, Haemangiomas, Vascular Malformations, Vasculitis]

Eczematous reaction within a port-wine stain

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A 23-year-old female patient presented with a large port-wine stain (PWS) located on the anteromedial surface of her right thigh that stretched to her right inguinal and pubic regions. The patient complained of an itchy and scaly reaction confined to the borders of the PWS that began 6 years ago and had a waxing and waning course. The surface of the PWS was uneven, while the periphery of the lesion was bright red with a slight elevation, there were blotchy pale and atrophic areas in the center. There were areas of crusting and scaling interspersed on the surface of the PWS. A punch biopsy revealed orthokeratotic hyperkeratosis, focal parakeratosis and crusting, lymphocyte exocytosis in the epidermis, spongiosis, and irregular acanthosis. There was a mild perivascular lymphocytic infiltration in the dermis with sparse eosinophils overlying capillary ectasia. Pathological findings were consistent with an eczematous reaction. The patient had no history of atopy or eczema, nor had received laser treatment for her PWS. She could not remember an eliciting factor for the eczematous reaction. Color duplex ultrasonography did not reveal any venous insufficiency, and there was no accompanying soft tissue overgrowth. Eczema subsided within days following topical corticosteroid therapy but frequent relapses were observed, necessitating intermittent use. The patient was advised to receive pulsed dye laser (PDL) treatment. PWS is a congenital vascular malformation (CVM) characterized by well-demarcated, bright or deep red macules and patches clinically, and by ectatic dermal capillaries pathologically. There have been some reports of eczematous reactions seen in CVMs, children with lesions located in the head and neck area comprise the majority. There are much fewer reports of adults with lesions in other locations, which led us to present and discuss our case. The pathomechanism of the eczematous reaction observed in CVMs is unclear. It is possible that the somatic mutations harbored by CVMs lead to a pro-inflammatory microenvironment. It has also been postulated that in grossly visible malformations with large vascular dilations, such as in the context of Klippel-Treanaunay syndrome, a pathogenesis similar to stasis dermatitis may be the case. In most cases reported in the literature, the eczematous reaction is confined to the borders of the vascular malformation. However, there are a few cases of children with a history of atopic dermatitis. Considering the predilection of atopic dermatitis to the head and neck area in children, eczematous changes observed in the CVMs in these cases may possibly be a collision dermatosis. There have also been some cases triggered by the inflammation following PDL treatment. Although the precise cause is not known, it is a benign and self-limiting condition. Most patients are responsive to a short course of topical steroids. In cases with frequent relapses, treatment with PDL often leads to permanent resolution of eczema.

Keywords: port wine stain, vascular malformation, eczema, nevus flammeus, Meyerson phenomenon

PP-39 [Cutaneous Oncology]

Association of carcinoma en cuirasse and carcinoma erysipeloides ın a patient with breast carcinoma

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INTRODUCTION & OBJECTIVES: Of all the carcinomas that metastasize to the skin, breast cancer is the one with the widest range of clinical lesions, ranging from carcinoma erysipeloides to carcinoma en cuirasse. A woman with primary right ductal breast cancer complicated with multiple organ metastases and peritoneal acid, diagnosed with carcinoma erysipeloides and carcinoma en cuirasse is presented here.

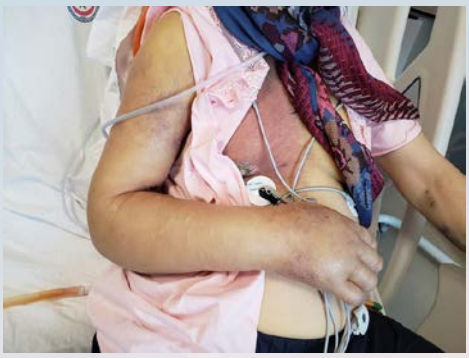
MATERIALS & METHODS: A 60-year-old female patient with primary right ductal breast carcinoma, was consulted with seriously hard, red and edematous skin lesions at the right upper torso, while she was hospitalised at the oncology clinic due to the multiple organ metastases, pleurisy and acid in the peritoneum. Dermatological examination revealed a diffuse, darkly colored, sharply limited erythema with stone-hard sclerotic with palpation covered the right side of the trunk including the mammarian tissue and extanding to the right side of the upper abdomen and back. There were sclerotic tissue with edema and crepitation at the rigth arm. A skin biopsy was planned with the preliminary diagnosis of carcinoma erysipeloides, carsinoma en cuirasse, but the patient was died immediately after her consultation.

RESULTS: From 5%–10% of the patients with breast cancer develop skin metastases. Of all the carcinomas that metastasize to the skin, breast cancer may be the one with the widest range of clinical lesions varying from papulonodules to patches with erythema mimicking erysipelas (inflammatory carcinoma) to woody induration with a peau d'orange appearance. The latter is often referred to as "en cuirasse " due to its clinical resemblance to the leather armor of a soldier (cuirassier). Inflammatory carcinoma (carcinoma erysipeloides) is characterized by lesions similar to erysipelas. While the histologic presence of invasive carcinoma invading dermal lymphatics is supportive of the diagnosis, it is not required, nor is dermal lymphatic invasion without typical clinical findings sufficient for a diagnosis of inflammatory breast cancer, as in our patient. Carcinoma en cuirasse is a diffuse infiltration of the skin that imparts an indurated and hidebound leathery quality to skin. This type mainly seen with the breast as within our patient.

CONCLUSIONS: Carcinoma erysipeloides, an inflammatory carcinoma, has many characteristic features that could be diagnosed easily by a dermatologist but its association with carcinoma en cuirasse, a sclerotic form is reported very rarely in the literature. This case here presented had a distinctive features that consistent with carcinoma en cuirasse and association with carsinoma erysipeloides. We wanted to remind as such very rare disease and emphasize the need for more studies.

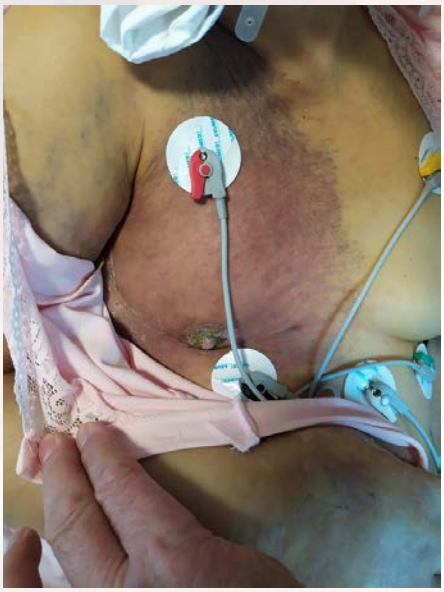
Keywords: Carcinoma erysipeloides, inflammatory carcinoma, breast cancer, skin metastase

Fig 1.



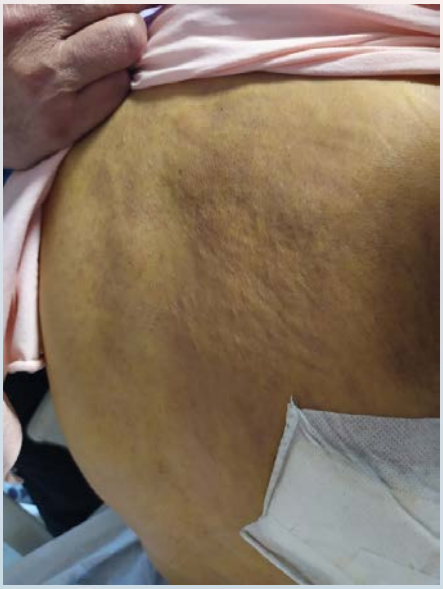
The skin on the lesions was stone-hard sclerotic with palpation and sclerotic tissue with edema and crepitation at the rigth arm

Fig 2.



Closer view of carcinoma erysipeloides and carcinoma en cuirasse

Fig 3.



There were sclerotic tissue with edema and crepitation at the rigth upper right back

PP-40 [Pharmacology and Skin-related Toxicology, Phlebology]

Subcutaneous fat necrosis following transcatheter arterial chemoembolization with drug-eluting beads

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A 65-year-old female patient presented to our clinic with the complaint of numerous painful subcutaneous lumps on her torso. Her complaints had begun a year ago. On physical examination, there were subcutaneous lobulated nodules that were hard and painful upon palpation, dispersed on the abdominal region. The biggest lump was roughly 10x10 cm wide, located in the right lower quadrant. On the skin overlying the lesion, there were patches of brownish discoloration with slight depression. The patient had a history of chronic hepatitis C virus infection and hepatocellular carcinoma diagnosed in 2018. Partial hepatectomy was performed shortly after diagnosis, and transcatheter arterial chemoembolization with drug-eluting beads (DEB-TACE) loaded with doxorubicin was performed in 2019. At the time of presentation, the disease had metastasized to vertebrae. Two punch biopsies were obtained from the biggest lesion, with suspicion of panniculitis and cutaneous metastasis. Pathological examination revealed foreign bodies in the deep dermis that were consistent with the microparticles used in chemoembolization, lipid necrosis, foreign-body type multinucleated giant cells, histiocytes, and chronic active inflammation.

The patient complained of pain despite nonsteroidal anti-inflammatory drug usage. Intralesional steroid injection was performed in two sessions, one month apart wih moderate reduction of pain and some softening of the nodules.

TACE is widely used in the treatment of liver tumors. By occluding the hepatic artery, it allows selective treatment of the liver, occluding blood flow to the tumor and delivering a sustained dose of chemotherapy. However, some particles used in embolization may reach the skin through extrahepatic collateral vessels, or through the hepatic falciform artery, which originates from the hepatic artery. There have been several reports of transient periumbilical skin rash following hepatic intraarterial chemotherapy infusion. However, fat necrosis and foreign body reaction following DEB-TACE is a very rare complication. Unlike conventional chemotherapy, DEBs are designed to release drugs slowly, which leads to a prolonged inflammatory reaction. It is important to keep it in mind as a delayed complication.

Keywords: TACE, DEB, embolization, fat necrosis

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