

PROGRAM & ABSTRACTS

ISAD 2016

**9TH GEORG RAJKA
INTERNATIONAL SYMPOSIUM ON
ATOPIC DERMATITIS**

May 19-21, 2016 - Sao Paulo, Brazil



“ Wayfarer, the only way
is your footsteps, there is no other.
Wayfarer, there is no way,
you make the way as you go.
As you go, you make the way
and stopping to look behind,
you see the path that your feet
will never travel again.
Wayfarer, there is no way – ”
only foam trails in the sea.

Antonio Machado (1875 - 1939)

From THE SOUL OF THE WORLD: A MODERN BOOK OF HOURS, edited by Phil Cousineau.
Translation from Spanish by Alan S. Trueblood, from SELECTED POEMS OF ANTONIO MACHADO

Dear Friends,

It is a great honor to welcome you to the 9th Georg Rajka International Symposium on Atopic Dermatitis in São Paulo.

The search for answers in atopic dermatitis made me think of the poem written by Antonio Machado. In medical research we are constantly exploring and discovering new roads. Along the way, we have to choose which paths we want to explore. In atopic dermatitis we went from the allergic theory, to the discovery of complex immunological pathways, skin barrier defects and now we have just begun exploring the role of the microbiome in atopic dermatitis. And the search will continue.

At this symposium you will notice a strong presence of patients and volunteers working behind the scenes. This has been the case for many years now during our local events of the Brazilian Atopic Dermatitis Association. It is indeed a great blessing to be able to work with such a special group of people. Patients themselves increasingly will have to be included in vital decisions concerning medical research and in the development of new drugs and treatments.

On the last day of the ISAD we will visit the University of São Paulo Medical School and commemorate the Centennial of the Department of Dermatology. I am deeply grateful to Prof. Cyro Festa, Prof. José Antonio Sanches and Prof. Valéria Aoki who made this session at the Department of Dermatology of the University of São Paulo Medical School possible.

In this symposium we will have the privilege of receiving experts in the field of atopic dermatitis from all over the world and we want to take advantage of this opportunity to exchange new ideas and experiences. We will do our best to provide an environment to make things happen. Let's take this opportunity to collaborate and explore this intriguing and fascinating disease together.

I wish you all a wonderful and productive symposium.



Roberto Takaoka, MD
ISAD 2016 General Chair

ISAD 2016

General Chair

Roberto **TAKAOKA** (Brazil)

Scientific Committee Chair

Valeria **AOKI** (Brazil)

Abstract Committee Chair

Raquel **ORFALI** (Brazil)

Abstract Committee Co-chair

Eric **SIMPSON** (USA)

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Alain **TAÏEB** (France)

Jean-François **STALDER** (France)

Martin **STEINHOFF** (Ireland)

Roberto **TAKAOKA** (Brazil)

Gail **TODD** (South Africa)

Christian **VESTERGAARD** (Denmark)

Hywel **WILLIAMS** (UK)

Andreas **WOLLENBERG** (Germany)

Jianzhong **ZHANG** (China)

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ISAD 2016 Program

Thursday, May 19, 2016, Renaissance Hotel Theater

Time schedule	Theme / Lecture	Speaker / Country
14:00 - 14:05	Prologue: "My Adorable Son"	Verônica SARNO (Brazil)
14:05 - 14:10	Introduction	Roberto TAKAOKA (Brazil)
14:10 - 14:20	Rajka Symposium	Susanne RAJKA (Norway)
14:20 - 14:40	AD Timeline - The History of Atopic Dermatitis	Johannes RING (Germany)
14:40 - 15:00	The Hanifin & Rajka Criteria Revisited	Jon HANIFIN (USA)
AD Around the World Chairs: Valeria AOKI (Brazil) & Alain TAÏEB (France)		
15:00 - 15:10	DENMARK	Christian VESTERGAARD
15:10 - 15:20	FRANCE	Alain TAÏEB
15:20 - 15:30	AFRICA	Gail TODD
15:30 - 15:40	INDIA	Murlidhar RAJAGOPALAN
15:40 - 16:00	Discussion	
16:00 - 16:30	Coffee-Break	
16:30 - 16:40	Music Performance Taiko + Samba	WADAIKO SHO (Brazil)
16:40 - 16:50	JAPAN	Norito KATOH
16:50 - 17:00	CHINA	Jianzhong ZHANG
17:00 - 17:10	CANADA	Danielle MARCOUX
17:10 - 17:20	BRAZIL	Valeria AOKI
17:20 - 17:35	Patient Satisfaction in AD	Julie BLOCK (USA)
17:35 - 17:55	Discussion	
17:55 - 18:00	Concluding remarks	Roberto TAKAOKA (Brazil)
18:00 - 19:00	Opening Cocktail (Renaissance Hotel)	

Friday, May 20, 2016, Renaissance Hotel America's Room

8:30 - 8:40	Opening	Valeria AOKI (Brazil) Raquel ORFALI (Brazil) Eric SIMPSON (USA)
8:45 - 9:05	How can AD research translate into better treatments and outcomes?	Hywel WILLIAMS (UK)
Immunology and Microbiome		
Chairs: Christian VESTERGAARD (Denmark), Maria SATO (Brazil), Heidi KONG (USA)		
9:05 - 9:25	State of Art: Immunology and AD	Christian VESTERGAARD (Denmark)
9:30 - 9:40	OC01 - A Novel Human Immune System Mouse Model for Human Atopic Dermatitis	Yan LI (France)

9:40 - 9:50	OC02 - Modulatory Effect of Vitamin D on Dendritic Cell Phenotype in Children with Atopic Dermatitis	Arturo BORZUTSKY (Chile)
9:50 - 10:00	OC03 - Evidence of regulatory myeloid dendritic cells and circulating inflammatory epidermal dendritic cells-like modulated by Toll-like receptor (TLR)-2 and TLR7/TLR8 in adults with atopic dermatitis	Raquel ORFALI (Brazil)
10:00 - 10:20	Microbiome and AD	Heidi KONG (USA)
10:20 - 10:30	Discussion	
10:30 - 11:00	Coffee-Break	
Skin Barrier		
Chairs: Alain TAÏEB (France), Kyu Han KIM (S. Korea) and Michael CORK (UK)''		
11:00 - 11:20	Barrier Defects in AD	Michael CORK (UK)
11:20 - 11:30	OC04 - Effect of water hardness and season of birth on the prevalence of atopic dermatitis in young children: a study within the danish national birth cohort''	Kristiane ENGBRETSEN (Denmark)
11:30 - 11:40	OC05 - High mobility group box 1 (hmgb1) protein downregulates flaggrin gene translation and protein expression, impair stratum corneum formation, and reduce epidermal growth	Uffe NYGAARD (Denmark)
11:40 - 11:50	OC06 - An organotypic model for assessing skin barrier function gives evidence of functional effect for the eczema candidate gene C11ORF30''	Sara BROWN (UK)
11:50 - 12:00	OC07 - Advances in understanding atopic dermatitis - A morphological and functional comparison with healthy skin	Simon G. DANBY (UK)
12:00 - 12:15	Discussion	
12:15 - 13:30	Lunch (Renaissance Hotel)	
13:30 - 14:30	Poster View (with authors on site)	
14:30 - 14:45	The Therapeutic Effects of Origami	Mari KANEGAE (Brazil)
Itch		
Chairs: Norito KATO H (Japan), Jianzhong ZHANG (China) and Martin STEINHOFF (Ireland)''		
14:50 - 15:10	Novel therapeutic approaches in pruritus	Martin STEINHOFF (Ireland)
15:10 - 15:20	OC08 - The Disease Cycle in Patients with Chronic Severe and Very Severe Itch Reported by Community Dermatologists in the United States	Martin STEINHOFF (Ireland)
15:20 - 15:30	OC09 - TLR 3 and its role in the itch scratch cycle of nodular prurigo- new insights into innate immune pathways of peripheral itch sensitization	Ian MCDONALD (Ireland)
15:30 - 15:40	Discussion	


15:40 - 16:00	Coffee-Break	
Evidence Based & Outcome Measures		
Chairs: Hywel WILLIAMS (UK), Jean-François STALDER (France) and Eric SIMPSON (USA)		
16:00 - 16:20	AD Outcomes	Eric SIMPSON (USA)
16:20 - 16:30	OC10 - Harmonising Outcome Measures for Eczema (HOME) STATEMENT TO ASSESS ATOPIC ECZEMA SYMPTOMS IN CLINICAL TRIALS"	Phyllis SPULS (Netherlands)
16:30 - 16:40	OC11 - Evaluation of the measurement properties of symptom measurement instruments for atopic eczema: a systematic review	Louise GERBENS (Netherlands)
16:40 - 16:50	OC12 - How patient-reported outcomes can be useful in routine practice in children with atopic dermatitis?"	Sebastian BARBAROT (France)
16:50 - 17:00	OC13 - Atopic dermatitis scores for dark skinned patients	John SU (Australia)
17:00 - 17:10	OC14 - Serum levels of thymus and activation-regulated chemokine as a biomarker for atopic dermatitis"	Koji MASUDA (Japan)
17:10 - 17:30	Discussion	
20:00 - 22:00	Gala Dinner (Renaissance Hotel) Brazilian Night Georg Rajka Medal Ceremony	

May 21, 2016, University of São Paulo Medical School		
8:30 - 9:30	AD Grand Rounds (Clinical Cases)	
	University of São Paulo Medical School Hospital - Dermatology Outpatient Clinic Medical Doctors only	
9:30 - 9:45	100th Year Celebration Department of Dermatology	Evandro RIVITTI (Brazil)
	University of São Paulo Medical School Theater All participants	Jose Antonio SANCHES Jr. (Brazil)
9:45 - 10:30	Discussion Panel	Jon HANIFIN (USA),
		Johannes RING (Germany),
		Norito KATOH (Japan),
		Carlo GELMETTI (Italy)
10:30 - 10:50	Coffee-Break	Valeria AOKI (Brasil)
10:50 - 11:10	New Perspectives in the Treatment of Atopic Dermatitis	Andreas WOLLENBERG (Germany)
Treatment & Education		
Chairs: Andreas WOLLENBERG (Germany) and Peter SCHIMID-GRENDELMEIER (Switzerland)		

11:10 - 11:20	OC15 - Efficacy and safety of crisaborole, a novel, topical, nonsteroidal, anti- inflammatory, phosphodiesterase 4 inhibitor in 2 phase 3 studies in children and adults with mild-to-moderate atopic dermatitis	Eric SIMPSON (USA)
11:20 - 11:30	OC16 - Topical corticosteroid phobia in atopic dermatitis: an international validation study of the TOPICOP SCORE	Jean-François STALDER (France)
11:30 - 11:40	OC17 - Preliminary results of the clothes trial: a randomised controlled trial of silk clothing for the management of eczema in children	Kim THOMAS (UK)
11:40 - 11:50	OC18 - Efficacy and safety of Dupilumab for moderate-to-severe atopic dermatitis in adults: a pooled analysis of two phase 2 clinical trials"	Eric SIMPSON (USA)
11:50 - 12:00	OC19 - Effects of oral and topical antibiotics in children with infected eczema in the community: The CREAM Study	Nick FRANCIS (UK)
12:00 - 12:10	Discussion	
12:10 - 12:25	Innovations in Patient Care in AD	Jean-François STALDER (France)
12:25 - 12:40	Education and AD	Uwe GIELLER (Germany)
12:40-13:00	Announcements:	Roberto TAKAOKA (Brazil) Johannes RING (Germany)
	Abstract awards	
	Final remarks	
	ISAD 2018	
13:00-15:00	Farewell Lunch (Melia Paulista Hotel)	

Wednesday, May 18, 2016

09h00 ~ 18h00	Preliminary Meeting
	09h00 ~ 12h00 For AD Non Profit organizations and health professionals who work in the field of education. To apply for the Preliminary Meeting, please, send email to info@isad2016.org
	14h00 ~ 18h00 Organization of Care in Atopic Dermatitis - The Role of AD Non Profit Organizations
	Design Thinking Workshop - Creating New Solutions for the Patient with Atopic Dermatitis
	Hotel Renaissance São Paulo - Yukon Room



Day 01 – HEAR

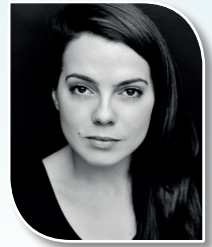
May 19, 2016

Renaissance Hotel São Paulo Theatre

14h00 – 18h00

Verônica Sarno (Actor)

Verônica Sarno has graduated with distinction from Drama Centre London in the MA Acting course, which included two months training in Russia at the Boris Shchukin Theatre Institute. In Brazil she attended to the BA Acting course at Escola Superior de Artes Célia Helena. Before her training she had worked with the amateur theatre company Folha em Branco in Brazil. Her professional debut was in the Brazilian version of the English play "Spur of the Moment" by Anya Reiss. The play was called "Sem Pensar", starred Denise Fraga and was directed by Luiz Villaça. In London Verônica's worked in the independent films "Once more with Filling" and "Alien Rage", in the pilot episode for the TV series "PUMPS", in the commercial "Kid on a Bus", in a corporate video for the British Council and in the play "Before the Sun Rises" at Theatre 503. Verônica has also worked as a production assistant in the theatrical productions "The Merchant of Venice" and "Protocols" in London and in Brazil in the production "Caisou da Indiferença das Embarcações" by Kiko Marques. She is currently working as a voice teacher at Oficina de Artes Rosina Pagan Drama School, running her own study group for actors O Trabalho do Ator and rehearsing the play "Ophelia e Seu Duplo" by André Corrêa.



My ADorable Son

Gitel Weber

*Congratulations! It's a boy!
So much excitement – so much joy!
It was the birth of my son on a Wednesday night
Those little features – what a wonderful sight.*

*It was a month later – I was proud as can be
Strolling outside with my baby so that everyone can see.
How cute he was in his carriage so new –
Short-sleeved polyester romper and tiny socks too.*

*He just had a bath – he smelled so fresh and clean.
I smeared him with baby lotion – he was the cutest I've seen!
I walked and strolled with my head held up high –
I thought he was noticed by every passer-by.*

*But then a while later (four months old was he)
I was no longer as proud as can be,
For "he had atopic dermatitis", the doctors said
When they looked at the rash from his toes to his head.*

*To go out shopping I did dread
For on his face he had a rash fiery-red.
The polyester rompers were packed away;
Now he had to wear long-sleeved cotton each day.*

*The five pediatricians and two derms that we went to
Said, "Smear cortisone, moisturizers, give antihistamine too".
Mother, neighbors, and friends had advice for me;
Also my mother-in-law, cousin, and landlady!*

*The more I heard, the more I got confused;
What does help? What method should be used?
The advice we all different – it was quite a riddle;
Everyone said opposite things – I was caught in the middle.*

*"Change the formula – use no cortisone on someone so small."
"Just use cortisone cream – the formula has nothing to do with it at all."
"Bathe him twice daily and he'll clear up – no doubt!"*

"Bathe him once a week – water dries the skin out!"

"Keep him undressed and out in the sun – Just try."

"Don't keep him in the sun – his skin is too dry."

"Just keep on nursing him – don't try to stop!"

"Don't drink milk when nursing – not even a drop!"

"Stop nursing him – he's allergic to certain food."

I was confused – and in a lousy mood.

I didn't feel like taking him out for strolls down the street;

"Oh, poor little baby!", said the old women I'd meet.

Wherever I went, no one did fail –

They all had advice, a story, a tale.

From all I heard, what did I gain?

At 10 months old, he still looked the same.

All the doctors with all their degrees

Had no advice or no cures for me.

What doesd this come from – this itch quite strange

"that happens when the weather does change".

This man was a doctor – a licenced M.D.;

But he couldn't begin to convince me

That because yesterday was cool & today was hot.

That's why my should like like that.

We went to nutricionists & such with our son.

Always on the look-out for something to be done.

We tried severals oils and diets galore

Anything different we hadn't tried before.

Everytime we tried something new, or when there was a change.

He would get somewhat better, but it was so strange –

After a while the eczema returned to his skin

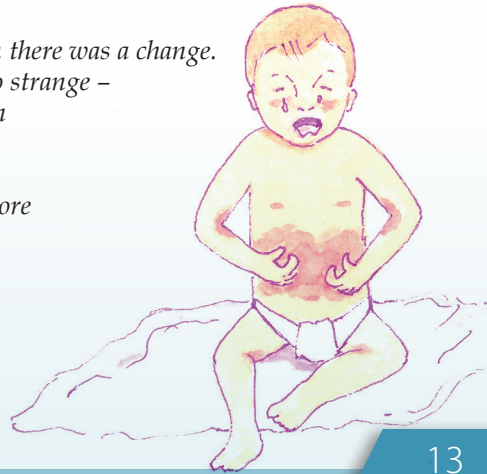
And became just as bad as it ever had been.

I could go on and on, and write more and more

But I won't do that – you'd find it a bore.

I'd like to end the poem, my friend,

But my son's life with eczema has no end!





Johannes RING (Germany)

AD Timeline - The History of Atopic Dermatitis

Professor Ring has been director of the Department of Dermatology and Allergy, Biederstein, Munich, since 1995. His major area of expertise is allergic and inflammatory skin disease. Together with Professor Heidrun Behrendt he founded ZAUM – Centre for Allergy and the Environment. In his role as dean of studies, he has formatively shaped medical training and education. He has also set up successful education program for patients suffering from neurodermitis and anaphylaxis and organized various large international conferences in Munich, including the Eur Derma Congr 2001 (6,000 participants) and World Allergy Congress 2005 (7,000 participants).

Having worked for seven years in the field of experimental immunology (W. Brendel) and allergology, in 1978 Professor Ring changed his focus to dermatology (O.Braun-Falco). Between 1990 and 1995 he was director of the Department of Dermatology and Allergy at the University Hospital Hamburg-Eppendorf. Professor Ring is on the board of several major professional associations. He is president of the German Society for Allergy and Clinical Immunology (DGAKI), the European Academy Dermatology and Venerology (EADV) and the Collegium Internationale Allergologicum (CIA). He is vice president of the World Allergy Organization (WAO).

Jon HANIFIN (USA)









Jon Hanifin is a board-certified dermatologist who received his medical degree from the University of Wisconsin Medical School-Madison in 1965. He received specialty Dermatology training from the University of California-San Francisco, where he also completed an NIH research fellowship in the Division of Hematology/Immunology. He joined the OHSU faculty in 1971, where his academic work includes clinical practice, research, and education.



He has a career-long interest in the research and management of atopic dermatitis. He has directed many national and international symposia and was a founding member of the International Society of Atopic Dermatitis (ISAD). Dr. Hanifin served on the Board of the National Psoriasis Foundation for 15 years, the Board of the Society for Investigative Dermatology from 1988-1991, and the Board of Directors of the American Academy of Dermatology from 1998-2002. In 1988 he helped found the National Eczema Association, serving as President until 1990 and continues on the Board of Directors.

Dr. Hanifin has received many honors, including the Royal Society of Medicine Visiting Professorship in London 1989-1990, the Dohi Memorial Lectureship from the Japanese Dermatological Association in 1994, and the American Academy of Dermatology Master Dermatologist in 2007. Dr. Hanifin has published more than 280 peer-reviewed articles.

Atopic Dermatitis Around the World

DENMARK		JAPAN	
	Christian VESTERGAARD		Norito KATOH
FRANCE		CHINA	
	Alain TAÏEB		Jianzhong ZHANG
AFRICA		CANADA	
	Gail TODD		Danielle MARCOUX
INDIA		BRAZIL	
	Murlidhar RAJAGOPALAN		Valeria AOKI

WadaikoSho



"Wadaiko", in Japanese, means "the art of Japanese drums". "Sho" means "to live". "WadaikoSho" is to live based on the art of the Japanese drums. A therapy that aims to develop the physical, mental and social health through taiko. Formed in 2002 by the music therapist Setsuo Kinoshita and by the sociologist Mitsue Iwamoto, they keep their studio in the Vila Mariana area in São Paulo, and seek to harmonize the brilliance of the Brazilian and Japanese cultures and the differences between them, both in their repertoire as in the group activities.



Julie BLOCK (USA)


Patient Satisfaction in Atopic Dermatitis

Julie Block, President and Chief Executive Officer of the National Eczema Association since 2010, has dedicated her career to the non-profit sector, and for the past several years, to patient-

health advocacy.

The immediate past-president of the Coalition of Skin Diseases, Julie is an active member of multiple national groups focused on skin diseases in the U.S. – the American Academy of Dermatology Atopic Dermatitis Guidelines Committee, Expert Resource, and Pruritus Work groups; the National Institute of Arthritis, Musculoskeletal and Skin Coalition; and, the Friends of the National Institute for Environmental Health Sciences Coalition. She serves on the LEO Pharma Patient and Scientific Review Board, and a variety of other ad-hoc pharmaceutical industry initiatives.

Julie's extensive non-profit management, strategy and development experience stems from leadership positions in education, medical technology, and the arts. Throughout her career, Julie has continued her involvement with causes she is passionate about as a volunteer including the American Cancer Society Relay for Life, the Susan G. Komen Breast Cancer Foundation, and Very Special Arts for children with special needs.



Day 02 – CREATE
Friday, May 20, 2016
Renaissance Hotel São Paulo
America's Conference Room



Hywel WILLIAMS (UK)

How can AD research translate into better treatments and outcomes?

Hywel co-directs the Centre of Evidence-Based Dermatology (CEBD) at the University of Nottingham with Professor Kim Thomas.

The CEBD includes the Cochrane Skin Group (identifying research gaps) and the UK Dermatology Clinical Trials Network (addressing those gaps through randomised controlled trials) and an information specialist (Douglas Grindlay) who helps to disseminate key results to a community of research users. Hywel has had a lifelong interest in atopic eczema (AE), initially in the field of epidemiology and then in evidence-based treatments and intervention studies. He has published over 200 articles on AE including original epidemiological research such as the UK refinement of Hanifin and Rajka's diagnostic criteria and the link between AE and social class and hard water, outcome measures such as the POEM scale, clinical trials such as different duration of topical corticosteroids and ion exchange water softeners, and systematic reviews such as house dust mite avoidance. Outside of dermatology, Hywel has just been appointed as the UK's Director of the National Institute of Health Research Health Technology Assessment Programme with responsibility for over 400 national clinical trials covering the whole of medicine and surgery. He freely admits to being slightly mad.

Christian VESTERGAARD (Denmark)



State of Art: Immunology and AD

Dr. Christian Vestergaard graduated from Aarhus University in 1998, after which he started his studies in Atopic Dermatitis and inflammation as a Monbusho Scholar at the University of Tokyo, Japan, in the laboratory of professor Kouji Matsushima. Dr. Vestergaard completed the studies as part of his ph.d. in the Dermatological research laboratory at the Department of Dermatology, Aarhus University Hospital. After achieving the ph.d. degree he was awarded a two year postdoctoral position from the Danish National Research council, which lead to the completion of the Danish Doctoral thesis with focus on inflammation. Dr. Vestergaards research still has focus on the inflammatory reaction in the skin and it's influence on skin-barrier function, but also on the epidemiology of co-morbidities in atopic dermatitis. Dr. Vestergaards research group also focuses on bullous pemphigoid, mastocytosis, and skin changes of malnutrition with phd students, MD student and master of science students.

Dr Vestergaard is National Coordinator of The Training in Dermatology in Denmark, and is an active teacher at the eczema school for Atopic Dermatitis patients and their parents in Aarhus

He serves as member of the Board in The Danish Association of Allergology and in the European Task Force on Atopic Dermatitis (ETFAD).



Heidi KONG (USA)

Microbiome and Atopic Dermatitis

Investigator and Head, Skin Microbiome Section, Dermatology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, USA

Dr. Kong received her undergraduate degree in biological sciences from Stanford University, and obtained her M.D. from Baylor College of Medicine. She completed her internship at Baylor College of Medicine and dermatology residency at Duke University Medical Center. After completing her clinical research fellowship training in the Dermatology Branch and the Duke-NIH Masters Program in Clinical Research, Dr. Kong became an Assistant Clinical Investigator in the Dermatology Branch in the Center for Cancer Research of the National Cancer Institute. She is currently a tenure-track Investigator in the Dermatology Branch. Dr. Kong's research focuses on the skin microbiome in healthy individuals and patients with dermatologic disorders, particularly individuals with atopic dermatitis and primary immunodeficiency disorders with eczematous skin conditions. Her interest is in understanding the interface between cutaneous microbes and the human host.

Michael CORK (UK)

Barrier Defects in Atopic Dermatitis

Dr Michael J Cork BSc (Hons), MBBChir (Dis), PhD, FRCP, is Head of the Academic Dermatology Group in the Division of Genomic Medicine, University of Sheffield Medical School. He is an Honorary Consultant Dermatologist at the Sheffield University Hospitals Trust and Sheffield Children's Hospital. His major research interests include the genetics regulation of skin barrier function in atopic dermatitis, gene-environment interactions in the development of atopic dermatitis and improving clinical outcomes in atopic dermatitis through education.





Mari KANEGAE (Brasil)

The Therapeutic Effects of Origami

Mari Kanegae attended Art School at "Escola de Comunicações e Artes" (ECA) at the University of São Paulo, Brazil.

She studied origami with master Toyoaki Kawai in Japan and studied other paper techniques like kirie, chiguirie and paper-kraft.

She has attended many events like the Origami Convention in New York and participated in the Southeastern Origami Festival in Charlotte, North Carolina, USA.

In 2002 she earned a scholarship by JICA (Japan International Cooperation Agency) and studied with origami masters Akira Yoshizawa, Saburo Kase and Isamu Asahi.

She was an Origami award winner at "Happy Encounter" organized by NOA (Nippon Origami Association)

Mari is an active volunteer at AADA (Brazilian Atopic Dermatitis Association) teaching origami for patients and their families.

Martin STEINHOFF (Ireland)

Novel therapeutic approaches in pruritus

Professor Steinhoff has studied Medicine and Human Biology (Theoretical medicine) in Germany where received his MD and MSc as well as PhD from the University of Marburg.

After residency in Internal Medicine and Dermatology, he became Assistant Professor of Dermatology at the University of Muenster in 2002, rising from assistant professor to full professor in only 6 years. He holds board certifications in dermatology, venerology, phlebology and allergy from Germany, in dermatology from the California Medical Board and Irish Medical council.



Prof Steinhoff is an established physician scientist with a long-standing background as a basic scientist studying mediators, pathways and their receptors that cause inflammation, autoimmune disease or cancer of the skin on a molecular level. He also uses in vivo and ex vivo models to study proof-of-principle concepts, and translate them into the human disease setting by performing human studies or clinical trials.

Prof Steinhoff started his current position as Professorial Chair of the Dept. of Dermatology and as Director of the UCD Charles Institute at University College Dublin in January 2014. His current research interests span Systems Medicine and cell signaling, molecular neuroscience, neuro-immunology, genomics, proteomics, biomarkers, new therapies.

Prof Steinhoff received several prestigious scientific awards for his research in Germany, USA and Ireland. To date, his group has published more than 300 articles, reviews and book chapters spanning basic science as well as clinical dermatology.



Eric SIMPSON (USA)

Atopic Dermatitis Outcomes

Dr. Simpson specializes in all aspects of general dermatology with special interests in chronic inflammatory skin diseases and skin cancer. As Director of the Clinical Studies Unit, he is involved in clinical research and is funded by the National Institutes of Health and industry partners to study new approaches to chronic skin disease treatment and prevention.

Dr. Simpson supports medical professional education and regularly instructs residents and medical students in dermatology. Additionally, he has published over 70 scientific articles in several high-impact peer-reviewed journals including the New England Journal of Medicine and The Lancet. His work is recognized internationally and he has spoken at over 20 international conferences about his approach to patient care and research at meetings in Europe, North and South America, and Asia.

Dr. Simpson volunteers in support of the National Eczema Association, where he serves as Co-Chair of the Scientific Advisory Committee. He also serves on the executive committee of the Harmonizing Outcome Measures in Eczema (HOME) – a group of patients, providers, and other stakeholders whose mission is to improve the quality of eczema research to better suit the needs of patients and policy-makers.

Dr. Simpson enjoys spending time with his wife and children, playing squash, camping, hiking, fishing, and biking.



Day 03 – DELIVER
University of São Paulo Medical School Hospital / Theater
8H30 – 13h00



Department of Dermatology of the University of São Paulo Medical School

The first Professor of the Department of Dermatology of the University of São Paulo Medical School was Adolpho Lindenberg, who presented the first lecture for medical students in February 26, 1916. His main research topics were tropical diseases, especially mycetomas and cutaneous leishmaniasis.

One hundred years after Prof. Lindenberg's lecture, the Department of Dermatology of the University of São Paulo Medical School receives each year, 175 medical students, and has two graduate courses for 3rd and 5th year medical students. The Department of Dermatology is also responsible for the dermatology residents (12 residents each year), and is the only post-graduate course in dermatology in the country.

We welcome all participants of the 9th Georg Rajka International Symposium on Atopic Dermatitis. It is a great honor to host this session of the ISAD as part of the commemoration of the Centennial of the Department of Dermatology of the University of São Paulo Medical School.



Celina Wakisaka Maruta
Professor of Dermatology
Department of Dermatology of the University
of São Paulo Medical School

Andreas WOLLENBERG (Germany)

New Perspectives in the Treatment of Atopic Dermatitis

Professor for Dermatology and Allergy, Head of
Pediatric Dermatology Unit at Ludwig Maximilian
University, Professor at LMU-München





Jean-François STALDER (France)

Innovations in Patient Care in Atopic Dermatitis

Prof. Jean-François Stalder heads the Department of Dermatology of the University of Nantes, France. Prof. Stalder is one of the creators of the SCORAD index and is currently involved in the study of corficofobia in atopic dermatitis.

Uwe GIELLER (Germany)

Education and Atopic Dermatitis

Prof. Uwe Gieler works as Deputy Director and senior clinical physician at the Clinic for Psychosomatics and Psychotherapy of the University Hospital Giessen and Marburg, Head of the Department of Dermatology Giessen (University Hospital Giessen and Marburg - Location Giessen).



Prof. Gieler also heads since 2001 the atopic dermatitis Training Academy Hessen-Thüringen in the nationwide AGNES project and is head and coordinator of psychotherapy training institution Marburg-Gießen Kassel State Medical Association Hesse.



Preliminary Meeting

Renaissance Hotel São Paulo – Yukon Room

Organization of Care in Atopic Dermatitis

ISAD 2016 Preliminary Meeting / May 18, 2016 / 9h00 - 12h00

Renaissance Hotel São Paulo - Yukon Room

9h00 - 9h10	Introduction	Roberto TAKAOKA (BRAZIL)
	Non-Profit Organizations:	
	Mission, Vision and Strategy	
9h10 - 9h20	AADA - Brazilian Atopic Dermatitis Association - São Paulo	Henrique ISHII (BRAZIL)
	AADA - Brazilian Atopic Dermatitis Association - Porto Alegre	
9h20 - 9h30	NEA - National Eczema Association	Julie BLOCK (USA)
9h30 - 9h45	Kumi Uri - Israeli AD Association	Shulamit BURSTEIN (ISRAEL)
10h00 - 10h15	Discussion	
10h15 - 10h45	Coffee Break	
10h45 - 11h00	FondationDermatiteAtopique	Helène PASSERINI (FRANCE)
11h00 - 11h10	Association Française de L'Eczema	Stephanie MERHAND (FRANCE)
11h10 - 11h25	Eczema Society of Canada	Amanda CRESSWEL-MELVILLE (CANADA)
11h25 - 11h40	Atopic Schools	Uwe GIELER (GERMANY)
11h40 - 11h55	Discussion	
11h55 - 12h00	Closing	

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Design Thinking Workshop

ISAD 2016 Preliminary Meeting / May 18, 2016 / 14h00 – 18h00

Renaissance Hotel São Paulo – Yukon Room

Design thinking is a creative innovation process originally used by designers to enhance the look and functionality of products. More recently, this methodology has also been used to tackle complex social and health care problems. Design thinking is a human-centered approach that, when applied to health care, involves creating solutions by listening closely to patients' needs and problems. Another important aspect of the design thinking approach is the co-development of solutions; which means involving all stakeholders in the process of generating ideas. In this workshop we will experience how design thinking can help create new solutions to improve the treatment of atopic dermatitis and increase patient satisfaction.

Workshop Moderators & Facilitators

Gisele RAULIK MURPHY (Brazil)

gisele@ducontact.com



Gisele Raulik Murphy is a partner at DUCO, a design management and innovation consultancy based in Curitiba (South of Brazil). Gisele gained her degree in Graphic Design from the Federal University of Parana (Brazil), obtained a Masters in Design Strategy and Innovation from Brunel University (UK), and her PhD on Design Policy from the University of Wales (UK). Gisele has worked for design centers both in Brazil and the UK (Centro Brasil Design, Design Council and Design Wales). In 2005 she established and coordinated the EU funded program SEE project, a collective of European design centers established to share experiences and expertise on policies for design and innovation. Since moving to Brazil in 2011 Gisele has established the design management consultancy DUCO, which was commissioned by the Uruguayan Government in 2013 to develop recommendations for a national design policy. More recently DUCO completed a detailed review of the design practices in key manufacturing sectors for the Brazilian government to inform national policies, together with a diagnostics about the design sector. Together with the DUCO team, Gisele has been running co-creation and design thinking workshops for various institutions as well as industry. She has continued her academic record and maintains teaching commitments at graduate and masters level at various universities in the South of Brazil. Gisele is currently member of the Board of the Brazil Design Center.



Carolina PIZATTO GIRARDI(Brazil)

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Carolina Pizatto Girard is a design researcher within DUCO. Carolina graduated in Graphic Design at Federal University of Parana and is currently completing a graduate program on Business Management at FAE Business School. Carolina was recently a visiting student at

Cambridge School of Art, England. She worked for the department of Communication and Sustainability in HSBC Brazil, has experience as a graphic designer for both national and international design studios, as well as practice on developing brand positioning research. Her interests include Service Design, Brand Management and Design Thinking.

Roberto TAKAOKA(Brazil)

Roberto Takaoka is a dermatologist from São Paulo, who has worked in the field of atopic dermatitis for more than 25 years. After finishing his Dermatology Residency at the University of São Paulo Medical School, he worked as a Research Fellow at the Oregon Health & Sciences University, supervised by Prof. Jon Hanifin. After returning to Brazil in 1990, he opened the Atopic Clinic at the University of São Paulo Medical School Hospital, which he continues to run to this day. Roberto founded the Brazilian Atopic Dermatitis (AADA) in 1997 after many years of experience with support groups for patients with atopic dermatitis at the University of São Paulo Medical School. AADA's current mission is to transform the disease into an opportunity for growth and self-development. Projects include the creation of support groups for patients and their families in other Brazilian cities, creation and distribution of educational materials, art workshops, and organization of scientific meetings for doctors and other health care professionals. Roberto is also interested in art and design and has attended courses on Innovation and Social Entrepreneurship at MIT and Stanford Graduate School of Business.



Brazilian Atopic Dermatitis Association

Associação de Apoio à Dermatite Atópica (AADA)

AADA was founded in 1997 following many years of experience with support groups for patients with atopic dermatitis (AD). The association is composed of patients and their families, doctors, psychologists, nurses, social workers and volunteers. AADA's current mission is to transform the disease into an opportunity for growth and self-development.

AADA's activities include: creation of educational material about AD; organization of support groups for patients and their families; art workshops: painting, origami, music; educational workshops: relaxation, skin hydration; and scientific meetings for doctors and other health care professionals.



www.aada.org.br
contact@aada.org.br

ISAD 2016 Volunteers

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ISAD 2016 Delegates' biosketchs

Alexander Egeberg

Title: MD, PhD

Affiliation: Dept. of Dermato-Allergology, Herlev and Gentofte Hospital, Denmark

Topics of interest: Atopic dermatitis, psoriasis, inflammation, pharmacology, cytokine signaling, epidemiology

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Alexander Egeberg is a medical doctor at the Department of Dermato-Allergology, Herlev and Gentofte Hospital. He has a PhD in Dermatology (Immunology) from the University of Copenhagen, focused on the epidemiology of psoriasis, and holds a post-graduate degree in Economics from Copenhagen Business School, focused on health economics and public health. He has extensive knowledge in publication planning and clinical trial designs, including pivotal data from phase I-IV-studies, and explorative/post-hoc analyses. His main research interest is inflammation in skin diseases, and the potential therapeutic and comorbid implications.



ISAD 2016 Abstracts

PT01

FREE AND BIOAVAILABLE 25-HYDROXYVITAMIN D ARE STRONGLY ASSOCIATED WITH SEVERITY OF ATOPIC DERMATITIS IN CHILDREN

Arturo Borzutzky^(1,2), Carlos A. Camargo Jr.⁽³⁾, Guillermo Perez-Mateluna⁽¹⁾, Cristián Navarrete-Dechent⁽⁴⁾, Carolina Iturriaga⁽¹⁾, Carolina Cabalin⁽¹⁾, Francisca Cristi⁽¹⁾, Sergio Silva-Valenzuela⁽⁴⁾, Cristián Vera-Kellet⁽⁴⁾, Lorena Cifuentes⁽⁵⁾, Rodrigo Hoyos-Bachiloglou⁽¹⁾, Sergio Niklitschek⁽⁴⁾, Juan Eduardo Carrasco⁽⁴⁾, María Laura Cossio⁽⁴⁾, Catalina Le Roy⁽⁵⁾.

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Funding: FONDECYT Chile grant 1130615, Iniciativa Científica Milenio Chile grant P09/016-F.

No conflicts of interest to disclose.

Keywords: free vitamin D, bioavailable vitamin D, SCORAD

Background: The association between vitamin D (VD) status and severity of atopic dermatitis (AD) remains uncertain. 25-hydroxyvitamin D (25OHD) and 1,25-dihydroxyvitamin D circulate bound to VD-binding protein (DBP) (85–90%) and albumin (10–15%) with less than 1% of circulating hormone in its free form. Recent studies suggest a stronger association of free (unbound) and bioavailable (free + albumin-bound) 25OHD with clinically relevant outcomes such as bone mineral density, but their potential role in AD severity has not been evaluated.

Objective: To explore the associations of free and bioavailable 25OHD with clinical severity of childhood AD, along with allergic biomarkers and *S. aureus* colonization of AD.

Methods: A cross-sectional study of free and bioavailable 25OHD in 101 children with AD from Santiago, Chile was performed. AD severity was evaluated by SCORAD. 25-hydroxyvitamin D (25OHD), DBP, albumin, total IgE, specific IgE to staphylococcal enterotoxins A and B, and eosinophil count were measured in sera. Skin culture was obtained from lesional eczematous skin. Free and bioavailable 25OHD were calculated as described by Powe et al, NEJM 2013; 369: 1991.

Results: Mean SCORAD was 32±29: 40% had mild, 45% moderate, and 16% severe AD. Mean 25OHD was 18.5±8.1 ng/ml, mean DBP levels were 483±96 ug/ml, and mean albumin was 4.5±0.3 g/dL. Mean free 25OHD was 3.08±1.35 pg/ml and bioavailable 25OHD 1.27±0.58 ng/ml. Free and bioavailable 25OHD were highly correlated with each other (r=0.99, P<0.001). Total 25OHD did not correlate with SCORAD (r=-0.04, P=0.67), or other clinical and laboratory variables. In contrast, free and bioavailable 25OHD strongly correlated with SCORAD (r=-0.61 and R=-0.60, both P<0.001), as well as eczema extension, intensity, pruritus and sleep loss (all P<0.001). Lower free and bioavailable 25OHD was associated with history of bacterial skin infections (both P<0.01). In addition, free and bioavailable 25OHD correlated with white blood count (both r=-0.27, P<0.01), eosinophil count (r=-0.46 and r=-0.45, both P<0.001), total IgE (r=-0.25 and r=-0.24, both P<0.05), and specific IgE against *S. aureus* enterotoxin B (r=-0.24 and r=-0.23, both P<0.05). Lower free and bioavailable 25OHD also were associated with skin colonization by *S. aureus* (both P<0.05).

Conclusions: Low concentrations of free and bioavailable 25OHD are associated with more severe AD, history of bacterial skin infections, higher serum biomarkers of allergic inflammation, and *S. aureus* skin colonization. Deficiency of bioavailable forms of VD may participate in AD pathogenesis and should be considered in future studies of the relation between VD status and AD.

PT02

GENE EXPRESSION OF EPIDERMAL TAPE STRIPPING SAMPLES TO ASSESS RESPONSE TO VITAMIN D SUPPLEMENTATION IN CHILDREN WITH SEVERE ATOPIC DERMATITIS: A PILOT STUDY

Carolina A. Cabalin⁽¹⁾, Guillermo Pérez-Mateluna⁽¹⁾, Carolina Iturriaga⁽¹⁾, Francisca Cristi⁽¹⁾, Sergio Silva-Valenzuela⁽²⁾, Cristián Vera-Kellet⁽²⁾, María L. Cossio⁽²⁾, Carlos A. Camargo Jr.⁽³⁾, **Arturo Borzutzky**^(1,4)

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No conflicts of interest to disclose. Keywords: tape stripping, skin biomarkers, vitamin D.

Background: Skin biopsy studies demonstrate that skin affected by atopic dermatitis (AD) shows changes in protein expression of the skin barrier, inflammatory cytokines and antimicrobial peptides. The tape stripping technique is a novel non-invasive sampling method of the stratum corneum of the skin that permits the analysis of different molecules through molecular biology techniques. We applied this novel technique to explore potential mechanisms for the reportedly beneficial effect of vitamin D (VD) supplementation on the severity of AD in some children.

Objective: To implement a new combined protocol of non-invasive tape stripping and RNA extraction from epidermal samples and analyze the effect of VD supplementation on Vitamin D Receptor (*VDR*), Cathelicidin Antimicrobial Peptide (*CAMP*) Vascular Endothelial Growth Factor (*VEGF*), and Thymic Stromal Lymphopoietin (*TSLP*) mRNA expression in the skin of children with severe AD.

Methods: In an ancillary study of the VIDATOPIC trial, samples of lesional and non-lesional skin from 6 children with severe AD were collected through tape stripping technique before and after 6 weeks of oral VD supplementation. We extracted total RNA from samples and measured the expression of *VDR*, *CAMP*, *VEGF* and *TSLP* genes through RT-PCR. We applied the $2^{-\Delta(\Delta C(T))}$ method to analyze the relative change of expression between lesional and non-lesional skin in each subject before and after VD supplementation.

Results: At baseline, mean SCORAD of the 6 children was 60 ± 10 and serum 25OHD was 48 ± 22 nmol/L. After 6 weeks of VD supplementation, 25OHD increased to 99 ± 20 nmol/L ($P < 0.05$). Tape stripping was well tolerated in all patients. Tape stripping samples yielded between 2 and 30 ng of RNA for each site. Although statistical power was limited, relative mRNA expression of *VDR* non-significantly increased after VD supplementation from 0.46 ± 0.28 to 1.10 ± 0.61 ($P = 0.13$). mRNA expression of other genes did not appear to change: *CAMP* (0.87 ± 0.22 to 2.14 ± 2.90 ; $P = 0.41$), *VEGF* (0.98 ± 0.24 to 1.20 ± 0.36 ; $P = 0.41$) and *TSLP* (1.60 ± 2.00 to 1.68 ± 2.40 ; $P = 0.80$).

Conclusions: This pilot study suggests that the analysis of mRNA relative expression from tape stripping of stratum corneum samples may permit a direct but non-invasive evaluation of skin biomarkers in AD patients. Further studies of mRNA expression in tape stripping samples are needed to evaluate the effects of VD supplementation on epidermal gene relative expression.

PT03

INVESTIGATION OF THE ROLE OF RIP1 KINASE AS A MEDIATOR OF INFLAMMATORY RESPONSE IN ATOPIC DERMATITIS

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*Conflict of interest: None declared

Background: Necroptosis is a form of programmed cell death, in which receptor-interacting protein (RIP)1 kinase and subsequent RIP3 kinase activation is a central pathway for its development. Necroptotic cells induce inflammation through the release of various cytokines or necrotic danger-associated molecular patterns. Recent reports indicated that mice with keratinocyte-specific necroptotic cell death exhibit severe chronic skin inflammation, which suggests the involvement of necroptosis in the pathogenesis of chronic skin inflammatory diseases, such as atopic dermatitis (AD).

Objective: We investigated the involvement of RIP1 kinase, key regulator of necroptosis, in the pathogenesis of AD.

Methods: We examined the effects of necrostatin-1, a specific inhibitor of RIP1 kinase, in house dust mite (HDM)-induced murine model with AD-like lesions and HaCaT cells stimulated with TNF- α , IFN- γ and HDM. Tissue expression of RIP1 kinase was also evaluated in human AD skin lesions by immunohistochemical staining.

Results: Protein expression of RIP1 kinase was significantly increased after HDM application in the ear tissues of mouse model with AD-like dermatitis. Administration of necrostatin-1 significantly reduced the severity of HDM-induced AD-like dermatitis and protein expression of RIP1 kinase in mouse model with AD-like dermatitis. Serum levels of histamine, total IgE, HDM-specific IgE, and IgG2a were significantly decreased compared with control mice. Gene expressions of several key pro-inflammatory cytokines including TNF- α , IFN- γ , IL-4, IL-5, IL-13, IL-17, and IL-31 were also decreased in the tissues of mouse ears. In addition, we found decreased gene expression of NK- κ B and Th2 chemokines, CCL-17 and CCL22 in HaCaT cells stimulated with TNF- α and IFN- γ . Interestingly, in relation to the RIP1-RIP3-MLKL (mixed lineage kinase domain-like protein) necroptosis pathway, dabrafenib (RIP3 inhibitor) and necrosulfamide (MLKL inhibitor) also decreased the expression of IL-33 and TSLP in HaCaT cells stimulated with HDM.

Conclusions: These results indicate the involvement of RIP1 kinase and necroptosis pathway in the pathogenesis of AD.

PT04

LACK OF ASSOCIATION OF THE PTPN22 GENE C1858T POLYMORPHISM WITH ATOPIC DERMATITIS IN CHILEAN CHILDREN

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Funding: FONDECYT Chile grant 1130615, Iniciativa Científica Milenio Chile grant P09/016-F.

No conflicts of interest to disclose. Keywords: PTPN22, autoimmunity, atopic dermatitis

Background: The *PTPN22* gene, located on the long arm of chromosome 1, encodes lymphoid tyrosine phosphatase (Lyp), a protein that participates in inhibiting T-cell activation. The *PTPN22* gene C1858T polymorphism has been associated with increased incidence of multiple autoimmune diseases. Atopic dermatitis (AD) is characterized by overactive T-cell responses and autoimmune phenomena against epidermal proteins have been observed in AD. In addition, AD has been associated with autoimmune diseases such as celiac disease, vitiligo, and alopecia areata, but the association with the *PTPN22* gene C1858T polymorphism has not been evaluated in AD.

Objective: The aim of this study was to evaluate the association of the *PTPN22* gene C1858T gene polymorphism with AD in children.

Methods: The study included 99 children with AD and 85 healthy non-atopic controls (HC). Genotyping of the rs2476601 (C1858T) *PTPN22* gene polymorphism was performed using TaqMan SNP genotyping assay by Real Time PCR (RT-PCR). Severity of AD was assessed by SCORAD.

Results: Mean age was 6.3 ± 4.0 years for AD and mean age was 6.2 ± 3.8 years for HC ($P=0.84$) 52% were male in AD and 48% in HC ($P=0.66$). In children with AD mean SCORAD was 32 ± 29 . The C1858T allele frequencies of cases and controls showed no deviation from Hardy-Weinberg equilibrium. Genotypes CC, CT, and TT of the *PTPN22* C1858T polymorphism presented frequencies of 78.8%, 20.2% and 1%, respectively, in the AD group, and 83.7%, 12.8%, and 2.3% in the control group ($P=0.35$). Comparison of the distribution of *PTPN22* C1858T alleles among patients with AD and HC revealed no statistically significant differences (OR=1.49, 95%CI=0.70- 3.20, $P=0.30$) for TT+CT vs. CC genotypes). No association was found either between *PTPN22* C1858T polymorphism and AD severity assessed by SCORAD ($P=0.38$).

Conclusions: We found no association between the *PTPN22* C1858T polymorphism and AD susceptibility in Chilean children.

PT05

Distribution and characterization of Interleukin-33 and its receptor ST2 in patients with atopic dermatitis

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Background: Interleukin-33 (IL-33) is a novel member of the IL-1 type family of cytokines that has been implicated in atopic dermatitis (AD). It binds to two receptor subunits; the IL-33-specific subunit ST2 and accessory protein IL-1RAcP which transduce IL-33-induced intracellular signalling via MAP kinases or NF- κ B, for example. In murine models, studies have demonstrated that IL-33 is released following irritation of AD skin thereby inducing a T-helper type 2 response, production of IL-4, IL-5 and IL-13. IL-33 is also involved in skin barrier repair. It activates various immune cells including eosinophils suggesting an important role for IL-33 during inflammation and pruritus in AD. ST2 is also expressed in the skin and central nervous system, but the precise function of ST2 in AD is still unknown.

Objective: Currently, we rely almost exclusively on *in vitro* work and mouse models as our source of information regarding the pathophysiological expression of IL-33 and ST2. To further understand which cell types express IL-33 and ST2 in humans, and to determine how the cytokine fits into the complex network of pruritic and inflammatory pathways in atopic dermatitis, we performed morphological and immunological studies in tissue and cells of patients with AD.

Methods: We used immunofluorescence and double-immunofluorescence to determine the distribution of IL-33 and ST2 in lesional and non-lesional skin of AD patients compared to controls. We will use FACS to confirm these results and characterize the infiltrating immune cells that produce IL-33 or carry the receptor subunit ST2.

Results: Increased numbers of IL-33-positive cells were found in the basal and suprabasal layer of the epidermis and many endothelial cells. Double-immunofluorescence verified colocalization of IL-33 with CD4+ T cells and macrophages but not human mast cells, which is contrary to the report that IL-33 is present in bone marrow-derived, murine mast cells.

Conclusions: Animal models and *in vitro* work provide an invaluable opportunity to understand the molecular and cellular basis of AD. In a translational setting, we demonstrated that IL-33 as well as its receptor are significantly upregulated in various skin and immune cells in AD skin. Thus, this novel cytokine may be a therapeutic target for the treatment of AD.

PT06

The Role of Eosinophils in Atopic Dermatitis

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Background: Eosinophils are often dominant inflammatory cells in atopic dermatitis, the roles remain uncertain.

Objective: To investigate the role and pathogenesis of eosinophils in atopic dermatitis.

Methods: MC903 (calcipotriol) was topical used on skin of WT and Δ dbl-GATA mice, the latter of which lack eosinophils, to develop atopic dermatitis-like syndrome. Clinical manifestations, histopathology, serum IgE, cytokines, Th1 and Th2 cells were determined. Affymetrix chips were used to compare mRNA and long non-coding RNA expression in samples of skin lesions. Enrichment analysis was carried out to find out the relevant pathways regulated genes.

Results: Atopic dermatitis like skin inflammation were both eminent in WT and Δ dbl-GATA mice; the initiation time in Δ dbl-GATA mice was longer. Histological analysis revealed epidermal hyperplasia with numerous eosinophils infiltration were identified in WT mice. Eosinophils were not detectable in the skin of Δ dbl-GATA. The serum IgE, TSLP and IL-6 level increased, which were more significant in WT. Th1 cells reduced after MC903 application, and in WT; the reduction was more obviously than Δ dbl-GATA. Th2 cells were not changed. In WT, 812 genes were up regulated and 503 genes down regulated after MC903 treatment. In addition, 92 and 62 long non-coding RNAs up or down regulated. In Δ dbl-GATA, We identified 1992 genes up regulated and 1439 genes down regulated. There were 186 and 439 long non-coding RNAs up or down regulated respectively. These genes correlated to JAK-STAT cascade, endothelial cell migration, et al. Among these genes, FOS and STAT3 seem like play an important role in both WT and Δ dbl-GATA group. Further enrichment analysis revealed that immune system process, immune response, cell adhesion, cell differentiation etc. changed obviously. Jak-STAT, PI3K-Akt, MAPK, NF- κ B, p53, TGF- β signaling pathway, Wnt signaling pathway and mTOR signaling pathway were significantly enriched. No significant differences was observed in clinical manifestation although these differential genes.

Two key genes, Fos and Stat3 were identified.

Conclusions: We speculated that eosinophils are immune regulated cells which served as a secondary, accelerated effect. Fos and Stat3 may be necessary in MC903 induced atopic dermatitis.

PT07

IL-17A producing ILC3s are increased in murine Atopic dermatitis mode

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Background: The skin constitutes the interface between the organism and the environment. The immunological barrier of the skin comprises both innate and adaptive immune system. During past several years, it has become clear that innate lymphoid cells (ILCs) play a role in homeostasis and inflammation of the skin in humans and mice. The ILCs lack expression of antigen-specific receptors as those expressed by T and B cells and are activated by specific cytokines. In the skin, ILC are well placed to sense keratinocyte-derived danger signals in an antigen-independent manner. Recent findings link ILC2 to atopic dermatitis (AD) and ILC3 to psoriasis

Objective: The goals of this study were to investigate whether ILCs are involved in house dust mite (HDM) induced atopic dermatitis (AD) and to look for molecular mechanisms of activation of ILCs.

Methods: We applied *Dermatophagoides farinae* extract (HDM) to the barrier-disrupted skin of NC/Nga mice twice a week for 2 weeks. Skin samples were obtained from dorsal back skin or ears to analyse ILCs and signals that stimulate ILCs. Flow cytometry, quantitative PCR and histology were used to identify, and quantitate ILCs and various cytokines.

Results: The prevalence of ILCs in skin was greater in the AD induced mice than in the control. The cell population with phenotypic ILC characteristics, lineage⁺ CD45⁺ cells was also increased in AD induced mice. ILCs from skin with AD produced significantly larger amounts of IL-13 as well as IL-17A. Unexpectedly, IL-17A producing ILC3s were dominant than IL-13 producing ILC2s at the site of inflamed skin. Moreover, blockade of IL-17A reduced symptom of AD in Nc/Nga mice.

Conclusions: IL-17A producing ILC3s are increased in HDM induced AD mice, suggesting potential role of ILC3s in the immune-pathogenesis of AD. Defining the IL-17-ILC3 axis in addition to ILC2 may represent a new target of AD.

PT08

EFFICACY AND SAFETY OF USTEKINUMAB TREATMENT IN ADULTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS – A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Background: Atopic dermatitis (AD) is the most common inflammatory skin disease, but treatment options for moderate-to-severe disease are still limited. Recent data suggest that AD is primarily immune-driven, with a strong skewing towards a Th2/Th22 response, but also with Th1 and Th17 contributions. However, the extent at which all these components contribute to the actual AD phenotype remains unclear. Whereas psoriasis has experienced a rapid development of targeted therapeutics, that also helped to define it as an IL-23/Th17 disease, specific therapeutics are not yet approved for

AD patients, and most tested agents are directed towards the Th2 axis. Ustekinumab is an IL-12/IL-23p40 antagonist that suppresses Th17 and Th22 activation, and is now commonly used to treat moderate-to-severe psoriasis.

Objective: As both acute and chronic AD lesions are associated with increased mRNA levels of IL-22 and IL-17 cytokines and associated products, we sought to assess safety and efficacy of ustekinumab in moderate-to-severe AD patients.

Methods: In this phase II, double-blind, placebo-controlled study, 33 patients with moderate-to-severe AD were randomly assigned to either ustekinumab (n=16) or placebo (n=17), with subsequent crossover at 16wks, and last dose at 32wks. Ustekinumab was given at the same dose as approved for psoriasis patients. Background therapy with mild topical steroids was allowed to promote patient retention. Study endpoints included clinical (SCORAD50) and biopsy-based measures of tissue structure and inflammation, using protein and gene expression studies.

Results: The ustekinumab group achieved higher SCORAD50 responses at 12wks, 16wks (the primary endpoint), and 20wks compared to placebo, but the difference between groups was not significant. Optimal clinical responses were observed 8wks after the administration of the second dose.

The AD molecular profile/transcriptome showed early robust gene modulation, with sustained further improvements until 32wks, only in the initial ustekinumab-group. Distinct and more robust modulation of Th1, Th17 and Th22 but also Th2-related AD genes was seen after 4wks of ustekinumab treatment (i.e. MMP12, IL-22, IL-13, IFN- γ , elafin/PI3, CXCL1, CCL17; $p < 0.05$). Epidermal responses (K16, terminal differentiation) showed faster (4wks) and long-term regulation (32wks) from baseline in the ustekinumab-group. No severe adverse events were observed.

Conclusions: Ustekinumab had clear clinical and molecular effects in moderate-to-severe AD, but conventional psoriasis dosing seems inadequate for AD, and clinical outcomes might have been obscured by a profound "placebo" effect, most likely due to background topical glucocorticosteroids. These data can be used to guide future trials with more appropriate ustekinumab dosing regimens in AD.

PT09

Atopic and non-atopic eczema: a hospital-based study

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Background: Atopic eczema (AE) is an inflammatory skin disease characterized by chronic recurrent dermatitis with profound itch. There are many differences between atopic eczema and non-atopic eczema. Most patients with atopic eczema have personal and/or family history of atopic diseases. Several criteria have been proposed for diagnosis of atopic eczema. Although the clinical features of childhood atopic eczema have been widely studied, there has been less large-scale study on adult/adolescent atopic eczema and non-atopic eczema.

Objective: To study the clinical features of adult/adolescent patients with chronic symmetrical eczema/ atopic eczema.

Methods: A hospital-based study was performed. Forty-two dermatological centers participated in this study. Adult and adolescent patients (12 years and over) with chronic symmetrical eczema or atopic eczema by clinical diagnosis were included in this study. A pre-designed questionnaire was used and completed by both patients and trained dermatologists, and the dermatologists were in charge of check, collection and signature of the completed questionnaires. The valid questionnaires were analyzed by EpiData 3.1 and SPSS 17.0 software.

Results: 2713 questionnaires were collected, and 2662 were valid (1369 male and 1293 female). According to our Chinese criteria for adult/adolescent atopic eczema, 60.3% patients were diagnosed as atopic eczema, while the other 39.7% were diagnosed as non-atopic eczema. The frequency of clinical features in atopic eczema patients were summarized as follows: pruritus (98.6%), xerosis (74.1%), disease influenced by environmental/emotional factors (73.9%), personal or family history of atopic diseases (61.4%), itching upon sweating (56.0%), flexural dermatitis (52.0%), visible flexural dermatitis (42.8%), food intolerance (38.2%), facial pallor/facial erythema (35.5%), intolerance to wool (30.2%), eczema/ atopic eczema before 12 years old (29.5%), scalp eczema/pityriasis (28.8%), urticaria/angioedema (26.8%), periauricular fissuring/eczema (25.8%), hand and/or foot dermatitis (24.7%), ichthyosis/palmar hyperlinearity/keratosis pilaris (23.3%), eyelid eczema (20.8%), eczema/ atopic eczema history before 2 years old (20.2%), perifollicular accentuation (19.5%), white dermatographism (19.0%), nummular eczema (18.4%), pompholyx of hand/foot (17.2%), liable to skin infections (16.8%), anterior neck folds (16.7%), cheilitis (15.0%), perineum eczema (14.3%), orbital darkening (11.4%), pityriasis alba (9.5%), breast eczema (7.9%), recurrent conjunctivitis (7.3%), Dennie-Morgan infraorbital fold (6.1%), anterior subcapsular cataracts (3.4%) and keratoconus (1.3%). The results showed that the incidence of most clinical features in atopic eczema was significantly higher than non-atopic eczema patients ($P < 0.05$), except the following: pruritus, white dermatographism,

Dennie-Morgan infraorbital fold and keratoconus.

Conclusions:

The clinical manifestations of atopic eczema are heterogeneous. There are many clinical features which are more frequent in atopic eczema than in non-atopic eczema.

PT10

ANTI-INFLAMMATORY EFFECT OF TOPICAL TETRACYCLINE IN ATOPIC DERMATITIS MOUSE MODEL

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Conflicts of interest: No

Background: Atopic dermatitis (AD) is the most common chronic skin disease characterized by chronic and relapsing itchy skin inflammation. Thymic stromal lymphopoietin (TSLP), highly expressed in acute and chronic AD, is considered as a new biomarker of AD. Tetracycline had shown to have anti-inflammatory properties.

Objective: The purpose of this study is to determine the effect of tetracycline on TSLP expression levels and whether the tetracycline would be an effective anti-inflammatory treatment for AD.

Methods: MC903-induced AD mouse models were used. Tetracycline 2% was applied topically on AD mice once a day for 14 days. Skin scoring of dermatitis, ear thickness and the histology image were performed to evaluate the severity of skin inflammation. Serum IgE and TSLP levels were determined by ELISA. The expression of TSLP and protease-activated receptor 2 (PAR2) were determined by Western blot. The mRNA levels of TSLP, IL-4, TNF- α and IL-1 β were measured by RT-qPCR.

Results: Topical 2% tetracycline significantly improved the skin lesions (dermatitis scoring, ear thickness and scratching frequency) and decreased the serum IgE level in MC903-induced mouse AD model. The mRNA of IL-4, IL-13 and TNF- α were also down regulated. Moreover, tetracycline significantly reduced the serum level of TSLP, and had an inhibitory effect on both TSLP mRNA and protein expression and PAR2 protein expression in lesions of mouse AD model.

Conclusions: Topical tetracycline can improve the symptoms of AD and regulate the inflammatory response, and this effect might be associated with suppressing TSLP expression through PAR2-NF- κ B pathway. Topical tetracycline might be a potential treatment for atopic dermatitis.

PT11

MODULATORY EFFECT OF VITAMIN D ON DENDRITIC CELL PHENOTYPE IN CHILDREN WITH ATOPIC DERMA-

TITIS

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Background: Dendritic cells (DCs) play a major role in the pathogenesis of atopic dermatitis (AD). Myeloid DCs (mDCs) and plasmacytoid DCs (pDCs) from adults with AD have abnormal phenotype and function, but DCs in children with AD have not been evaluated. Vitamin D (VD) deficiency has been associated with higher AD incidence and severity, and randomized trials suggest VD supplementation may improve some children with AD. VD inhibits DC differentiation, maturation and activation, but the molecular basis for VD effects on AD is unclear.

Objective: To explore phenotypic characteristics of mDCs and pDCs from children with AD and evaluate the role of VD in the modulation of DC allergic phenotype.

Methods: Phenotype of peripheral blood mDCs and pDCs was assessed by flow cytometry in 16 AD children and 9 healthy controls (HC). Expression of surface-bound IgE and its high-affinity receptor (FcεRI), co-stimulatory molecule CD86, and the cutaneous lymphocyte antigen (CLA) were assessed. Whole blood from 8 AD children was cultured with 1,25(OH)2D3 or vehicle and DC phenotype was evaluated 24h later. AD severity was evaluated by SCORAD; total IgE and 25-hydroxyvitamin D (25OHD) were measured in sera.

Results: AD patients were age 7±5 years, with SCORAD of 41±15, while HC were age 11±3 years. IgE was significantly higher in AD vs HC (513±379 vs. 44±53, $P<0.001$); serum 25OHD did not differ (29.9±7.4 vs. 28.2±6.2, $P=0.56$). In AD patients there was a significant inverse correlation between SCORAD and circulating total DCs (Rho=-0.75, $P=0.001$) and mDCs (Rho=-0.52, $P=0.04$). IgE+ and FcεRI+ pDCs and CLA+ mDCs were increased in AD patients (all $P<0.01$). Mean fluorescence intensity (MFI) of IgE and FcεRI was higher in mDCs from AD patients (both $P<0.01$). MFI of CD86 and CLA in mDCs and pDCs were not different between groups. Children with AD and low VD status (25OHD <30 ng/ml) had significantly increased FcεRI+ mDCs than children with VD sufficiency (79±10 vs. 69±14, $p<0.03$). In vitro culture with 1,25(OH)2D3 significantly downregulated FcεRI in mDCs ($p=0.02$) and surface-bound IgE in mDCs ($p=0.05$) and pDCs ($p=0.03$) of children with AD.

Conclusions: In children with AD, DC subtypes have phenotypic abnormalities, with differential expression of allergic and activation markers that participate in AD pathogenesis. Low VD in AD may be associated to increased mDC allergic activation. In vitro, VD induces tolerogenic properties in DCs from children with AD, suggesting a potential mechanism of how VD supplementation may ameliorate AD.

PT12

A Novel Human Immune System Mouse Model for Human Atopic Dermatitis

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Background: Atopic dermatitis (AD) is a chronic and relapsing inflammatory disease of skin affecting both children and

adults worldwide. Several mouse models of AD have greatly advanced the understanding of the mechanism behind and elucidated a predominant T helper type 2 (Th2) response. However, considerable differences between mouse and human immune system pose major limitations of using these models for evaluations of potential therapies. Human Immune System (HIS) mice offer significant promise for modelling human immune-related diseases. Multiple hematopoietic lineages are stably reconstituted in multiple tissues (including skin) in HIS mice. Nevertheless, human AD model is intrinsically difficult to be established in current generation of HIS mice due to 1) lack of lymph node (LN), 2) poor development human Th2 cell, 3) and rare antibody class-switching to IgE.

Objectives: To develop a novel HIS mice for modelling human AD and its subsequent treatment

Methods: A mTSLP transgene driven by keratin-14 promoter was extensively backcrossed onto the Balb/c Rag2^{-/-}IL2R-gamma^{-/-}Sirpa^{MOD} (BRGS) background to create TSLPtg-BRGS mice. Human CD34⁺ hematopoietic stem cells (HSC) were injected intrahepatically into newborn pups of TSLPtg-BRGS mice and were analysed 12 weeks later for humanization. Mice with more than 10% human cell reconstitution in the peripheral blood were further observed for the development of dermatitis and compared to control (non-tg) BRGS HIS mice.

Results: TSLPtg-BRGS HIS and non-tg BRGS HIS mice differ by two main features. First, lymphoid tissue induced (LTI) cells are increased in TSLPtg-BRGS mice which allow for robust LN development. As such, Th2 development and antibody class switching are significantly enhanced in TSLPtg-BRGS HIS mice. A second characteristic of TSLPtg-BRGS HIS is the notable development of skin inflammations that resembles AD. AD exclusively developed in TSLPtg-BRGS after 5-6 months of human cell engraftment, but not in non-humanized mice, proving the importance of human adaptive immunity in AD initiation. Extensive infiltration of human hematopoietic cells was observed in skin of TSLPtg-BRGS HIS mice, and IgE+ B cells and IgE bound human mast cells/basophils were found in draining LNs.

Conclusions:

The TSLPtg-BRGS HIS mouse model reproduced the major features of human AD. This novel HIS model with functional human immune system and spontaneous AD development provides a platform to better understand pathophysiological mechanisms for this disease and to evaluate potential new treatment modalities for AD.

PT13

Evidence of regulatory myeloid dendritic cells and circulating inflammatory epidermal dendritic cells-like modulated by Toll-like receptor (TLR)-2 and TLR7/TLR8 in adults with atopic dermatitis

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Background: Atopic dermatitis (AD) is a chronic, inflammatory skin disease, characterized by intense pruritus and xerosis. In AD, dendritic cells (DC) play essential role in tissue inflammation, especially a particular subset of myeloid dendritic cells (mDC), the inflammatory epidermal dendritic cells (IDEC). Recent data show that IDEC are also located in the dermis and produce different array of cytokines and chemokines. A better understanding about the traffic and function of these IDEC to the inflamed skin in AD remains to be elucidated.

Objective: The aim of the present study was to assess the phenotype and function of mDC and IDEC-like cells in peripheral blood mononuclear cells (PBMC) of patients with AD, regarding the cytokine response (IL-10, TNF and IFN- γ) under staphylococcal enterotoxin B (SEB) and TLR (2, 4 and 7/8) activation.

Methods: We selected 21 AD patients (aged 18-65 years; male/female: 13/8) and 21 controls (aged 21-41 years; male/female: 8/13) for phenotypic and functional ratings of mDC and IDEC-like cells in PBMC. Expressions of Fc ϵ RI, CD36, TNF, IFN- γ and IL-10 in mDC were analyzed, under stimuli of staphylococcal enterotoxin B (SEB), TLR2 (Pam3CSK4), TLR4 (LPS) and TLR7/8 (CL097) agonists by flow cytometry.

Results: Main findings of AD patients included: enhanced IL-10 frequency in mDC under TLR4 (LPS) stimuli; elevation of IDEC-like cell frequency with TLR2 (Pam3CSK4) stimuli, augmented *ex vivo* frequency of IFN- γ , and of IL-10 with TLR7/8 (CL097) stimuli of IDEC-like population.

Conclusions: The characterization of an IDEC-like population in AD shows pro-inflammatory profile in *ex vivo* condition,

influencing the adaptive response. In addition to this inflammatory role, the findings suggest a regulatory impact on T cells through IL-10, induced by the agonist mimicking single stranded RNA virus. The present study corroborate the relevance of IDEC-like cells in the perpetuation of inflammation in AD through skin homing, and reinforces the need for a better understanding of the basis of its pathogenesis, including the contribution of viral infections for disease perpetuation.

PT14

ASSOCIATIONS OF SINGLE NUCLEOTIDE POLYMORPHISMS OF CORNULIN, REPETIN AND SMALL PROLINE- RICH PROTEINS WITH ATOPIC DERMATITIS RISK AND COURSE

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Background: FLG mutations are well known risk factor of AD. It appears that disturbances in the genes encoding cornified envelope proteins other than FLG are involved in AD pathogenesis.

Objective: Search for associations between SNPs of cornulin (*CRNN*), repetin (*RPTN*), small proline-rich proteins (*SPRR1A*, *SPRR1B*, *SPRR3*) genes and AD course and risk, also independently of filaggrin (*FLG*) mutations.

Methods: In the groups of 159 AD patients and 108 healthy volunteers polymorphisms in *CRNN* gene (rs941934), *RPTN* gene (rs2845544), mutations in *FLG* gene (R2447X, S3247X) were analyzed by TaqMan Genotyping Assay, polymorphisms in *RPTN* gene (rs28441202, rs3001978, rs12117644), *SPRR1A* gene (rs1611753, rs1611764), *SPRR1B* gene (rs2070964), mutations in *FLG* gene (2282del4, R501X) were analyzed by PCR-RFLP method, polymorphisms in *SPRR3* gene (rs28989168) by allele-specific PCR.

Results: We have found 26 heterozygotes and 5 homozygotes of 2282del4, 2 heterozygotes of S3247X, no carriers of R501X or R2447X FLG mutations. 2282del4 FLG mutation enhanced AD risk nearly 3 times ($p=0,015$; $OR=2,97$) and was associated with AD severity ($p=0,045$), elevated IgE levels ($p=0,035$), eosinophilia ($p=0,016$). A-allele of *CRNN* (rs941934) enhanced AD risk 2 times ($p=0,0076$; $OR=2,09$) and was associated with severe course of AD ($p=0,04$), elevated IgE levels ($p=0,05$), eosinophilia ($p=0,02$) and concomitant asthma ($p=0,026$). CC genotype of *RPTN* (rs3001978) enhanced AD risk nearly 0,4 times ($p=0,042$; $OR=0,38$). The patients with CC genotype of *RPTN* (rs3001978) presented stronger pruritus than those with CT genotype ($p=0,02$). AA genotype and A-allele of *RPTN* (rs28441202) were associated with early onset of AD ($p=0,025$; $p=0,005$). CC genotype of *SPRR1B* was associated with elevated IgE levels ($p=0,01$). After excluding carries of FLG mutations the CC genotype of *RPTN* (rs3001978) was associated with severe course of AD ($p=0,05$) and concomitant asthma ($p=0,04$), *SPRR1B* with elevated IgE levels ($p=0,005$) and an extra 24-bp repeat in the central domain of *SPRR3* with early onset of AD ($p=0,02$).

Conclusions: Our results indicate SNPs of *CRNN* (rs941934) and *RPTN* (rs3001978) genes may be a new important factors in AD pathogenesis influencing AD risk and course, at least in the Polish population. Further studies are needed to confirm usefulness of these polymorphic variants as the prognostic, genetic markers in AD.

PT15

ATOPIC DISEASES AND EPITHELIAL CANCERS IN PATIENTS WITH ICHTHYOSIS VULGARIS

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Background: Ichthyosis vulgaris (IV) is a hereditary scaling skin condition due to inherited loss-of-function mutations in the gene encoding the epidermal structural protein, filaggrin. While the association between IV and atopic dermatitis is well established, whether filaggrin deficiency alone determines non-atopic comorbidities is unknown.

Objective: To investigate the association between IV and selected barrier and non-barrier-related comorbidities such as

atopic disorders, skin cancer, and HPV-related cancers in a nationwide population data base.

Methods: All Danish citizens between 1997 and 2012 with a diagnosis of IV were identified (n=323), and matched with controls. Conditional logistic regression was used to compute odds ratios (ORs) with 95% confidence intervals.

Results: IV was significantly associated with atopic dermatitis (adjusted OR=107.42; 78.58-146.84), asthma (adjusted OR=1.84; 1.27-2.67), non-melanoma skin cancer (adjusted OR=3.59; 1.83-7.03), actinic keratosis (adjusted OR=6.05; 1.84-19.96), and cervical cancer (adjusted OR=12.79; 2.78-58.78).

Conclusions: Our study suggests that complete epithelial flaggrin deficiency predicts an increased risk of certain epithelial cancers, warranting a new awareness of possible comorbidities in patients with IV.

PT16

The Effects of Emollients on Skin Barrier Function – A framework for Comparator Trials

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Background: Moisturizer use is a mainstay of treatment in atopic dermatitis (AD), and is currently also investigated for the primary prevention of the disease. Newly developed emollients contain ingredients purported to improve the skin barrier function, however studies directly comparing the skin barrier effects of different emollient formulations are missing in the literature.

Objective: In order to design future emollient comparison trials, our objective was to estimate the effect that routine over-the-counter emollients have on various skin barrier parameters. These data provide a framework for future research aimed at identifying the optimal emollients and treatment regimen for this patient population.

Methods: Using a randomized observer-blind forearm-controlled study design, adult subjects with clear to moderate AD were randomized to apply one of four emollients (Cetaphil Cream, Aveeno Eczema Therapy Moisturizing Cream, CeraVe Moisturizing Cream and Vaseline 100% Pure Petroleum Jelly) to non lesional skin on one arm and no emollient to the opposite arm for four weeks. Skin barrier measurements were made at baseline and at four weeks and included capacitance, pH and trans-epidermal water loss (TEWL) before and after tape stripping.

Results: Overall 22 patients with AD participated in the study. When grouped together, emollients had the following effects in treated Vs. non-treated arms at 4 weeks (paired t-test): Mean capacitance increased (43.3 Vs 38.6 arbitrary units, p=0.0027); mean pH increased (5.61 Vs 5.36, p=0.001); mean TEWL decreased (10.65 Vs 11.6 g/m²h, p=0.19); mean post-tape stripping TEWL decreased (30.6 Vs 32.7 g/m²h, p=0.5). We observed similar effects per emollient, yet other than Cetaphil cream these effects were not statistically significant probably due to a lack of power. Comparing skin barrier functions of the treated arms at baseline to measurements conducted on the same arms following 4 weeks of treatment yielded a similar direction of effect without reaching statistical significance.

Conclusions: Even simple and cost-effective emollients can lead to improvements in some skin barrier parameters. However, the observed effect sizes were small. Skin hydration may be the parameter most readily changed by emollient therapy. The unexpected increase in pH we observed after emollient application needs to be reproduced and further examined. Comparison to baseline in emollient studies may not be the best approach given the variability in measurement over time. Comparing treated to non-treated arms at the same visit may be a superior approach. The data generated by this study will help design and power future studies comparing emollients.

PT17

CHARACTERISATION OF THE SKIN BARRIER DEFECT IN ATOPIC DERMATITIS USING *IN VIVO* ATR-FTIR MOLECULAR SPECTROSCOPY

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Background: Attenuated total reflectance (ATR)-Fourier transform infrared (FTIR) spectroscopy is a molecular spectroscopic technique that can be used to investigate the surface properties of human skin *in vivo*.

Objective: To compare the molecular structure of the skin of atopic dermatitis (AD) patients to the skin of healthy controls non-invasively using a fibre-based FTIR device.

Methods: In a cohort of 56 patients with AD, and a control group of 20 volunteers with healthy skin (no skin conditions or atopy), the clinical and biophysical properties of six different skin sites (cubital fossa, volar forearm, wrist, back of hand, palm, and lower leg) were assessed. The levels of urocanic acid, pyrrolidone carboxylic acid and free amino acids, were determined in tape-strip samples taken from the volar forearm as a measure of natural moisturising factor (NMF) levels. All participants were genotyped for the 5 most common European filaggrin gene mutations.

Results: The FTIR spectra of AD patients exhibited prominent changes at several wavelengths associated with the components of natural moisturising factor (1600, 1410, and 1340 wavenumbers). Absorbance at 1340 cm^{-1} correlated significantly with NMF levels determined at the volar forearm ($r=0.7705$, $p<0.0001$) and was further evaluated as an AD biomarker. The highest absorbance at 1340 cm^{-1} was observed on the cubital fossa, followed by the forearm, wrist, back of hand, palm, and leg in decreasing order. On the forearm FTIR determined NMF levels increased 4-fold with increasing depth into the stratum corneum (SC), achieved by repeated tape-stripping. Throughout the depth of the SC, NMF levels were on average 29% lower in AD patients compared to controls. The difference between AD patients and controls was lowest at the surface (5.574 ± 0.289 AU compared to 7.195 ± 0.677 AU). Similar FTIR measurements at the surface of the cubital fossa revealed highly significant differences ($p<0.0001$) between patients (7.968 ± 0.554 AU) and controls (12.347 ± 0.831 AU). Moreover measurements on the cubital fossa could predict the presence of filaggrin gene mutations (ROC area under the curve $86\pm 0.03\%$). FTIR determined NMF levels were significantly correlated with disease severity (SCORAD, $r=-0.5529$, $p<0.0001$), visual dryness ($r=-0.7117$, $p<0.0001$), erythema ($r=-0.6220$, $p<0.0001$), skin hydration ($r=0.5146$, $p<0.0001$), TEWL ($r=-0.4509$, $p<0.0001$), skin surface pH ($r=-0.3687$, $p<0.0001$) and SC lipid structure (determined by FTIR, $r=0.5678$, $p<0.0001$).

Conclusions: ATR-FTIR is a useful technique for the rapid and non-invasive characterisation of the skin barrier defect in AD.

PT18

THE NEONATAL EPIDERMAL BARRIER: DEVELOPMENT OF SUPERFICIAL CHYMOTRYPSIN-LIKE PROTEASE ACTIVITY AND NATURAL MOISTURISING FACTORS

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Background: The infant stratum corneum (SC) is thinner, and immature in both structure and function compared to adults throughout the first year of life. This vulnerable period coincides with the onset (<1 year of age) of skin manifestations such as atopic dermatitis. From birth, the SC enters a maturation phase of rapid hydration and acid mantle formation. Considering the reported homeostatic action of these functional properties, the observations suggest underdeveloped or transitional mechanisms underlying neonatal epidermal barrier differentiation and desquamation.

Objective: To monitor the functional properties of the SC throughout the neonatal period, in conjunction with the determination of superficial chymotrypsin-like protease activity (such as kallikrein-7 [KLK-7]) and the level of filaggrin-derived natural moisturising factors (NMF).

Methods: Full-term, healthy neonates ($n=115$) recruited to the oil in baby skincare (OBSerVe) randomised controlled trial underwent a full SC assessment at birth (<72 hours old) and at 4 weeks of age ($n=39$, no oil control group) using a portfolio of minimally invasive instrumentation, techniques and methodology. To place the results in neonates into context, a cohort of unrelated adults ($n=20$) was recruited.

Results: In conjunction with the increase in SC hydration and skin-surface acidification over the neonatal period, transepidermal water loss (TEWL), superficial KLK-7 activity and NMF significantly elevated from birth beyond the levels observed in adult skin. At birth, KLK-7 activity and NMF both significantly correlated with TEWL ($r=0.26$ [KLK-7]/ -0.38 [NMF]), SC hydration ($r=-0.30/0.50$) and skin-surface pH ($r=0.25/-0.54$). Neonates with impaired epidermal barrier function at birth (>75th percentile TEWL) demonstrated significantly elevated KLK-7 activity (1.41 nU/ μ g) and reduced levels of NMF (139.80 nmol/mg) compared to subjects within the lower TEWL percentiles (KLK-7: 0.90 nU/ μ g; NMF: 277.90 nmol/mg).

Conclusions: The biophysical, biological and functional properties of the developing neonatal SC are transitional from birth to 4 weeks of age and differ to adults. The elevation in KLK-7 activity during this period occurs via a mechanism seemingly independent from skin-surface pH. The presence of impaired barrier function with elevated protease activity and reduced NMF at birth suggests why certain infants are predisposed to epidermal barrier breakdown and the development of AD.

PT19

HIGH MOBILITY GROUP BOX 1 (HMGB1) PROTEIN DOWNREGULATES FILAGGRIN GENE TRANSLATION AND PROTEIN EXPRESSION, IMPAIR STRATUM CORNEUM FORMATION, AND REDUCE EPIDERMAL GROWTH

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Background: Since the discovery of increased susceptibility to atopic dermatitis (AD) due to filaggrin gene mutations, the regulation of this gene and the encoded protein has been of major interest. Mutation or not – all patients with AD have decreased levels of filaggrin in the upper epidermis in part explained by the influence of pro-inflammatory cytokines. The epidermal derived “alarmin” high mobility group box 1 (HMGB1) protein is upregulated in the skin of AD patients. HMGB1 has dual functions possessing both pro-inflammatory capacities as a cytokine and significant transcriptional repressor properties as an intracellular nuclear factor.

Objective: We investigated the possible impact of HMGB1 on gene transcription, protein expression and epidermal differentiation across three distinct keratinocyte *in vitro* models.

Methods: Primary keratinocytes from healthy donors were used in submerged monolayer cultures, 3D human epidermis equivalents and 3D human skin equivalents. All keratinocyte models were subjected to 96 hours stimulation with HMGB1 (100 μ M) using IL-4 (50 ng/mL) as positive control of regulation and vehicle as negative control. RT-qPCR of 16 gene targets including 8 from the epidermal differentiation complex e.g. filaggrin, involucrin and loricrin was performed alongside immunohistochemistry to evaluate protein expression and lastly Ki67 and HE staining to assess proliferation, growth and stratum corneum formation.

Results: Stimulation with HMGB1 (100 μ M) significantly downregulated the gene transcription of filaggrin, involucrin and loricrin across all three keratinocyte models. Immunohistochemical staining revealed that HMGB1 stimulation significantly downregulated the filaggrin and loricrin expression in the upper epidermis surprisingly surpassing the effects observed from IL-4. However, involucrin was not convincingly regulated. HMGB1 increased the Ki67 positive nuclei count compared with the negative control, albeit significantly decreased total epidermal thickness, epidermal thickness w/o stratum corneum and lastly diminished stratum corneum formation.

Conclusions: We believe that HMGB1 plays a significant role in the AD pathophysiology due to negative regulation of structural proteins, stratum corneum formation and epidermal growth. HMGB1 may contribute to an aggravation of the skin barrier dysfunction in atopic dermatitis, and could be of great interest in the scientific and clinical community.

PT20

AN ORGANOTYPIC MODEL FOR ASSESSING SKIN BARRIER FUNCTION GIVES EVIDENCE OF FUNCTIONAL EFFECT FOR THE ECZEMA CANDIDATE GENE C11ORF30

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Background: Skin offers unique opportunities for translational research because this organ can be cultured *in vitro*, but models require careful optimisation for the study of disease-specific mechanisms. Genome-wide association studies have consistently replicated an eczema risk locus on chromosome 11q13.5 which acts independently of the well known mutations in the gene encoding filaggrin (*FLG*). However, the most strongly associated variant at 11q13.5 lies within an intergenic region >38kb upstream of the nearest candidate gene, *C11orf30*. *C11orf30* encodes EMSY, a nuclear protein involved in transcriptional regulation; variants have been associated with asthma and inflammatory bowel disease but its role in skin is unknown. Our previous transcriptome analyses have shown significant down-regulation of *C11orf30* mRNA in atopic skin.

Objective: We aimed to optimise a skin organotypic culture model to produce a functional barrier with measurable parameters of relevance to atopic eczema; we then used this model to investigate the effects of *C11orf30* knockdown on epidermal barrier function.

Methods: Human primary keratinocytes were extracted from skin samples and plated on to a dermal equivalent composed of fibrin matrix with matched-donor primary fibroblasts and lifted to the air-liquid interface to stimulate differentiation and barrier formation. *C11orf30* expression was knocked down using siRNA (Dharmacon). Barrier function was assessed using dye penetration (lucifer yellow CH dilithium salt, Sigma Aldrich) and transepidermal water loss. The model with *C11orf30* knockdown was compared with an established *FLG* knockdown model as well as untreated and non-targeting controls.

Results: We have achieved *C11orf30* knockdown in human primary keratinocytes and importantly the knockdown persists to day 10 in organotypic cultures, as demonstrated by quantitative PCR (mean 67% knockdown compared with non-targeting controls) and Western blotting. Histologically, *C11orf30* knockdown is associated with thickening of the stratum corneum and parakeratosis. Functionally, *C11orf30* knockdown results in increased dye penetration after 4 hours in comparison to controls, similar to the dye penetration in *FLG* knockdown models reported previously. Transepidermal water loss measurements also show profound differences in the *C11orf30* and *FLG* knockdown models compared to controls.

Conclusions: We have optimised an organotypic skin culture model to assess the functional effects of genes that may play a role in the barrier dysfunction that characterises atopic skin. Preliminary data support *C11orf30* as an eczema risk gene and provide, for the first time, evidence of the effect of EMSY on skin barrier formation, indicating a possible mechanism in the aetiology of atopic eczema.

PT21

EFFECT OF WATER HARDNESS AND SEASON OF BIRTH ON THE PREVALENCE OF ATOPIC DERMATITIS IN YOUNG CHILDREN: A STUDY WITHIN THE DANISH NATIONAL BIRTH COHORT

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Background: Previous studies have proposed an increased prevalence of atopic dermatitis in children living in regions with hard domestic water as well as in children born in the fall and winter.

Objective: To evaluate a possible association between atopic dermatitis and, respectively, domestic water hardness and season of birth in a large cohort of children. Moreover, to evaluate whether the presence of filaggrin gene mutations could affect this relationship.

Methods: A total of 52 950 children from the Danish National Birth Cohort were analyzed. Information on outcome and confounders were obtained from questionnaires. Water hardness data was provided by the Geological Survey of Denmark and Greenland and linked to the children's municipality code. A random subpopulation of 897 children was genotyped for the four most common filaggrin gene mutations and analyzed.

Results: Fully adjusted analyses showed a higher relative risk of atopic dermatitis in children born in the fall (aRR 1.24; 95% CI 1.17-1.31) and winter (aRR 1.18; 95% CI 1.12-1.26) than in the spring (reference group). Crude data analyses showed a lower risk of atopic dermatitis in children living in regions with the softest water (RR 0.89; 95% CI 0.80-0.99) and a higher risk in children born in regions with the hardest water (RR 1.13; 95% CI 1.01-1.28). Fully adjusted trend tests showed a 1% (aRR 1.01; 95% CI 1.00-1.01) increased risk of atopic dermatitis for each increasing degree of water hardness (range °dH 6.60-35.90). No effect of filaggrin gene mutations was found.

Conclusions: We showed that season of birth and domestic water hardness significantly affected the risk of atopic dermatitis within the first 18 months of life. The presence of filaggrin gene mutations appeared not to affect these results, but the analyses were compromised by low study power. Our findings support that exogenous stressors on the skin in early life affect the risk of atopic disease.

PT22

ADVANCES IN UNDERSTANDING ATOPIC DERMATITIS – A MORPHOLOGICAL AND FUNCTIONAL COMPARISON WITH HEALTHY SKIN

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Background: Breakdown of the skin barrier is a central event in the development of atopic dermatitis (AD). Modern imaging modalities such as Optical Coherence Tomography (OCT) provide a fast and non-invasive method of studying the skin barrier and the effects of treatments on it. A comparison of skin between AD and unaffected volunteers has never been carried out. This information will be useful for characterising the disease process and how treatments affect it.

Aim and Objectives: The aim of this study is to understand both the morphological and functional characteristics of AD skin and compare it with unaffected volunteers. For this, parameters of the skin sub-layers such as thickness and roughness were measured using OCT and quantified for comparison.

Methods: Four unaffected (no previous history of AD) and four AD volunteers were recruited with Fitzpatrick skin type between I-III. The study utilised a commercially available CE marked Fourier domain dermatological OCT system with 20kHz A-scan rate and 1300nm centre wavelength (Michelson Diagnostics Ltd., UK). OCT images were captured from skin sites such as the antebrahium, carpus, elbow, cheek, protrusion blepharochalasis eyelid and popliteal fossa. From these images, morphological parameters such as epidermal thickness and average mean roughness of both the upper-layer and epidermal-dermal junction (EDJ) were calculated using an image segmentation and analysis algorithm developed by Michelson Diagnostics. These parameters were compared between skin sites from unaffected and AD volunteers. Similarly, angiographic OCT images were acquired of the microvasculature at each skin site.

Results: The mean thickness of the epidermal layer for AD volunteers (115-170µm) was higher by 24-70% compared to unaffected volunteers (81-115µm). This thickening is supported by a lack of superficial microvasculature in the case of eczematous skin. Contrary to the hypothesis that eczema skin layers would be rougher due to scratching, the average mean roughness of upper-layer and EDJ was observed to be up to 30% lower for AD volunteers. The effect of skin swelling resulted in higher thickness and skin smoothing for AD volunteers. It was also noted, that the non-AD skin sites in AD volunteers had similar morphological parameters to unaffected volunteers.

Conclusions: Localised swelling of the skin in AD volunteers resulted in higher epidermal thickness and a reduction in vascular perfusion to the upper layers of skin. Quantification of the differences between the skin in those with and without AD is a prerequisite for studying the effects of therapies on the skin in AD.

PT23

Epidermal Overexpression of Protease-activated Receptor-2 (PAR₂) Results in Atopic-like Dermatitis *in vivo*

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Background: Activation of the protease-activated receptor-2 (PAR₂) has been implicated in inflammation, pruritus, and skin barrier regulation, all characteristics of atopic dermatitis (AD), as well as Netherton syndrome with similar characteristics. However, understanding the precise role of PAR₂ has been hampered by the lack of appropriate mouse models.

Objective: We used a recently established conditional mouse model with epidermal overexpression of PAR₂ (PAR₂OE) to study the spontaneous and inducible effects of epidermal PAR₂ upregulation and stimulation on skin inflammation, itch, and barrier dysfunction in AD, *in vivo* and *ex vivo*.

Methods: PAR₂OE and littermate WT mice were characterized by a wide array of dermatological, neurophysiological, and immunological assays. Repeated topical application of house dust mites (HDM) was performed to mimic the well-known disease exacerbation in AD patients after HDM exposure

Results: PAR₂OE newborns display no overt abnormalities, but spontaneously develop dry skin, severe pruritus, and eczemas. Dermatological, neurophysiological, and immunological analyses revealed the hallmarks of AD-like skin disease. Skin barrier defects were observed before onset of skin lesions. Application of HDM onto PAR₂OE mice triggered pruritus and the skin phenotype. PAR₂OE mice display an increased density of nerve fibers, increased nerve growth factor and endothelin-1 expression levels in the skin, which may explain our findings of a higher susceptibility of PAR₂OE mice to various pruritogens.

Conclusions: PAR₂, probably activated by exogenous and endogenous proteases, is critically involved in the pathophysiology of inflammation, barrier dysfunction, and pruritus in AD. Thus, keratinocyte-derived PAR₂ appears to be an important link in neuro-epidermal communication with the keratinocyte-protease-PAR₂ system

PT24

Non-invasive method to study pruritus in mice using iontophoresis

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Background: Pruritus is one of the major symptoms in dermatology world-wide, and its treatment is still a challenge. Different approaches are used to investigate pruritogen-induced scratching behavior and acute pruritus in mice. Difficulties for interpretation of sensory sensations such as pain versus itch derive from the fact that reactions towards pruritic and painful stimuli overlap at different locations in mice. Also, intradermal injection (i.d.) of compounds is an invasive procedure, thus can lead to misinterpretation of the effectiveness and specificity of a pruritogen and can induce pain-related behavior. These impairments of the invasive injection procedure can have significant impact on the development of a future candidate to treat pruritus. Recently, LaMotte et al. established the cheek model: pruritogens and pain mediators are i.d.

injected into the shaved skin of the cheek. Thereby the investigator has the possibility to distinguish between scratching (itch-related behavior) and whipping (pain-related behavior) in rodents. Here, we present a further advancement of the LaMotte cheek model.

Objective: To establish the efficacy of iontophoresis as a technique for cutaneous administration of pruritogens *in vivo*.

Methods: We used iontophoresis to apply pruritogens (histamine, 5-HT, SLIGRL) or an algogen (bradykinin) on the shaved skin of the cheek and monitored side-specific scratching behavior in mice. After defining the polarity of the pruritogens we applied 5-HT, SLIGRL and bradykinin from the cathode, and histamine from the anode on the shaved skin of the cheek.

Results: All tested pruritogens induced scratching behavior in mice in a concentration depending fashion. Although i.d. injection of pruritogens results in a greater scratching response per 30 min as compared to iontophoresis, non-invasive iontophoresis was well reproducible, showed significant scratching responses as compared to controls, was less invasive, non-painful and highly consistent.

Conclusions: Iontophoresis is an effective method for in-vivo testing of cutaneous pruritogens. Compared with i.d. injection it is non-invasive and non-painful. Another advantage of using this approach is that only peripheral nerve fibers become activated and can therefore distinguish between peripheral and central pathways of acute and chronic pruritus.

PT25

Proteomic evaluation of the keratinocyte secretome upon stimulation with pruritic substances

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Background: Itch (pruritus) is the most common symptom in dermatological practice, affecting 22% of the population over the course of their lives. Recent research has highlighted numerous new mechanisms behind non-histaminergic itch; a characteristic symptom of many dermatological and systemic conditions (e.g. atopic dermatitis, psoriasis, kidney and liver diseases). The exact mediators responsible for this type of pruritus have not been identified, although various substances (e.g. proteinase-activated receptor agonists, endothelin-1) have been implicated. Interestingly, a key component of these novel pathways is the interaction between various non-neuronal and neuronal cells, partly in the epidermis.

Objective: To identify novel mediators released by keratinocytes upon stimulation with pruritogenic substances using a proteomics based approach.

Methods: Normal human keratinocytes from three donors were stimulated with known pruritogens for 24hrs at near confluence (90%). Using a proteomic approach we investigated the secretome using mass spectrometry.

Results: Our results showed that the secretome of keratinocytes contains upwards of 2000 proteins, and between 160 to 1000 change significantly ($p < 0.05$) upon pruritogenic treatment.

Conclusions: Although many of these proteins are not considered to be extracellularly localized, and indeed some of them may be derived from cellular detritus, their careful evaluation may lead to the discovery of novel pruritogenic markers.

PT26

The Disease Cycle in Patients with Chronic Severe and Very Severe Itch Reported by Community Dermatologists in the United States

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Background: Severe and very severe chronic pruritus (SCP) is a frequent complaint received by dermatologists. There are few studies on the disease cycle experienced by patients with SCP.

Objective: We sought to understand the length of pruritus episodes for patients experiencing SCP symptoms as reported

by physicians.

Methods: 3,577 United States dermatologists from an AMA database were invited to participate in an email screener that queried patient load for various dermatological conditions, without revealing pruritus was the focus of the screener. 275 of 291 respondents reported 10 or more chronic pruritus patients per year. These respondents then participated in an on-line questionnaire containing 55 questions. 212 of 275 respondents completed the survey.

Results: Surveyed dermatologists reported that their patients with SCP experienced disease cycles that were 1) intermittent, with itch episodes lasting from a few weeks to a few months, 2) intermittent, with itch episodes lasting six months, or more, 3) continuous, year-round, or 4) experience with patient is too time-limited to know the disease cycle in 21%, 25%, 44% an 9% of cases, respectively.

Conclusions: Community dermatologists in the United States report that patients with severe and very severe chronic pruritus (SCP) experience lengthy disease cycles. Dermatologists indicated that in patient cases that were not too time limited to understand the disease cycle, nearly 50% (48.3%) of patients with SCP endured itch on a continuous basis

PT27

TLR3 and its role in the itch scratch cycle of nodular prurigo- new insights into innate immune pathways of peripheral itch sensitization.

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Background: Itch (pruritus) is the most common symptom in dermatology. As a defining symptom of atopic dermatitis (AD), itch is associated with very significant physical and psychological morbidity, and can lead to prurigo lesions. Our understanding of itch, and its pathophysiology is still far from complete. Toll-like receptors (TLRs) are cellular sensors designed to recognize molecular danger signals associated with exogenous or endogenous threats. Recent studies have demonstrated TLR3 to be significant in the regulation of itch signaling (Liu et al 2012, Borkowski et al 2015). A detector of double stranded RNA, TLR3 not only acts as an innate biosensor of viral pathogens but also responds to endogenous damage associated molecular patterns including RNA released from injured epidermal keratinocytes. We hypothesise that scratching, which leads to epidermal damage and the release of RNA from keratinocytes contributes to the peripheral sensitization of itch via the activation of TLR3.

Objective: In this study we aimed to: 1) Identify key itch mediators released from keratinocytes following activation of TLR3. 2) Evaluate the expression of TLR3 in chronically scratched skin of AD patients with nodular prurigo.

Methods: Normal human epidermal keratinocytes (NHEKs) from four healthy donors were treated with the ligand of TLR3 Polyinosinic:polycytidylic acid (Poly(I:C)) at different concentrations. Secretome analysis was performed at 4 and 24 hours post treatment using ELISA. Itch rating was recorded using the itch visual analogue scale. The expression of TLR3 in lesional and non-lesional was performed using immunofluorescence.

Results: Stimulation of NHEKs with Poly(I:C) resulted in release of IL-6 and Endothelin (ET), while nerve growth factor (NGF) was not detected. Immunofluorescence verified increased immunoreactivity for TLR3 in lesional skin of patients with nodular prurigo (mean VAS score 6.8), compared with perilesional (non-scratched) skin and healthy skin controls.

Conclusions: Previous studies have demonstrated that TLR3 is minimally expressed in normal skin (Baker et al 2003). In this study we have shown increased epidermal expression of TLR3 in chronically scratched, itchy skin of nodular prurigo. Kido et al 2014, demonstrated ET-1 to be an important mediator in non-histaminergic itch. It's expression was also shown to be increased in lesional skin of nodular prurigo patients. We demonstrated that NHEKs stimulated with Poly(I:C) release ET1. Therefore TLR3 may act as an important receptor in the itch-scratch-cycle, acting not only as a sensor of injured, scratched epidermal skin but also, through its increased expression and release of potent pruritogens (ET-1) and pro-inflammatory cytokines.

PT28

CASE-CONTROL STUDY OF THE ASSOCIATION OF OBESITY AND ABDOMINAL OBESITY WITH ATOPIC DERMATITIS IN CHILEAN CHILDREN

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Background: Overweight and obesity have been associated with higher rates of atopic dermatitis (AD), and some investigators have proposed recent increases in obesity as a possible explanation for concurrent increases in AD prevalence. However, studies to date show conflicting results and there is little information on this association in Latin America.

Objective: To evaluate the association of nutritional status and abdominal obesity with AD in Chilean children.

Methods: We conducted a case-control study in 101 children with AD and 101 healthy controls (HC). Overweight was defined as BMI-for-age Z-score $\geq +1$ and $< +2$ and obesity as BMI-for-age Z-score $> +2$ as per WHO standard definitions. Abdominal obesity was defined as waist circumference/height ratio (WHR) > 0.5 . AD severity was assessed by SCORAD. Eosinophil blood counts, total IgE, and 25-hydroxyvitamin D (25OHD) were measured in children with AD.

Results: Median age was 5 years (interquartile range 3-9) in cases and controls ($P=0.91$). 53% of children with AD and 48% among HC were female ($P=0.48$). No significant differences in terms of BMI Z-score were found between children with AD and HC (mean BMI-for-age Z-score $+1.1 \pm 1.3$ vs. $+1.2 \pm 1.2$, $P=0.40$). Among children with AD, 23% were overweight and 28% obese, while 28% of HC were overweight and 26% obese ($P=0.44$ and $P=0.78$, respectively). No children had undernutrition (BMI Z-score < -2). Sixty percent in each group had abdominal obesity ($P=0.95$). Girls with AD had higher rate of abdominal obesity than HC (70% vs 52%), while boys with AD had lower rate of abdominal obesity than HC (52% vs 69%), but neither comparison was statistically significant ($P=0.06$ and $P=0.09$, respectively). Children with AD had slightly lower height-for-age Z-score than HC (-0.12 ± 1.23 vs. $+0.1 \pm 0.84$, $P=0.15$), but this was significant only for children < 8 years (-0.19 ± 1.1 vs. $+0.23 \pm 0.87$, $P < 0.02$). Among children with AD ≥ 8 years, higher BMI Z-score was associated with higher SCORAD ($\rho=0.38$, $P < 0.03$), and higher BMI Z-score and WHR correlated with higher eosinophil count ($\rho=0.35$ and $\rho=0.38$, both $P < 0.05$). Higher BMI Z-score and WHR did not correlate with total IgE or 25OHD among children with AD.

Conclusions: Chilean children with AD had similar rates of obesity and abdominal obesity rates as healthy controls. In older children, obesity and abdominal obesity were associated with increased AD severity.

PT29

MEASUREMENT PROPERTIES OF QUALITY-OF-LIFE MEASUREMENT INSTRUMENTS FOR INFANTS, CHILDREN AND ADOLESCENTS WITH ECZEMA: A SYSTEMATIC REVIEW

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Conflicts of interest:

All authors are ordinary members of the HOME initiative. Christian Apfelbacher is a member of the HOME Executive Committee. Carsten Flohr is a member of the Scientific Advisory Board of HOME. Aaron Drucker is involved with the development of a novel quality of life assessment instrument for atopic dermatitis that is as yet unpublished. The authors declare that they have no other competing interests.

Background: Quality of life (QoL) is one of the core outcome domains identified by the Harmonising Outcome Measures for Eczema (HOME) initiative to be assessed in every eczema trial. There is uncertainty about the most appropriate QoL instrument to measure this domain in infants, children and adolescents.

Objective: To systematically evaluate the measurement properties of existing measurement instruments developed and/or validated for the measurement of QoL in infants, children and adolescents with eczema.

Methods: A systematic literature search in PubMed and EMBASE retrieved studies on measurement properties of eczema QoL instruments for infants, children and adolescents. For all eligible studies, we judged the adequacy of the measurement properties and the methodological study quality with the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) checklist. Results from different studies were summarized in a best evidence synthesis and formed the basis to assign four degrees of recommendation.

Results: 17 articles reporting on 24 instruments were included. While no instrument could be recommended for use in all eczema trials, the US version of the Childhood Atopic Dermatitis Impact Scale (CADIS), a proxy-reported instrument, has the potential to be recommended depending on the results of further validation studies. All other instruments, including all self-reported ones, lacked significant validation data.

Conclusions: Currently, no QoL instrument for infants, children and adolescents with eczema can be highly recommended. Future validation research should primarily focus on the CADIS, but also attempt to broaden the evidence base for the validity of self-reported instruments.

PT30

RISK OF TYPE 2 DIABETES MELLITUS IN PATIENTS WITH ATOPIC DERMATITIS: A POPULATION- BASED COHORT STUDY

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Background: Atopic dermatitis (AD) is a chronic inflammatory skin condition that has recently been associated with sedentary lifestyle. Interestingly, a higher prevalence of cardiovascular comorbidities and type 2 diabetes mellitus (T2DM) has been observed in patients with AD, but additional studies are warranted to determine the nature and cause of this relationship.

Objective: We investigated the risk of T2DM in adult patients with mild and severe AD, respectively, taking use of medication into account.

Methods: We used nationwide registers to identify adult patients with a hospital diagnosis of AD. Each patient was matched 1:5 with controls. Incidence rate ratios (IRRs) with 95% confidence intervals were estimated by Poisson regression models.

Results: A total of 27,300 patients with mild AD and 2,779 patients with severe AD were identified and matched with 148,428 controls. Patients with severe AD had a higher baseline prevalence of smoking, comorbidities such as hypertension and inflammatory bowel disease, but also use of prescription medication including topical and systemic corticosteroids, when compared to the mild AD and the reference groups. Risk of T2DM was increased in severe AD (IRR 1.39 [1.11-1.74]), however after adjustment for corticosteroid use, the estimates became non-significant (IRR 1.03 [0.82-1.29]). In patients with mild AD the adjusted risk of T2DM was significantly reduced (IRR 0.74 [0.68-0.82]). Furthermore, we found a positive dose-dependent association between potency of prescribed topical and systemic corticosteroids and risk of T2DM.

Conclusions: This study suggests that patients with severe AD have a higher occurrence of T2DM, likely due to increased

use of topical and systemic corticosteroids. Patients with mild AD have a significantly decreased risk of T2DM. Increased focus on comorbidities in patients with severe AD, and awareness of long-term adverse effects of both systemic and topical corticosteroids is warranted.

PT31

USING SOCIAL NETWORKS TO UNDERSTAND PARENT AND FAMILY PRIORITIES FOR PEDIATRIC ATOPIC DERMATITIS RESEARCH

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Background: Patient-centered research can rapidly advance our knowledge of how best to treat and manage moderate to severe atopic dermatitis in children, and help ensure that clinical insights derived from findings are relevant to, and accepted by, patients and their caregivers. This approach to research requires input and involvement from patients and families who have “lived expertise” that can inform treatment strategies and research hypotheses. Traditional methods for soliciting such input rely upon face-to-face interviews or small focus groups. However, the social web affords new opportunities for effectively and meaningfully engaging large numbers of patients and families in the research process.

Objective: To determine if the global community of parents networked via social media can be organized and utilized to provide input on priorities for research from the standpoint of parents of children with moderate severe eczema

Methods: Global Parents for Eczema Research (GPER), a collaborative of parents impacted by childhood eczema created in 2015 with support from the Patient Centered Outcomes Research Institute, embarked upon a research priority setting process in 2015. Parents who were part of a GPER Facebook group were asked to submit their priorities for research to an online database by responding to the question, “What questions about the treatment or management of moderate to severe eczema in kids would you like to see answered by research?”. To increase the size of potential respondents to a later priority setting poll, English-speaking users who self-identified as parents of children with eczema were located using the demographic micro-targeting functions of social media and Web advertising platforms. Other members of Facebook groups for parents of children with eczema (in addition to GPER) were also targeted with posts to their respective Facebook group pages. Parents identified through these strategies were then invited to participate in the 7-question online survey (poll) which was open for the period December 23 2015 to January 29, 2016. The survey asked about their top 2 choices for research study from the list of topics submitted earlier by other parents.

Results: Parents submitted 42 research topics to the online database which were culled and consolidated to remove repeats and topics that weren't research related. The 42 submitted topics addressed 16 separate themes which were ultimately included in the survey. During the 1-month period that the poll was “open”, 204 parents submitted responses and 202 were from unique IP addresses. This approach yielded broad participation from parents throughout the world: 17 total countries were represented in the survey. The survey results indicate clear preferences for patient and family-centered research: two topics were chosen by a full 70% of respondents.

Conclusions: Web-based approaches to parent and patient input afford a broader and more efficient degree of participation in research priority setting. Such approaches can highlight opportunities for partnership with families on clinical research that addresses pragmatic questions of relevance to patients and families impacted by moderate to severe eczema in kids.

PT32

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND OTHER COMORBIDITIES OF CHILDHOOD ECZEMA

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Background: Several studies have shown an association between eczema and Attention-Deficit/Hyperactivity Disorder (ADHD) although the mechanisms and time sequence remains unclear. There is limited information on the association between eczema and other mental and neurological disorders.

Objective: To explore if preschool eczema was associated with ADHD or other neurological disorders requiring pharmacotherapy in school-age, and to analyze if eczema in other ages was associated with ADHD.

Methods: From the BAMSE birth cohort 3,606 children were included in the analyses. At 1, 2, 4, 8, 12 and 16 years of age their parents answered questionnaires regarding eczema the last year. Information on prescribed medications during school-age (10-18 years of age) was derived by record linkage to the Swedish Prescribed Drug Register (SPDR).

Results: A total of 1,178 (32.7%) of the children had preschool eczema (eczema at 1, 2 and/or 4 years), and 162 (4.5%) of the children had used ADHD medication in school-age. Preschool eczema was not associated with ADHD medication in school-age (crude Odds Ratio (OR) 1.16; 95% Confidence Intervals (CI): 0.83-1.61). There were no significant association between preschool eczema and use of antidepressants, migraine drugs or antiepileptics in school-age. Infantile eczema, school-age eczema or eczema ever up to 16 years of life was not associated with ADHD medication in school-age.

Conclusions: The previously described association between eczema and ADHD could not be confirmed in this large population-based birth cohort study. In addition, there were no significant associations between preschool eczema and medications for depression/anxiety/phobia, migraine or epilepsy in school-age.

PT33

The Patient-Oriented Eczema Measure Of Eczema Severity In Young Children: Responsiveness And Minimal Clinically Important Difference

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Background: The Patient-Oriented Eczema Measure (POEM) has been recommended as the core patient-reported outcome measure for trials of eczema treatments. This recommendation is more likely to be followed by investigators planning trials of eczema treatments if the POEM's responsiveness to change can be demonstrated, and the size of a minimal clinically important difference (MCID) can be established across a range of eczema patient populations.

Objective: To assess the responsiveness to change and determine the MCID of POEM in young children using data from the Choice of Moisturiser for Eczema Treatment (COMET) trial.

Methods: COMET was a UK-based randomized feasibility trial, designed to determine the feasibility of recruiting young children (from one month to less than five years of age) with eczema from primary care into a clinical trial testing emollient treatments. Parents completed weekly Patient-Oriented Eczema Measure (POEM) and monthly Parent Global Assessment (PGA) measures. Responsiveness to change by repeated administrations of the POEM was investigated in relation to parent-recalled change using the PGA.

Five methods of determining the MCID of the POEM were employed:

- The mean change between baseline and follow-up in POEM scores for the subgroup of children identified as minimally improved (within-patient score change)
- The mean difference in POEM change scores between subgroups of children identified as minimally improved and unchanged (between-patient score change)
- The POEM score that optimally discriminates between minimally improved and unchanged subgroups of children (sensitivity and specificity method)
- The change in POEM scores between baseline and follow-up, divided by the SD of the baseline scores (effect size estimate)
- Half of the standard deviation of the baseline POEM scores.

The minimally improved and unchanged subgroups were identified by parental response to the PGA.

Results: Successive POEM scores were found to be responsive to change in eczema severity. The MCID of the POEM change score, in relation to a slight improvement in eczema severity as recalled by parents on the PGA, estimated by the within-patient score change (4.27), the between-patient score change (2.89) and the sensitivity and specificity method (3.00) was

similar to the one half standard deviation of the POEM baseline scores (2.95) and the effect size estimate (2.50).

Conclusions: The Patient-Oriented Eczema Measure (POEM) as applied to young children is responsive to change and the MCID is around 3. This study will encourage the use of POEM and aid in determining sample size for future RCTs of treatments for eczema in young children.

PT34

QUALITATIVE STUDIES IN ATOPIC ECZEMA: A SCOPING REVIEW

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Background: Atopic eczema (syn. atopic dermatitis) is very common, affecting around one in five children and one in ten adults. Despite a considerable evidence-base informing the aetiology, treatment and epidemiology of AE, there is limited qualitative research exploring the experiences of patients and carers of children living with AE. No systematic reviews have been published synthesising these experiences. Such a review may help inform clinical practice.

Objective: (1) To scope and map the existing qualitative literature on AE, and (2) to identify potential research gaps for future studies.

Methods: We searched Medline and CINAHL from inception to July 2015 for papers that had used qualitative methods of data collection and data analysis focusing on AE where participants were either patients with AE, carers of children with AE or health professionals treating AE patients. Two reviewers independently decided which studies met these criteria. Citation searching of key papers in Google scholar was conducted to identify additional papers.

Results: We screened 2153 titles and abstracts. Of these, 37 full texts were obtained and 22 papers met our criteria. The papers were on (i) parents of children with AE (n=14), (ii) adults with a mixture of skin conditions including AE (n=6), and (iii) both adults and children with AE (n=2). The papers varied widely in their aims and focus, with the largest grouping focusing on the theme of information and healthcare needs of parents of children with eczema (5 papers), revealing frustration with conventional healthcare and treatments and a mismatch between the agendas of carers and professionals. However, three of these included qualitative research as part of questionnaire development or process evaluation and reported little qualitative data. The second largest grouping focused on the theme of impact of eczema on the family (2 papers). The majority of papers used either focus groups or interviews. Although formal assessment of quality of papers was not carried out in this scoping review, it was apparent that several of the papers would not have scored highly on reflexivity, presentation of methods and results.

Conclusions: There is relatively little qualitative research into this common condition and the available literature is variable in quality and scattered in focus. Further research could helpfully focus on patients/carers' understandings of AE and its treatment and management.

PT36

THE EFFECTS OF SUPERFINE MERINO WOOL ON MILD TO MODERATE ATOPIC DERMATITIS

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Background: Atopic dermatitis (AD) affects one in four children and disease severity can be affected by clothing. Woollen clothing has been traditionally considered as an irritant to be avoided in AD, but there has been limited research to examine this claim. Wool fibres are the most strongly hygroscopic of common apparel fibres and this property may be of benefit in AD. Its physical properties, however, have been shown to vary depending on fibre diameter.

Objective: To examine the effects of superfine merino wool on mild to moderate AD in children under 3 years of age.

Methods: A 12-week, randomized, assessor-blinded, cross-over, prospective, cohort study comparing superfine merino wool ensembles with standard 100% cotton clothing in 39 patients aged 4 months to 3 years with mild to moderate AD. Recruitment took place in a paediatric dermatology outpatient clinic in Melbourne, Australia, after ethics approval. Participants were assigned to wool or cotton clothing and assessed 3 weekly for 6 weeks, before crossing over to wear the other clothing material for a further 6-week period, with similar 3 weekly reviews. The primary endpoint was the SCORAD after each 6-week period, with ADSI and IDQOL as secondary endpoints to measure AD severity and quality of life.

Results: Overall, compared with baseline, superfine merino wool ensembles were associated with a reduction in mean SCORAD (-4.4 (95% CI=-6.8, -2.1) at 3 weeks and -7.5 (-10.1, -5.0) at 6 weeks). A similar significant change was observed in ADSI and IDQOL scores. The greatest improvement was seen, during the period when wearing wool, for the group that started with cotton, when they changed to wool. Conversely, the group that started with wool showed a worsening of eczema when changed over to cotton in the second half of the study.

Conclusions: The findings support a place for superfine merino wool in the management of childhood atopic dermatitis.

PT37

Lessons from the inpatient management of refractory AD in a tertiary hospital

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Background: Atopic Dermatitis (AD) is a chronic, relapsing and inflammatory skin disease, managed on an outpatient basis. However, refractory patients evolve with potentially serious complications, requiring inpatient management. Main indications for hospitalization include erythroderma, cutaneous/systemic bacterial infections, eczema herpeticum (EH) and refractory response to treatment. In our population, bad adherence and poor social conditions are also contributing factors to hospitalization.

Objective: The objective of this study was the evaluation of clinical features, complications and evolution of hospitalized AD patients.

Methods: Thirty-seven AD patients, hospitalized at the Dermatology Ward from a tertiary university hospital from December 2013 to December 2015 were included in the study. A retrospective analysis of medical records was performed, with focus on clinical severity at admission and discharge (SCORAD and EASI), duration of hospitalization, reported bacterial or viral infections, use of systemic antibiotics, erythroderma and laboratory tests (IgE and eosinophilia).

Results: Demographic data showed 14 women and 23 men, ages varying from 10 months to 62 years old (median 16yo). Eight days was the average duration of hospitalization, and 21% of the patients (8 of 37) had history of at least one hospitalization within the last two years. As for acute complications at admission, 92% (34 of 37) of the individuals had secondary cutaneous bacterial infection, treated with first choice antibiotics such as cephalosporins or sulfamethoxazole-trimethoprim. However, 4 of 37 patients (11%) required intravenous antibiotics (three received oxacyllin and one vancomycin). Moreover, six of 37 individuals (16%) had EH, and were successfully treated with acyclovir. Analyzing AD severity, 43% (16 of 37) of the patients had erythroderma; SCORAD at admission varied from 44.2 to 85.2 (mean 75.13), and EASI varied from 8.1 to 72 (mean 38.41). At discharge, patients showed a relevant reduction of the scores: SCORAD reached 7.0-73.4 (mean 42.41) and EASI 0-47.6 (mean 18.71). Laboratory analysis demonstrated high levels of circulating IgE (mean value 20,099 IU/ml - normal up to 100 IU/mL) and eosinophilia (mean value 13,9% - normal range from 1% to 5%). Circulating IgA, IgM, IgG, C3 and C4 were also tested and remained at normal levels.

Conclusions: Refractory AD may require hospitalization. Main causes for inpatient management rely on bacterial infections, EH and erythroderma. Despite descriptions of increasing methicillin-resistant *Staphylococcus aureus* infections in the community, the majority of our population still responds to first choice antibiotics. AD refractory patients with complications reach a good recovery during hospitalization, evolving with important clinical improvement within a week.

PT38

OCULAR MANIFESTATIONS IN PATIENTS WITH ATOPIC DERMATITIS

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Background: Atopic dermatitis is a chronic inflammatory skin disease that affects genetically predisposed individuals. The incidence of atopic dermatitis in the US population varies around 3%. Ocular involvement occurs in 25% to 40% of patients. The possible eye complications in patients with atopic dermatitis are dermatitis of the eyelid, blepharitis, keratoconjunctivitis, keratoconus, uveitis, anterior and posterior subcapsular cataracts, retinal detachment and ocular herpes simplex.

Objective: The aim of this study is to analyze the symptoms and ocular findings in patients with atopic dermatitis.

Methods: Sixty-four eyes of 32 patients with atopic dermatitis were evaluated at the Outpatient Clinic of the Department of Ophthalmology at a Tertiary Hospital. Patients were referred from the Department of Dermatology of the same hospital. Patients were submitted to slit lamp examination and a questionnaire on ocular symptoms was applied. The signs and symptoms were graded from 1 (very slight or absent) to 5 (severe), and in some cases only as present or not. Descriptive and statistical analyses were performed. Inclusion criteria were confirmed diagnosis of atopic dermatitis, age between 5 and 50 years; and exclusion criteria were patients with no follow-up, patients with previous eye surgery, and contact lens users.

Results: Symptoms included itching (graded 1.8); foreign body sensation (1.33); red eye (1.26); tearing (0.69); photophobia (0.63); and ocular secretion (graded 0.4). Clinical grading for papillary conjunctivitis was 0.67; meibomitis was 0.46; and for blepharitis was 0.43. Clinical ocular findings were lid eczema in 31.1%; eyelash loss in 18.75%, eyelid margin teleangiectasia in 18.7%; and limbal Horner-Trantas nodules in 12.5% of the patients.

Conclusions: Patients with atopic dermatitis may have severe signs and ocular symptoms. Itching was the most significant symptom, followed by foreign body sensation and red eye in our patients with atopic dermatitis.

PT39

OCULAR SURFACE PROFILE IN PATIENTS WITH ATOPIC DERMATITIS

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Background: Atopic dermatitis (AD), also known as eczema, is a chronic relapsing skin disease, frequently associated with other atopic conditions, that affects children and adults. In the last years, the prevalence of AD increased steadily in developed countries, with 15-30% of children and 2-10% of adults affected. Ocular involvement in AD occurs in 25% to 40% of patients, and it is a significant cause of ocular morbidity, with eye and eyelid involvement. The most severe ocular surface manifestation of this disease has been termed atopic keratoconjunctivitis (AKC), which can cause alterations in the ocular surface of affected patients. Beyond the eyelid alterations, AKC can damage the ocular surface. The cornea is usually affected by keratitis and ulcerations that result in opacities and corneal neovascularization. The conjunctival scarring can be clinically relevant and result in atrophic conjunctiva and secondary dry eye.

Objective: The aim of this study is to analyze the ocular surface profile in patients with atopic dermatitis.

Methods: Sixty-six eyes of 33 patients with atopic dermatitis from the Department of Dermatology were examined at the Outpatient Clinic of the Department of Ophthalmology of a Tertiary Hospital. The Ethics Committee approved the study, and all subjects signed an informed consent form before being enrolled in this study. The tear film break-up time (BUT), Schirmer I test and the ocular surface staining pattern with rose Bengal and fluorescein were evaluated, according to the method of Van Bijsterveld.

Results: The Schirmer I test was 15.22 mm (SD = 8,49 mm); BUT was 8,59 seconds (SD = 2,90); vital staining score with rose Bengal was 0,67 (SD = 0,76) and with fluorescein 0,76 (SD = 0,89).

Conclusions: In the present study, patients presented milder findings in the ocular surface profile compared to world population with atopic dermatitis.

PT40

Serum levels of thymus and activation-regulated chemokine as a biomarker for atopic dermatitis

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Background: Thymus and activation-regulated chemokine (TARC) is a member of the Th2 chemokine family. TARC is over-produced in atopic dermatitis (AD) patients, and its serum levels are higher in individuals with AD than in healthy controls.

Objective: The purpose of this study was to examine whether serum levels of TARC can assess the severity of AD and be used in the clinical evaluation of AD.

Methods: A total of 41 AD patients were enrolled. Data were collected prospectively regarding age, sex, clinical skin score (Eczema Area and Severity Index [EASI]) and laboratory parameters such as TARC, LDH, eosinophil and total IgE. In addition, data from follow-up visits were collected.

Results: Mean serum TARC values were 974.6 in the mild AD group, 2656.5 in the moderate AD group and 9194.5 in the severe AD group. Compared with other laboratory parameters, the serum TARC level was significantly correlated with EASI ($P < 0.01$). In the majority of patients, TARC and EASI changed in a congruent manner during follow-up.

Conclusions: The serum TARC level may represent a suitable biomarker for monitoring of AD severity in daily practice.

PT41

THE Harmonising Outcome Measures for Eczema (HOME) STATEMENT TO ASSESS ATOPIC ECZEMA SYMPTOMS IN CLINICAL TRIALS

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Background: The profusion of outcomes for clinical trials of atopic eczema (AE) (syn. atopic dermatitis) is a major obstacle to comparing and combining studies for patient benefit. A core outcome set (COS) for AE is needed so that trials can be compared and combined. The global Harmonising Outcome Measures for Eczema (HOME) initiative has already defined clinical signs, symptoms, quality of life and long-term control as the four core outcome domains that should be measured in all AE trials.

Objective: To report the consensus process to select a core instrument to assess symptoms in AE trials.

Methods: Following the process described in the HOME roadmap, we performed two systematic reviews to (i) identify all instruments used in AE treatment clinical trials and to (ii) assess the quality of identified instruments. Both systematic reviews were supplemented by results of a patient survey and a patient pre-meeting to identify the most important symptoms. The reviews and patient information was then used as a basis for structured discussions with a group of 70 stakeholders (51.5% clinicians, 18.2% patients, 12.1% methodologists, 18.2% pharmaceutical industry representatives) from 13 countries of different parts of the world (Asia, Europe, Australia, South America, United States) at the international HOME consensus meeting (Malmö, Sweden 2015). Consensus was reached if less than 30% of the voters disagree.

Results: In total, the systematic reviews identified 18 validated instruments, five of which had sufficient evidence of va-

lidity to be considered for the final COS (paediatric Itch Severity Scale (ISS), Patient-Oriented Eczema Measure (POEM), Patient-Oriented SCORAD (PO-SCORAD), Self-administered Eczema Area and Severity Index (SA-EASI) and adapted SA-EASI). Patients in the survey and at the meeting identified itch, sleep loss, dryness, redness/inflamed skin and irritation as the most important symptoms that should be measured. Voting resulted in consensus that the Patient-Oriented Eczema Measure (POEM) should be used as the core instrument to measure symptoms (87.5% agreed).

Conclusions: All relevant stakeholders are encouraged to comply with the consensus to use POEM as the chosen instrument to measure the core domain of symptoms in all future AE clinical trials. Other instruments of interest can be used in addition to POEM.

PT42

EVALUATION OF THE MEASUREMENT PROPERTIES OF SYMPTOM MEASUREMENT INSTRUMENTS FOR ATOPIC ECZEMA: A SYSTEMATIC REVIEW

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Background: Symptoms have been identified as a core outcome domain for atopic eczema (AE) trials. Various instruments exist to measure symptoms in AE, but they vary in quality and there is a lack of standardization between clinical trials.

Objective: To systematically evaluate the quality of the evidence on the measurement properties of AE symptom instruments to inform consensus discussions within the Harmonising Outcome Measures for Eczema (HOME) initiative regarding most appropriate instruments for the core outcome domain symptoms.

Methods: A systematic literature search was performed in MEDLINE and EMBASE to identify development (inauguration) and validation studies of AE symptom instruments. The methodological quality of the included studies was evaluated using the Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist; the results of the studies on measurement properties were evaluated against predefined criteria for good measurement properties. A best evidence synthesis according to COSMIN was performed to draw an overall conclusion on quality of the instruments and to provide recommendations to inform the international consensus process in selecting the most appropriate instruments.

Results: Eighteen instruments were identified and evaluated. When the quality and results of the studies were considered, only five of these instruments had sufficient validation data to consider them for the core outcome set for the core outcome domain symptoms. These instruments had at least 2 required quality items in the best evidence synthesis, i.e. the paediatric Itch Severity Scale (ISS), Patient-Oriented Eczema Measure (POEM), Patient-Oriented SCORAD (PO-SCORAD), Self-administered Eczema Area and Severity Index (SA-EASI) and adapted SA-EASI.

Conclusions: ISS (paediatric version), POEM, PO-SCORAD, SA-EASI and adapted SA-EASI are currently the most well validated instruments for capturing patient-reported symptoms and therefore have the potential to be recommended as core symptom instruments in future clinical trials. More validation work is needed for all of these instruments. This information was used to inform the HOME consensus meeting (Malmö, Sweden 2015).

PT43

How patient-reported outcomes can be useful in routine practice in children with atopic dermatitis?

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Background: The importance of patient-reported outcomes (PROs) is increasing in research. However, there is still a lack of data to evaluate whether PROs may also be useful in routine practice to help patients to identify/monitor signs and symptoms and support shared decision-making with clinicians. In atopic dermatitis (AD), it is unclear whether the frequent collection of PROs presents a different picture of disease severity over time compared to less frequent collection of clinician-reported outcomes (i.e. a 8 week period between 2 visits) and whether capturing PROs could help patients/clinicians to predict a flare.

Objective: To compare disease severity over time using PRO data with clinician-reported data at baseline and 8 weeks. To assess to what extent capturing PRO data could predict flares.

Methods: We used data from a 12 week multicenter, randomized open label study trial aiming to assess the interest of using two emollients on flare prevention in children with AD (n=335, mean age 4.08 years (range 2.0 - 6.9)). A flare was defined as the need to escalate the treatment as assessed by the investigator. We compared areas under the curve of the Patient-Oriented Scoring of Atopic Dermatitis (PO-SCORAD) and SCORAD using Pearson correlation coefficient (r). We compared the mean PO-SCORAD score assessed in patients who had a flare in the following 7 days with those who did not have a flare using logistic regression.

Results: Despite the high correlation between PO-SCORAD and SCORAD (r=0.874), the disease severity assessed by twice-a week PO-SCORAD collection over a 8 week period was significantly higher than the severity assessed by the clinician between baseline and the 8 weeks visit (r=0.537 ; p=0.002). The mean PO-SCORAD score in patients who had a flare in the following 7 days was higher compared to those who did not have a flare (13.85 (SD 11.05) vs 7.13 (SD 7.27) (OR [IC95%] 1.07 [1.05; 1.08] (p<0.0001)).

Conclusions: We showed that the regular collection (2 times per week) of PROs described a different picture of the disease severity compared to a conventional clinician-reported assessment at each visit. Furthermore, our results suggested that capturing PROs might help patients anticipate a flare one week prior to the event and help them to potentially start anti-inflammatory treatment earlier in order to prevent the flare. Our results provided some new findings on the potential usefulness of PROs in clinical practice.

PT44

Atopic dermatitis scores for dark skinned patients

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Background: Atopic dermatitis (AD) scoring systems appeared unreliable in dark skinned patients in a previous study performed using photographs.¹

Aim: We seek to improve the validity of the previous study by performing it in real life patients and to investigate the reliability of a novel grey-scale.

Method: Twenty-five AD patients each attended a one-day scoring exercises based in either Sydney or Melbourne. Each patient was scored by 5 dermatology doctors using the Eczema Area Severity Index (EASI)², objective-Scoring Atopic Dermatitis score (oSCORAD), Physician Global Assessment (PGA) and a grey-scale composed of four shades of grey. Patients also self-completed the Dermatology Life Quality Index (DLQI) and the Patient-Oriented Eczema Measure (POEM). A Mexameter was used for their baseline melanin indices. Ten randomly chosen patients were re-scored for intra-rater reliability

testing. Reliability was analysed using the intra-class correlation coefficient (ICC). Contribution of score components to their overall variability was analysed with the co-efficient of variance (CV).

Results: There were 14 dark skinned patients (melanin index >200) and 11 light skinned patients (melanin index of ≤ 200). The inter-rater ICCs of each score were: EASI 0.83 (95% CI 0.66-0.94) in light skinned patients and 0.77 (95% CI 0.60-0.91) in dark skinned patients; oSCORAD 0.68 (95% CI 0.44-0.88) in light skinned patients and 0.74 (95% CI 0.54-0.89) in dark skinned patients; PGA 0.80 (95% CI 0.62-0.93) in light skinned patients and 0.70 (95% CI 0.49-0.87) in dark skinned patients; the grey-scale had an inter-rater ICC of 0.64 (95% CI 0.40-0.84) for dark skin patients. Intra-rater ICCs of all scores were excellent in all skin types. Separate erythema component calculations showed that erythema did not contribute to the scores' variability. The SCORAD's erythema components had higher inter-rater variations than the EASI's.

Conclusions: Life scoring patients allowed for overall superior scoring reliability than virtual scoring using photographs. The EASI score had excellent inter-rater reliability for all skin colors, while the SCORAD had good reliability for all skin colors.

PT45

EFFECT OF VITAMIN D SUPPLEMENTATION ON THE SEVERITY OF ATOPIC DERMATITIS IN CHILDREN: THE VITADROPIC RANDOMIZED CONTROLLED TRIAL

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Background: Observational studies have shown vitamin D (VD) deficiency is common among patients with atopic dermatitis (AD) and is associated with increased severity. However, results of randomized trials of VD supplementation in AD patients are equivocal.

Objective: To determine the efficacy of VD supplementation to decrease clinical severity of AD.

Methods: A randomized, double-blind, placebo-controlled trial was conducted in Santiago, Chile. We randomly assigned 101 children aged 2-17 years with active AD (SCORAD 10-103) to weekly oral vitamin D3 (VD3) or placebo for 6 weeks. Patients were recruited between May and October of 2014. Blocked randomization was used with stratification by AD severity. Weekly dose of VD3 was adjusted by age: 8000 IU for ages 2-5.9 years; 12000 IU for ages 6-11.9 years; and 16000 IU for ages 12-17.9 years. The primary endpoint was improvement in SCORAD index at 6 weeks. Analysis was performed by intention-to-treat.

Results: Mean age was 6.3 ± 4.0 years and baseline SCORAD was 32 ± 29 . Age, gender, baseline SCORAD, eosinophil count and total IgE levels were not significantly different between groups. At baseline, 57% of children were VD deficient (<50 nmol/L): 250HD was 47 ± 20 nmol/L in supplementation arm and 46 ± 21 nmol/L in placebo group ($P=0.86$). A total of 99 children (98%) completed the 6-week follow-up assessment. Change in 250HD at 6 weeks was $+43.4 \pm 34.5$ nmol/L with VD3 supplementation and $+2.3 \pm 21.2$ nmol/L with placebo ($P<0.001$); however, 46% of subjects taking placebo increased 250HD at week 6. Change in SCORAD at 6 weeks was not different between VD and placebo groups (-5.3 ± 11.6 vs. -5.5 ± 9.9 , $P=0.91$). There were no significant between-group differences in changes of total IgE, eosinophil count, or *S. aureus* colonization rate. Subgroup analysis by age, baseline 250HD, or atopic status did not reveal between-group differences in SCORAD change. Rate of adverse events and use of medical co-intervention during trial also did not differ between

groups. When reanalyzing data by change in 250HD, regardless of treatment assignment, subjects with increased 250HD between baseline and 6 weeks had significant improvement in SCORAD (-7.1 ± 9.8 vs 1.8 ± 12.1 , $P=0.02$), eczema extension ($P<0.01$) and pruritus ($P<0.01$) compared to those with stable or decreased 250HD.

Conclusions: Among children with AD, weekly VD supplementation improved VD status but did not improve AD severity significantly better than placebo, with both groups showing improvement. However, a longitudinal increase in 250HD concentration, regardless of treatment assignment, was associated with a significant reduction in AD severity. (ClinicalTrials.gov number NCT01996423)

PT46

PILOT FEASIBILITY STUDY: CHILDREN PREFERENCE IN THE CHOICE OF GALENIC FORMULATION IN ATOPIC DERMATITIS: IMPACT ON TREATMENT ADHERENCE

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Background: The prescription of an unsuitable galenic formulation can be a significant obstacle to treatment observance in AD.

Objective: We suggest that taking into account patient/parent preference in the choice of their galenic formulation is both feasible and useful for patient compliance.

Methods: A prospective, bicentric, descriptive study included children with mild to moderate AD. Feasibility, patient acceptance, autonomy and declared adherence were measured by questionnaires. Physical examination was performed at D30 and D90

• 4 different excipients were proposed according to the lipids ratio (A:21%, B:32%, C:66%, D: 88%) for emollients and topical steroid preparation.

After consent the child chose his/her favorite excipient

Results:

22 patients: 10 girls, 12 boys, (8,2 years old range 3-15), were followed during 105 days in a private practice (n=6) and in a hospital setting (n=16).

Patients choices were equally broken down into the three less greasy preparations (27% of the patients for A, 32% for B, 27% for C, 14% for D.

At D0, 91% of the patients were highly satisfied. They appreciated the simplicity and the innovative aspect of the protocol.

• The doctor's and patient's choices were different in 14 cases (64%) and similar in 8 cases (36%). The children declared that the chosen treatment was preferred to the previous imposed one at D30 and D90 in respectively 86% and 95% of the cases. Adherence was declared to be good in 73% of cases at D30 and 85% of cases at D90. A 43% improvement in the patients' SCORAD was observed at D30 and a 60% at D90. Finally, the child's autonomy, defined as the capacity to apply their local treatments on their own, was rated as 45% at D0, 72% at D30 and 70% at D90.

Conclusions:

Despite the low number of patients, the lack of a control group and a mostly qualitative assessment, this original pilot study shows that child with AD can easily choose the most suitable galenic formulation for himself/herself. The child's choice is different to the caregiver's choice in 2 out of 3 cases. Our results suggest a positive impact on patient autonomy and therapeutic adherence. We propose that caregivers should include the child in the choice of their galenic formulation. A future study with a larger number of patients and a control group will enable us to obtain more precise information on the impact of this approach on adherence.

PT47

Risk of myocardial infarction, ischemic stroke and cardiovascular death in patients with atopic dermatitis

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Background: Atopic dermatitis (AD) is a chronic inflammatory skin condition. While a possible increased risk of cardio-

vascular disease in AD patients has been suggested, it remains unknown whether the risk is explained by inflammation or lifestyle factors.

Objective: We investigated the risk of major adverse cardiovascular events (MACE), i.e., myocardial infarction (MI), ischemic stroke, and cardiovascular death in patients with mild and severe AD, respectively.

Methods: Data were collected through Danish nationwide administrative registers. Patients with a hospital diagnosis of AD were identified as cases, and matched with controls. Incidence rate ratios (IRRs) were estimated with 95% confidence intervals (95% CIs) by Poisson regression analysis.

Results: We identified 26,898 patients with mild AD, 2,527 patients with severe AD, and 145,372 matched controls. Patients with severe AD had a higher baseline prevalence of comorbidities, cigarette smoking, alcohol abuse, and medication use, respectively, compared to the mild AD and reference groups. In patients with mild AD, the risks of MI, ischemic stroke, cardiovascular death and MACE were significantly reduced in fully adjusted analyses. For severe AD, the sex- and age-adjusted IRRs were 1.39 (0.95-2.03), 1.51 (1.08-2.10), 1.46 (1.07-2.02), and 1.53 (1.23-1.91), respectively. However, in the fully adjusted analysis the estimates became insignificant.

Conclusions: Patients with severe AD had a higher prevalence of MACE when compared to controls, but this difference was explained by comorbidities and lifestyle factors. Patients with mild AD had a significantly decreased risk of MACE compared with matched controls.

PT48

Early aggressive intervention on infantile atopic dermatitis inhibits the development of food allergy

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Background: Recent studies indicated that infantile atopic dermatitis might be one of the most important risk factors for food allergy and might cause atopic march thereafter.

Objective: The aim of this study is to explore whether early intervention on the infantile atopic dermatitis might have a protective effect on the onset of food allergy in later life.

Methods: Retrospective chart survey was applied for all 26 infants who admitted for treatment of severe atopic dermatitis to the National Center for Child Health and Development, Tokyo between April 2011 and March 2013. All of them received proactive treatment with potent topical steroids and achieved sustained clearness from skin rash thereafter. They were divided into two groups of the early intervention group (EI) admitted before 5 months old, and the late intervention group (LI) admitted at 5 months old or later. Primary outcome was the incidence of food allergy in each group at 18 months of age.

Results: There were no difference between both groups in the severity of eczema on admission, age of eczema onset and parental atopic disposition. Incidence of food allergy (defined as having a positive result of food provocation test, a history of immediate reaction due to any specific food intake or any food specific IgE (immuno CAP) level higher than 50 UA/ml) in EI was 50% (6 out of 12) and that of LI was 100% (14 out of 14) ($p < 0.01$).

Conclusions: Early aggressive intervention on infantile atopic dermatitis significantly reduced the incidence of food allergy at 18 months old.

PT49

LONG-TERM SAFETY OF CRISABOROLE, A NOVEL, NONSTEROIDAL, TOPICAL, ANTI-INFLAMMATORY, PHOSPHODIESTERASE 4 INHIBITOR IN CHILDREN AND ADULTS WITH MILD-TO-MODERATE ATOPIC DERMATITIS

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Background: Atopic dermatitis (AD), a chronic inflammatory skin disease affecting children and adults, often requires long-term topical treatment. Unfortunately, topical therapies are associated with potential safety concerns and have not changed over the past 15 years. Crisaborole Topical Ointment, 2% (Anacor Pharmaceuticals, Inc., Palo Alto, CA), is a novel nonsteroidal, topical, anti-inflammatory phosphodiesterase 4 (PDE4) inhibitor currently being investigated for the treatment of AD to address the need for a more targeted and safe long-term treatment.

Objective: To assess the long-term safety results of patients as young as 2 years of age with mild-to-moderate AD who were included in an open-label extension study.

Methods: After completing a 28-day Phase 3 pivotal study (301: NCT02118766; 302: NCT02118792), patients who opted to continue treatment were enrolled in a multicenter, open-label, long-term, 48-week safety study (303). Every 4 weeks patients were assessed for AD severity using the Investigator's Static Global Assessment (ISGA) scale and were treated as needed with 4-week cycles of crisaborole. Investigators initiated each On-Treatment Period based on severity of AD (ISGA \geq 2 [Mild]). Safety measures included assessment of adverse events (AEs), serious adverse events (SAEs), vital signs, physical examinations, and clinical laboratory results.

Results: Study 303 enrolled 517 patients, who had a mean age of 11.7 years. During the open-label extension and the pivotal studies, \geq 1 treatment-emergent AE (TEAE) was reported by 65% of patients, most of which were considered unrelated to treatment (93.1%) and were mild (51.2%) or moderate (44.6%) in severity. Analysis of the frequency and severity of TEAEs over time (four 12-week treatment periods) was well balanced, indicating a favorable safety profile for long-term treatment of crisaborole. None of the 9 treatment-emergent SAEs (7 of which occurred in the extension study) were considered treatment-related. Treatment-related AEs were reported by 10.2% of patients; with atopic dermatitis (3.1%), application site pain (burning/stinging, 2.3%), and application site infection (1.2%) as the most frequently reported events. Only 33 patients (6.4%) interrupted or discontinued treatment because of TEAEs, although only 9 patients (1.7%) discontinued the study because of TEAEs during the long-term period. Review of clinical laboratory and vital sign results did not identify any safety signals. There were no cutaneous adverse reactions reported, such as telangiectasia, application site atrophy, or hypopigmentation. Crisaborole demonstrated a similar safety profile across age groups.

Conclusions: Crisaborole demonstrated a favorable safety profile for the long-term treatment of patients \geq 2 years or older with mild-to-moderate AD.

PT50

TREATMENT OF ATOPIC DERMATITIS (TREAT) REGISTRY TASKFORCE: AN INTERNATIONAL eDELPHI EXERCISE TO IDENTIFY A CORE SET OF DOMAINS AND DOMAIN ITEMS FOR NATIONAL ATOPIC ECZEMA REGISTRIES

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Background: Atopic eczema (AE) is one of the most common inflammatory skin disorders with a major impact on health-related quality of life. Moderate-to-severe patients require photo- or systemic immunomodulatory therapies to induce disease remission and long-term control. The current evidence to inform clinical management stems from a small body of clinical trials and observational studies, despite the frequent and off-label use of these treatment modalities.

Objective: Using an e-Delphi approach, the international TREAT Registry Taskforce therefore seeks to find consensus between key stakeholders internationally on a minimum set of domains and domain items to inform the design of future AE research registries that collect real world data of children and adults on photo- and systemic immunomodulatory therapies.

Methods: The TREAT Taskforce identified key domains and domain items by review within the Steering Group but also invited all e-Delphi participants to add to this list in Round 1. Participants from six stakeholder groups were invited: doctors, nurses, non-clinical researchers, patients, industry representatives and regulatory body representatives. The e-Delphi comprises 3 sequential online rounds. In each round, participants are asked to rate the importance of proposed domains and domain items. In Round 1, this is done independently, while in Round 2 the scores of others in the same stakeholder group and in Round 3 across all participants are visible, allowing participants to adjust their original score accordingly. A final consensus meeting will be held with representatives of each stakeholder group.

Results: 479 people accessed the online survey, of which 410 (86%) completed round 1. Responses were received from 335 (70%) doctors, 30 (6%) nurses, 16 (3%) researchers, 76 (16%) patients, 16 (3%) industry representatives and 6 (1%) regulatory body representatives, of in total 39 countries. Rounds 2 and 3 will follow in February and March 2016, and the results of the e-Delphi presented at the ISAD.

Conclusions: With the results of this Delphi study we will be able to identify the minimum set of domains and domain items to capture in research registries of AE in children and adults on photo- and systemic immunomodulatory therapies.

PT51

FREQUENT EMOLLIENT USE AND ATOPIC DERMATITIS ARE SIGNIFICANTLY ASSOCIATED WITH INCREASED URINARY LEVELS OF LOW MOLECULAR WEIGHT PHTHALATE METABOLITES AND PARABENS IN DANISH CHILDREN

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Background: Low molecular weight phthalate diesters and parabens are often found in cosmetic products and may have endocrine disrupting effects. Two recent studies suggested that high urinary levels of phthalates could be associated with filaggrin gene mutations and atopic dermatitis. However, it is unknown whether the difference is explained by increased use of emollients and topical medication to treat pruritic and inflamed skin, and/or whether the impaired skin barrier allows chemicals to easier penetrate.

Objective: We evaluated the relationship between filaggrin gene mutations, atopic dermatitis and use of emollients, respectively, with urinary concentrations of phthalate metabolites and parabens in Danish children.

Methods: A total of 845 Danish children between 4 and 9 years old were examined. Urinary concentrations of phthalate metabolites and parabens were determined. Children were genotyped for filaggrin gene mutations R501X, 2282del4 and R2447X. Information about atopic dermatitis and use of emollients was collected from questionnaires completed by parents.

Results: A total of 17.5% of the children reported frequent use of emollients. Phthalate metabolite and paraben levels were generally higher in children with frequent use of emollients compared to uncommon use. For example, urinary levels of monoethyl phthalates and methylparaben were, respectively, 42.2% (CI95%: 32.4-52.8%) and 253% (CI95%: 204, 310%) higher in frequent emollient users when compared to infrequent and never users. While there was no effect of

common filaggrin gene mutations, children with atopic dermatitis had 14.7% (CI95%: 8.98-20.7%) and 46.4% (CI95%: 23.9, 73.2 %) higher urinary levels of respectively, monobutyl phthalates and propylparaben when compared to children without atopic dermatitis.

Conclusion: This study showed that both emollient use and atopic dermatitis were associated with significantly increased internal phthalate and paraben exposure. While cosmetic products do not always declare their contents of phthalates and other ingredients, guidelines on (preventive) skin barrier restoration with emollients should consider the selection of chemicals and their possible endocrine disruptive effects.

PT52

IN SILICO MATHEMATICAL FRAMEWORK TO DEVISE EFFECTIVE STRATEGIES FOR EARLY DETECTION, PREVENTION AND TREATMENT OF ATOPIC DERMATITIS

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Background: Effectiveness of current treatment strategies for prevention, and induction of remission, of atopic dermatitis (AD) are yet to be confirmed, mainly due to a lack of mechanistic understanding on how genetic and environmental risk factors for AD trigger its onset and progression. An integrated quantitative understanding of the AD pathogenesis lies beyond the ethical and practical reach permitted only by the current clinical and experimental studies. Dynamical *in silico* reconstructions of the pathogenesis of AD, when integrated with the clinical and experimental studies, will help to overcome this problem by implementing an exhaustive system-level interrogation of the mechanisms for AD onset and progression.

Objective: To demonstrate the scientific and clinical utility of *in silico* predictions obtained by mathematical and exhaustive investigation of personalised effective treatment strategies to prevent the progression, and to induce the remission, of AD.

Methods: We constructed a mathematical model that describes the interplay between skin barrier function, immune responses and inflammation, which are the three main key elements contributing to AD onset and progression. We computationally simulated the AD pathogenesis of patients with different combinations of risk factors, and validated our *in silico* predictions using an AD mouse model we created by inducing epidermis-specific Stat3 mutation. The disease dynamics were evaluated by evolution of gene expression profiles and of disease markers, upon pathogenic challenges to the murine skin.

Results: Our *in silico* simulation effectively reconstructed the different stages of AD achieved by genetic and environmental risk factors: Single genetic risk factors trigger an early asymptomatic phenotype that can progress to severe clinical symptoms when environmental challenges are applied; Combinatorial existence of risk factors dramatically increase the susceptibility of the patients to develop allergy in response to environmental triggers.

To devise effective treatments for distinctive patient cohorts, classified by their risk factors and disease stages, we defined early warning signals to detect when the pro-active treatment should be applied to stop incipient AD flares in asymptomatic high-risk patient cohorts.

In silico simulation further predicted the effectiveness of preventive emollient treatment in decreasing the risk of developing AD, and the optimal treatment regimens to achieve remission of AD. Our AD mouse experiments demonstrated, in accordance with our model predictions, that severe AD symptoms develop after allergic sensitization induced by exposures to environmental challenges.

Conclusion: Our novel mathematical framework serves as an effective tool to extensively explore better treatment strategies for effective prevention of progression of AD.

PT53

IMPACT OF SEVERITY OF ATOPIC DERMATITIS ON THE QUALITY OF LIFE OF PATIENTS AND CAREGIVERS

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Background: Atopic dermatitis (AD) is a relapsing and chronic inflammatory dermatosis, with intense itch and eczematous lesions, which range from mild to severe. Several aspects of the disease and its treatment can lead to a negative impact on the quality of life of patients and their caregivers. Defining the impact of the disease on the daily life of patients and their caregivers is important for the appropriate management of dermatosis.

Objective: To assess the impact of AD on the quality of life of patients and their relatives and its relationship with the severity of the disease.

Methods: Transversal study with AD patients, selected by convenience method, from August to December 2015. Included patients that agreed to participate, during a regular follow-up visit, with age ranged 4 to 14 years old. They attended appointments and responded to questionnaires: (Children's Dermatology Life Quality Index, CDLQI) for the children and their respective caregivers (Dermatitis Family Impact Questionnaire, DFIQ). The severity of atopic Dermatitis was determined by the AD score index (SCORAD) and was graded as mild (score < 25), moderate (≥ 25 to ≤ 50) or severe (> 50). The data were analyzed using Statistica 10.0 software. Chi-square, Pearson, and Kruskal-Wallis tests were applied. The level of statistical significance for all tests was $p < 0.05$.

Results: Seventy-seven patients were included, with mean age of $8,1 \pm 2,75$ (4 to 14 years old) and 50,6% were girls. Mild, moderate, and severe AD were diagnosed in 21 (27%), 31 (40%), and 25 (32%) children, respectively. The quality of life index for patients ranged from 0 to 22, with a median of 7,0; for families, from 0 to 28, with a median of 8,0. Correlation coefficient between the SCORAD value and the quality of life was $r=0,508$ for children and $r=0,524$ for caregivers. Quality of life indexes for family according to sex of patients was $9,4 \pm 7,3$ for girls and $7,7 \pm 5,7$ for boys ($p=0,5$) and for patients was $7,9 \pm 4,9$ for girls and $7,1 \pm 4,6$ for boys ($p=0,6$). Quality of life indexes for patients according to AD severity were: $4,3 \pm 3,0$ on mild AD, $7,5 \pm 4,2$ on moderate AD and $10,2 \pm 5,2$ on severe AD ($p=0,0001$). Quality of life indexes for families were: $4,5 \pm 5,4$ on mild AD, $8,3 \pm 5,9$ on moderate AD and $12,3 \pm 7,3$ on severe AD ($p=0,0005$).

Conclusions: Quality of life indexes for patients and caregivers were inversely proportional to the severity of AD.

PT54

THE EFFECTS OF ORAL VITAMIN D SUPPLEMENTATION ON ATOPIC DERMATITIS: EVALUATION OF 42 CHILDREN IN WINTER MONTHS

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Background: Clinical and epidemiological studies have shown that vitamin D (VD) deficiency may be associated with atopic dermatitis (AD) severity. Some have suggested that VD supplementation promotes changes in immunity and in the integrity of the epidermal barrier, leading to clinical improvement in AD and representing an adjuvant treatment.

Objective: To determine the effects of vitamin D supplementation on the severity of atopic dermatitis.

Methods: A prospective study with patients under 14 years old with AD, selected by convenience, examined from June 2013 to November 2015. Disease severity was determined by the SCORAD (scoring atopic dermatitis) index and classified as mild (score <25), moderate (>25 to <50), or severe (>50). Serum VD levels were classified as sufficient (>30ng/ml), insufficient (29 to 21ng/ml), and deficient (<20ng/ml). Children with VD deficiency were treated with a 50.000 IU capsule of VD, once a week, for 4 weeks and then 15.000 IU capsule of VD, once a week, for 8 weeks. Patients with insufficient VD levels received 15.000 IU capsule of VD, once a week, for 12 weeks. All children and parents received similar education about AD and basic skin care with emollients and topical medications. Statistical analysis included the Wilcoxon and the McNemar tests.

Results: Forty-two patients met the inclusion criteria, and 24 (57,1%) were female. All of them were evaluated for the first time in the winter. Mild, moderate, and severe AD were diagnosed in 28 (66.7%), 8 (19.0%), and 6 (14.3%) children, respectively. No children had sufficient VD levels. Vitamin D deficiency was observed in 27 individuals (64.2%). Of these, 17 (63.0%) presented mild, six (22.2%) moderate, and four (14.8%) severe AD. Insufficient VD levels were found in 15 cases (35.8%), mild in 11 (73.4%), moderate in two (13.3%), and severe in two (13.3%). After supplementation, 35 patients presented mild (83.3%) and seven moderate AD (16.7%). Serum VD levels were classified as sufficient in 24 children (57.1%), insufficient in 14 (33.3%) and deficient in four (9.6%). There were no adverse effects. Median VD levels were 37 ng/ml in mild AD and 21 ng/ml in moderate, ($p<0,05$). Median SCORAD before and after VD supplementation were 23.9 e 13.0, respectively, showing a statistically significant improvement ($p<0,05$).

Conclusions: Levels of 25-hydroxyvitamin D were deficient or insufficient in all children, and vitamin D supplementation improved their atopic dermatitis.

PT55

HELPING PATIENTS LIVING WITH ATOPIC DERMATITIS

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Background: atopic dermatitis produces psychosocial and emotional involvement in patients and they family. So that, emotional support becomes necessary in all treatment phases of atopic dermatitis, and educational activities are of excellent help in disease control.

Objective: our group is working nowadays with some integrating activities with the purpose to strenght the knowledge and disease self acceptance.

Methods: working activities are, as follows: 1. Clown doctors – these activities, with clown doctors performance, who explains about atopic dermatitis through playful activities as theaters, jokes and games. There are strong children's participations in these activities. 2. Cooking activities – this space is rich in changing experiences between parents, as fun and learning for the kids. This integration between kids and food sharing, allows changes in feelings of pain and prejudice onto feelings of solidarity, compassion, love-giving, reciprocity and hope. At the moment when all the participating people, wich are AD patients or not, put their hands at the food and share it, this lets all participants to see themselves as the same manner, facing the most intimate action of human being: let the food to get into their body and so, work internally. 3. Animals assisted activities (AAA) – with participation of trained animals, in educational meetings. This activity has been show very integrative. Children have shown great interest in interacting with the dog who performs this activity. To touch and play with the dog helps to ward off animal's prejudice, which is usually strong and present.

Results: activities results in dialogue facilitation with pediatric patients, leaving to better understanding about AD.

Conclusions: there are well known good effects from playful activities in educational groups of AD. These activities comprise an efficient way to lessen the stress and turns disease in something less harmful and little bit fun.

PT56

EFFICACY AND SAFETY OF CRISABOROLE, A NOVEL, TOPICAL, NONSTEROIDAL, ANTI-INFLAMMATORY, PHOSPHODIESTERASE 4 INHIBITOR IN 2 PHASE 3 STUDIES IN CHILDREN AND ADULTS WITH MILD-TO-MODERATE ATOPIC DERMATITIS

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Background: Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by red eczematous lesions, which predominantly presents with mild-to-moderate disease severity (up to 90%). Phosphodiesterase 4 (PDE4) enzyme is overactive in inflammatory cells of patients with AD; leading to disease exacerbation.

Objective: To assess the safety and efficacy from 2 identically designed, multicenter, double-blind, vehicle-controlled phase 3 studies in patients with mild-to-moderate AD (301: NCT02118766 and 302: NCT02118792) treated with the novel, nonsteroidal, topical, anti-inflammatory PDE4 inhibitor Crisaborole Topical Ointment, 2%.

Methods: Patients ≥ 2 years old with mild-to-moderate AD were randomized 2:1 to receive crisaborole or vehicle twice daily with evaluation on Days 8 (D8), 15, 22, and 29. Primary and secondary efficacy endpoints analyzed AD disease severity based on the Investigator's Static Global Assessment (ISGA). The primary endpoint defined success in ISGA as "clear/0" or "almost clear/1" with ≥ 2 -grade improvement from baseline. Supportive efficacy endpoints examined time to improvement in pruritus, severity of pruritus, and signs of AD. Improvement in all signs and symptoms of AD was defined as "none/0" or "mild/1" with ≥ 1 -grade improvement from baseline.

Results: Studies 301 and 302 enrolled 503:256 and 513:250 crisaborole/vehicle patients, respectively. Key baseline characteristics did not differ across all groups/studies (pooled data: mean age, ~ 12 years; mean BSA, $\sim 18\%$; ISGA, $\sim 40\%$ "mild/2" and $\sim 60\%$ "moderate/3"). At D29, more crisaborole-treated patients achieved ISGA success than those treated with vehicle (301: 32.8% vs 25.4%, $P = 0.038$; 302: 31.4% vs 18.0%, $P < 0.001$), with a greater percentage of "almost clear/1" or "clear/0" ISGA scores (301: 51.7% vs 40.6%, $P = 0.005$; 302: 48.5% vs 29.7%, $P < 0.001$). Crisaborole-treated patients achieved success in ISGA and improvement in pruritus earlier than vehicle-treated patients ($P < 0.001$). For all clinical signs of AD, a greater proportion of crisaborole-treated patients achieved success by D29 (301, crisaborole vs vehicle; 302, crisaborole vs vehicle) erythema: 62.8% vs 46.1%, 54.9% vs 33.9%; induration/papulation: 57.7% vs 54.8%, -51.9% vs 40.2%; exudation: 41.0% vs 33.3%, 38.1% vs 27.2%; excoriation: 63.0% vs 51.8%, 57.2% vs 44.2%; lichenification: 51.7% vs 46.5%, 51.4% vs 35.3%). Most treatment-related adverse events (AEs) were mild and included application site pain (pooled: 4.4% vs 1.2%) and upper respiratory tract infection (pooled data: 3.0% vs 3.0%). AEs resulted in study discontinuation in 1.2% of crisaborole and vehicle patients.

Conclusions: Crisaborole represents a novel, efficacious, and safe treatment for patients ≥ 2 years of age with mild-to-moderate AD.

PT57

TOPICAL CORTICOSTEROID PHOBIA IN ATOPIC DERMATITIS: AN INTERNATIONAL VALIDATION STUDY OF THE TOP-COP SCORE

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Background: Topical Corticosteroid-phobia (TCP) is a frequent and widespread phenomenon, leading to poor treatment adherence in patients with atopic dermatitis (AD). TOPICOP score (TOPICOP CorticosteroidPhobia) is composed of 12 questions assessing the different domains of TCP (fears, beliefs and reluctant behavior to use topical steroids). TOPICOP score showed excellent psychometric properties in a previous study but needed international validation.

Objective: To evaluate the feasibility and comprehensibility of the TOPICOP score in a large international population of AD patients and to compare TCP profiles between countries.

Methods: After giving formal consent, consecutive patients (or parents of children under 7) with AD completed a TOPICOP score (maximum score: 100) before the consultation from May 2014 to August 2015. Additional questions asked included the time needed to fill in the form, the global intelligibility and the comprehensibility of each question. Data were collected using an electronic device (iPad) and uploaded via internet to the research center. Quantitative data were described using mean and SD and qualitative data using proportions. Adequate statistical tests were performed to compare the data.

Results: 1564 questionnaires were administered to patients or parents of children with AD [mean age 10.7 years (SD 12.3)] in 19 centers from 15 different countries. 1236 participants (79%) declared needing less than 5 minutes to fill in the form. The proportion of participants who declared having perfectly or very well understood the questions was 81%. Mean TOPICOP score was 45 (SD 20). Three countries (Ukraine, Poland and Taiwan) showed significantly higher TOPICOP scores compared to the mean. Five countries (Germany, Brazil, Japan, Denmark) showed significantly lower TOPICOP scores compared to the mean. Looking at the assessment of the different domains of TCP, we showed that the levels of fears were higher than the mean in Canada and Japan even though reluctant behavior scores were lower than the mean.

Conclusions: This international survey demonstrated that the 12-item questionnaire (TOPICOP) presents a good comprehensibility and feasibility despite linguistic and cultural differences. For the first time, we can assess this worldwide phenomenon using the same TCP questionnaire.

The fact that fears and behavior can diverge is evidence that all the dimensions of TCP have to be detected. Caregivers can thus propose the most personalized and convincing discourse to the patient. In the fight against the failure to treat AD, TOPICOP could be an effective tool to better manage the obstacles to treatment adherence by adapting the education to the patient profile.

PT58

PRELIMINARY RESULTS OF THE CLOTHES TRIAL: A RANDOMISED CONTROLLED TRIAL OF SILK CLOTHING FOR THE MANAGEMENT OF ECZEMA IN CHILDREN

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Background: The role of clothing in the management of atopic eczema (AE) is poorly understood.

Objective: To evaluate the effectiveness of silk therapeutic clothing over a period of six-months for children with AE.

Methods: Parallel group, randomised controlled trial of children (1 to 15 years) with moderate to severe AE recruited in five UK centres (Nov 2013 to May 2015). Randomisation (1:1) to usual care, or usual care plus 100% sericin-free, knitted silk undergarments, was stratified by age and recruiting centre and used a secure web-based system. Three sets of garments were supplied per participant (worn daily for up to 6-months). Primary outcome was assessed at baseline, 2, 4 and 6 months, by nurses blinded to treatment allocation using the Eczema Area Severity Index (EASI), which was log-transformed for analysis. Secondary outcomes included patient-reported eczema severity (Patient-Oriented Eczema Measure (POEM)) and number of skin infections.

Results: Three hundred children were randomised (42% female, mean age 5 years). EASI was assessed at least once at follow up for 282/300 (94%) children. Garments were worn for at least 50% of the time by 82% of participants in the silk clothing group. Geometric mean EASI scores at baseline, 2, 4 and 6 months were 8.4, 6.6, 6.0, 5.4 for usual care and 9.2, 6.4, 5.8, 5.4 for silk clothing. There was no evidence of any difference between the groups (ratio of geometric means averaged over study visits = 0.95, 95% CI 0.85 to 1.07). This confidence interval is approximately equivalent to a difference of -1.5 to 0.5 in the original EASI scale units. There was a small improvement in the POEM score: difference in means averaged over all follow up visits was -2.4 (95% CI -3.5 to -1.3). The number of participants reporting at least one skin infection was 39 (28%) and 36 (25%) for usual care and silk clothing respectively.

Conclusions: These preliminary results suggest that silk clothing is unlikely to provide additional benefit to usual care. Small differences in the unblinded secondary outcome (POEM) are most likely to be the result of response bias.

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EFFICACY AND SAFETY OF DUPILUMAB FOR MODERATE-TO-SEVERE ATOPIC DERMATITIS IN ADULTS: A POOLED ANALYSIS OF TWO PHASE 2 CLINICAL TRIALS

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Background: Atopic dermatitis (AD) is characterized by Th2 cytokine-mediated inflammation (interleukin [IL]-4 and IL-13). Dupilumab, a fully-human anti-IL-4 receptor- α monoclonal antibody, inhibits IL-4 and IL-13 signaling.

Objective: To evaluate safety and efficacy of dupilumab 300mg weekly in adults with moderate-to-severe AD inadequately controlled with topical agents, using pooled data from two phase 2 trials (NCT01548404; NCT01859988).

Methods: Patients enrolled in a 12- or 16-week randomized, double-blind, placebo-controlled, phase 2 study received weekly subcutaneous placebo or dupilumab. Efficacy analyses included least squares (LS) mean percent change from baseline in Pruritus 5-Dimension (5-D) Scale, pruritus Numeric Rating Scale (NRS), Eczema Area and Severity Index (EASI), and SCORing Atopic Dermatitis (SCORAD); proportion of patients who achieved EASI improvement $\geq 50\%$ (EASI-50), $\geq 75\%$ (EASI-75), or $\geq 90\%$ (EASI-90); and proportion of patients who achieved SCORAD improvement $\geq 50\%$ (SCORAD-50),

≥75% (SCORAD-75), or ≥90% (SCORAD-90). Pooled efficacy and safety were assessed through Week 12.

Results: Demographic and clinical characteristics were balanced between dupilumab (n=118) and placebo (n=115) groups. At Week 12, dupilumab resulted in significant improvement (reduction) vs placebo in Pruritus 5-D (-41.7% [1.9%] vs -9.8% [1.9%], $P<0.0001$) and pruritus NRS (-52.8% [3.0%] vs -8.0% [3.1%], $P<0.0001$), with significant improvements in both by Week 2 ($P<0.0001$). At Week 12, improvement (reduction) in EASI was greater with dupilumab than placebo (-73.6% [3.7%] vs -23.2% [3.7%]; $P<0.0001$); for SCORAD, improvement (reduction) was also greater for dupilumab versus placebo (-56.64% [2.628] vs -15.72% [2.651]; $P<0.0001$). Significantly higher proportions of dupilumab-treated patients compared with placebo achieved EASI-50 (85.6% vs 32.2%; $P<0.0001$), EASI-75 (61.0% vs 13.9%; $P<0.0001$), and EASI-90 (34.7% vs 6.1%; $P<0.0001$) responses; more dupilumab-treated patients compared with placebo achieved SCORAD-50 (62.7% vs 15.7%; $P<0.0001$), SCORAD-75 (26.3% vs 2.6%; $P<0.0001$), and SCORAD-90 (6.8% vs 0.0%; $P=0.0045$) responses. The pooled incidence of treatment-emergent adverse events (TEAEs) through Week 12 was 81.4% with dupilumab and 80.9% with placebo. The three most common TEAEs (MedDRA Preferred Term) in the dupilumab group were nasopharyngitis, (32.2% dupilumab; 22.6% placebo), headache (14.4% dupilumab; 7.8% placebo), and conjunctivitis (9.3% dupilumab; 1.7% placebo).

Conclusions: In this pooled analysis in adults with moderate-to-severe AD, dupilumab significantly and markedly improved clinical outcomes and showed early efficacy in pruritus relative to placebo, and had a favorable safety profile.

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Effects of oral and topical antibiotics in children with infected eczema in the community: The CREAM Study

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Background: *Staphylococcus aureus* is strongly associated with eczema and approximately 40% of eczema flares are treated with antibiotics. However, a recently updated Cochrane review of antimicrobials for eczema found only low quality, conflicting evidence to support antibiotic treatment for eczema flares.

Objective: To determine whether treating children with clinically infected eczema with oral or topical antibiotics in addition to treatment with emollients and topical corticosteroids is effective.

Methods: Multicentre, blinded, randomised controlled trial in general practices and dermatology clinics in the UK. Children (3 months to <8 years) with eczema (UK working party criteria) and a clinical suspicion of infection were randomised to oral flucloxacillin and topical placebo, topical fusidic acid and oral placebo, or oral and topical placebos, all for 1 week. Outcomes were ascertained at 2, 4 and 12 weeks. The Patient Oriented Eczema Measure (POEM) at 2 weeks was the primary outcome. Other outcomes included the Eczema Area and Severity Index (EASI), the Dermatitis Family Impact (DFI) instrument, quality of life, parent-rated daily symptom severity, adverse effects and skin swabs.

Results: 113 children (36 oral antibiotic, 37 topical antibiotic, 40 placebo) were randomised. The mean (SD) baseline POEM score was 15.0 (5.4), 103 (92.0%) had one or more features suggestive of infection and 78 (69.6%) had *S. aureus* cultured from the skin. Oral and topical antibiotics resulted in a 1.52 (95% CI -1.35, 4.40) and 1.49 (95% CI -1.55, 4.53) increase (worsening) in POEM score at 2 weeks respectively (relative to control and controlling for baseline POEM score). Eczema Area and Severity Index (EASI) scores were also higher (worse) in the intervention groups (0.20 (95% CI -0.12, 0.52) and 0.42 (95% CI 0.09, 0.75) for oral and topical antibiotics respectively) at 2 weeks. Analyses of impact on the family, quality of life, daily symptom scores, and longer-term outcomes were all consistent with the main findings. There were no significant differences in adverse effects.

Conclusions: We found that oral and topical antibiotics have no effect, or a harmful effect, on subjective eczema severity in children with clinically infected eczema in the community. The confidence intervals around our estimates exclude a meaningful beneficial effect (POEM MCID is 3). Most children had some evidence of infection and *S. aureus* cultured from the skin, but eczema (and infection) severity was generally mild and therefore our results may not be generalisable to children with more severe infected eczema.

A RANDOMIZED, CONTROLLED, INVESTIGATOR-BLINDED STUDY TO EXPLORE THE EFFECT OF A NEW DAILY EMOLLIENT PRODUCT ON THE MICROFLORA OF THE SKIN AFTER WASH STRESS IN HEALTHY ADULTS**Hans Stettler**¹, Peter Kurka¹, Caroline Manger², Stephan Bielfeldt², Klaus-Peter Wilhelm², Florian Brill³, Holger Lenz¹¹Bayer Consumer Care AG, Peter Merian Strasse 84, Basel, Switzerland, e-mail: hans.stettler@bayer.com, phone: +41 61 58 272 7745

Background: Skin microbes contribute to the skin's innate defense by producing anti-microbial peptides. Commensal bacteria like *Staphylococcus epidermidis* were shown to inhibit colonization and biofilm formation of *Staphylococcus aureus*. The newly developed daily emollient formula contains a prebiotic ingredient (α -oligoglucan) shown *in vitro* to selectively support beneficial cutaneous bacterial strains like *Micrococcus kristinae* and *Corynebacterium xerosis* leading to a competitive inhibition of growth of pathogenic bacteria like *S. aureus*.

Objective: The purpose of this study was to assess the influence of the test product on the microflora of the inner forearms of 20 healthy subjects after wash stress with 10% Sodium Dodecyl Sulfate and single product application in comparison to untreated skin sites.

Methods: Quantification of total bacteria as well as occurrence of *Micrococcus* and *Corynebacterium* species belonging to the commensal skin flora was performed after wash stress (baseline) and at several time points after application (2h, 4h, and 6h) by taking dermal swabs and performing microbiological methods such as culturing of microorganisms and counting colony forming units (CFU).

Results: Analysis of viable bacteria revealed that the total number of bacteria increased slightly from baseline (test product: 1.73 log CFU; untreated area: 1.59 log CFU) over the 6 hours after application of the test product (test product: 1.93 log CFU; untreated area: 1.81 log CFU). No statistically significant differences were found between the CFU differences to baseline on skin treated with test product and untreated skin at any post-treatment time point as measured after 2, 4 or 6 hours. After application of test product, the number of subjects with *Micrococcus* species on their skin increased by about 70 % (from 10 to 17 after 4h and 6h), while it remained on a comparative level on the untreated skin. The number of subjects with *Corynebacterium* species on their skin increased about 3 times (from 5 to 15 after 6h), while it only increased about 2 times (from 5 to 11 after 4h and 6h) on the untreated skin.

Conclusions: Within 6 hours after application of the new daily emollient product no influence on the total number of viable bacteria was found. A slight positive effect on the commensal skin microflora was observed, represented by an increase in the occurrence of *Micrococcus* and *Corynebacterium* species. Therefore, the new daily emollient product showed a tendency to rebalance the skin microflora after washing supporting a healthy microflora.

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