BIODERMA
CONGRESS **REPORTS**

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LEADERSHIP TRAINING WORKSHOP

Speakers: Prof. Carle Paul, Dr. Myrto Trakatelli and Dr. Lise Boussemart

Reports written by Dr. Déborah Salik

1. Objectives - shared values and participant expectations

To start, the participants introduced themselves and said what they expected to get out of the workshop.

Next, they brainstormed to establish the core values of the workshop: trust, caring, listening, kindness, indulgence, patience, firmness, respect, experience, impartiality, confidentiality, sharing emotions, honesty, self-criticism, tolerance, reflection, spontaneity, efficiency, non-judgement.

2. Leadership and emotional intelligence, leadership styles, the concept of personal impact

"Leadership is the art of persuading people to work toward a common goal" - D. Goleman

The concept of social intelligence was first brought to light by E. Thorndike.

In 1980: H. Gardner introduced the concept of multiple intelligences.

In 1990: P. Salovey and J. D. Mayer coined the term "emotional intelligence".

In 2000: R. Boyatzis and D. Goleman developed a model of emotional intelligence, broken down into domains and competencies, and evaluated and validated the tool.

How important is emotional intelligence in leadership situations?
The vast majority of the skills developed in higher education are cognitive skills. They provide a core set of technical skills leading to a diploma. Future differentiation will be based on emotional skills, i.e.

- Self-management: motivation, self-knowledge, emotional control, confidence, and a desire to grow
- Flexibility
- Communication: listening, conveying messages
- Organisational efficiency: leading projects and involving others

The dimensions of emotional balance according to R. Davidson are as follows:

- Self-awareness

- Positive outlook
- Attention
- Resilience
- Social intuition
- Sensitivity to context

There are 12 competencies of emotional intelligence:
The key domains in social and emotional intelligence are as follows:

- Ability to describe how my emotions affect my actions
- Ability to analyse the factors affecting my emotions
- Awareness of the connection between how I feel and what is happening
- Awareness of my emotions in the present moment
- Knowledge of my strengths and weaknesses

There are various styles of leadership: coercive, authoritative/visionary, democratic/inclusive, and coaching/mentoring.

The main objectives in leadership are trust, authenticity, empathy, and logic. Trust is central to building relationships in leadership.

The concept of leadership is influenced by personal impact. This is the positive or negative individual impact we have as a leader in a relationship.

There is no impact on age, gender, nationality, culture, biography or reputation, but this is part of personal impact.

However, certain aspects can be modulated: physical presence, clothing, appearance, listening skills, competence, language and choice of words, politeness, and courtesy.

3. Listening and dialogue, the attachment-separation cycle, sharing experiences as a leader

There are three levels of listening

- I listen to understand
- I listen to respond
- I listen to speak

Similarly, there are various types of listeners. We can adopt an attentive, intermittent, distracted, weak, elective, opportunistic, confirmation bias, deficit-based, contradictory, or convergent approach.

In listening and understanding, some cues can be important, such as eye contact, facial expressions, nodding, and body language. The listener should avoid interrupting and external distractions (text messages, telephone calls) should be eliminated. No judgement, no interpretation.

It is necessary to create a transition cycle and establish a connection. We attach to a secure base. We establish connections with people, values, and objectives. When change occurs, we are separated from the things and people to which/whom we are connected. We experience emotions in response to change that vary in intensity.

Unresolved grief/losses can prevent us from fully connecting with other people.

4. The principle of secure base leaders (insurance metaphor)

A secure base leader may be a person, a connection, or a goal – something that creates a feeling of protection. They are a source of energy that will inspire us and enable us to take risks and achieve fulfilment. We can take the example of a parent and their child.

The components of our secure base are essential for learning and making sense of things; they influence the way we think.

A secure base leader offers help. They are a good listener who deciphers verbal and non-verbal cues and is attentive to needs. Rather than defending a position, they ask questions to learn more. They do not think for others. *"They have unconditional positive regard toward the other person"* - C. Roger. They see potential, even if the other person does not. They are reliable and available to the other person and will encourage them if they have any problems.

5. The types of empathy

Empathy is the intuitive ability to put ourselves in another person's shoes and sense what they are feeling. It is a powerful tool for emotional intelligence.

There are three types of empathy:

- Emotional: perceiving another person's emotions, pain and perspective and the events and forces that influence them
- Cognitive: understanding their point of view
- Compassionate: responding to another person's distress with compassion

Empathy helps us understand other people and ourselves. It is essential in human relations and in doctor-patient and leader-team relationships.

It is a skill that can be developed through mirror neurons.

Here are a few techniques for cultivating empathy during a consultation:

- Smile, sit down, and be fully present
- Perceive the emotions expressed by the patient

- Non-verbal communication: attention and listening
- Verbal communication: summarise and show support, using the patient's lexicon and positive vocabulary

- Paraphrase to welcome the emotions heard
- Adapt to the person and their emotions

- For carers: adapting to patients (capacity to understand and personality type)
- Adaptation capacity varies from one carer to another
- Impact of current stress level
- Skill with endless room for improvement
- Tools: training, active listening, therapeutic communication, hypnosis, role-playing, simulation

6. Coaching

There are no right or wrong answers here.

It is important to create space to encourage exploration and ask open-ended and hypothetical questions, to redirect the attention of the person asking the question. This helps clarify the unknown and lowers the stakes when it comes to deciding whether to adopt a particular course of action; it also invites us to consider different possibilities.

There are various types of questions to ask:

- Forward-looking questions, which inspire action and move us in the direction of change.
- Reflective questions, aimed at introspection and self-reflection, encouraging us to see a person, ourselves or a situation from another point of view.
- Questions based on visualisation, which activate the imagination, make things more tangible, and bring us back to our bodies and our ability to feel.
- Appreciative inquiry, which helps us visualise what is possible, helps to eliminate real or perceived obstacles, and encourages an ideal state or positive thinking.

7. Conflict management

Conflict can be defined as a difference between two or more people, causing tension, an emotional response or disagreement when trust is broken or absent.

Conflict is caused by the breakdown of a relationship or the inability to deal with loss or grief.

Who am I when faced with a conflict?

Analyse the conflict, and identify the

- Conflict
- Conflict management style
- Other person's conflict management style
- Objectives
- Other person's objectives

What is the other person's goal? Where is the tension?

What are your areas of common interest?

To negotiate with "difficult" people, we can try using the "noble storytelling" technique, considering the:

1. Difficulties encountered by this person in their professional and personal life
2. Types of emotions this person is experiencing that are contributing to their difficulties
3. Aspects of this person that we really appreciate
4. Hopes we have for this person that would allow them to be happy and fulfilled
5. And then coming up with two or three questions in relation to this noble story

There are also eight principles of conflict management:

1. Create a connection with the other person: connect emotionally
2. Put the "fish on the table"
3. Separate the person from the problem: never create an enemy
4. Identify the needs and desires of the other person and yourself
5. Maintain a sincere desire to help the other person
6. Find a common goal
7. Find options and make proposals and concessions
8. Reach an agreement while cultivating a positive relationship

GENETICS AND GENODERMATOSES

Speakers : Dr. C. Devin, Prof. Florent Grange, Dr. Aude Nassif, Dr. Laura Fertitta and Dr. Arnaud Porquet

Report written by Dr. Déborah Salik

Role of sulphation defects in the pathophysiology of systemic mastocytosis

Mastocytosis is a disorder characterised by mast cell infiltration in organs. The WHO classification distinguishes between cutaneous mastocytosis and systemic mastocytosis (indolent, aggressive, with clonal haematological disease).

The pathophysiology is generally known as being linked to a mutation in the KITD816V gene, but this alone does not explain the different phenotypes of the disease. Other genes and signalling pathways are probably involved

This study focused on a patient with a form of congenital aggressive systemic mastocytosis, which accounts for less than 0.05% of mastocytosis cases and could be genetic in origin. He had a KIT mutation, multi-organ involvement (skin, bone marrow, liver, spleen), and recurrent anaphylaxis

An analysis of his exome found a homozygous, loss-of-function SLC26A2 variant (R279X (c.C835T, pArg279Trp). This variant is responsible for a sulphation defect in solid cancers, which probably plays a role in cancer plasticity. Inhibition of sulphation increases KIT proliferation and phosphorylation.

Sulphate reduces KIT proliferation and phosphorylation.

A second transcriptomic study in 33 patients with sporadic systemic mastocytosis showed a decrease in the PAPSS2 transcript (tumour suppressor gene).

These two genes regulate cell proliferation and tyrosine phosphorylation and could be new therapeutic targets in mastocytosis.

Knowledge and preventive habits of xeroderma pigmentosum (XP) patients in Nepal

XP is a particularly rare condition in Nepal. All the patients affected exclusively have the XPC pR415X mutation in its homozygous state, suggesting a founder effect of this mutation. This variant is characterised by the occurrence of extremely early carcinomas.

The aim of this study was to assess the preventive habits of XP patients in Nepal:

- Most families were aware of the role of the sun, but 9/30 did not know about UV rays.
- 30% of patients did not work or go to school.
- 20% applied sunscreen.
- Only two patients had a protective mask.

There is therefore a lack of knowledge as well as inadequate access to healthcare and sun protection. The obstacles are related to poverty, lack of health insurance, early school leaving, social exclusion, isolation, and distance from medical clinics. There is therefore a need to inform and educate the population (parents, families, youth workers) and put in place social and community assistance.

This study helped identify needs in order to improve the provision of care.

Identification of predicted pathogenic variants of antimicrobial response genes in isolated or syndromic hidradenitis suppurativa (HS)

The genetics of Verneuil's disease still remain unclear.

We reported an association between HS and gene variants involved in immune deficiency and/or immune response.

Regarding genetic factors, the following have been found:

- 30-40% familial forms
- Predominantly female patients
- 18 mutated genes already described in association with HS
- High-throughput sequencing of 74 candidate genes was performed in 201 HS patients. Eight homozygous variants were found, i.e. XIAP, LACCA, IFIH1, IRF2BP2, RNF213, NLRP1, OTULIN and IKBIP

A new hypothesis has been put forward: HS may be associated with immune deficiency genes.

Mortality in neurofibromatosis type 1 patients with subcutaneous neurofibromas: a case-control study

Neurofibromatosis type 1 (NF1) is an autosomal dominant genodermatosis linked to mutations in the NF1 gene (tumour suppressor gene).

There is a constant presence of tumours such as neurofibromas (NFs), which are

- Cutaneous (NFc), subcutaneous (NFsc) or deep-seated (NFp)
- Plexiform and internal neurofibromas (NFi)

Patients develop malignant peripheral nerve sheath tumours (MPNSTs), which are the main cause of death. The formation of these MPNSTs appears to be based on the conversion of NFp to dysplastic NFs.

The number of NFsc is independent of mortality, but if the number of NFsc is greater than 10, then there is a risk associated with the presence of NFi.

A risk phenotype can therefore be described in the presence of one NFi or more than 10 NFsc. The aim of this study was to investigate the mortality of NF1 patients as a function of these phenotypes.

Case-control studies in patients with at least two NFsc:

Results:

- No difference in mortality according to the number of NFsc
- No difference with NFi
- Of the 16 deaths: five MPNSTs and two cases of breast cancer.

The presence of NFsc > 2 was associated with a significant increase in mortality (five MPNSTs among the patients who died).

Vascular dysplasias in neurofibromatosis type 1 (NF1)

The prevalence of vascular dysplasias (VDs) in NF1 ranges from 0.4 to 6.4%.

The most common are renal artery stenosis and arterial aneurysm, with frequent arterial disease. The complications can include stenosis, aortic narrowing, Moyamoya disease or a life-threatening aneurysm/pseudoaneurysm.

The frequency of these abnormalities is unknown and there are no recommendations for screening.

The study presented was conducted on 123 patients with 210 vascular dysplasias.

Study results:

- The number of vascular lesions was greater in children than in adults, with multiple lesions observed.
- Cerebral and renal lesions were more frequent in adults, whereas cervical lesions were more common in children. The VDs observed tended to be stenoses or aneurysms.
- Moyamoya was in third position.
- Four of the 123 patients died.
- There was an association between optic pathway gliomas and cerebral vascular dysplasias.

In conclusion:

VD is common (18.5%) and is often asymptomatic in NF1 patients. In the event of optic pathway glioma, systematic screening for cerebral VDs is necessary. If a VD is present, screening for VDs in other regions should be performed.

GENETIC TESTING FOR MELANOMA AND SEBACEOUS CARCINOMA

Speakers: Dr. M. Saint-Jean, Dr. Lucie Peuvrel and Dr. C. Abadie

Report written by Dr. Déborah Salik

Oncogenetic consultation

The basic working tool is the patient's family pedigree, which is created during the consultation. Based on this consultation, we can determine whether there is a suspected genetic predisposition:

- if yes: a genetic analysis should be offered to the person in the family with the highest probability of prediction (index case).
- if no: the family should be advised with regard to monitoring.

The oncogenetic consultation should be carried out with the patient's agreement and informed consent.

The genetic test involves DNA sequencing from blood and a buccal smear, followed by a laboratory analysis of the DNA sequencing results, after which the patient is called in for a consultation.

The consultation takes place in parallel with a consultation with a psychologist.

If a genetic predisposition is identified:

- There is an alteration in a gene, known as a pathogenic variant or pathogenic variation (the word "mutation" is no longer used).
- This abnormality is constitutional, in all the patient's cells, with a risk of transmission to offspring.
- In oncogenetics, the predisposition gene is in one of the two copies (of maternal or paternal origin). The probability of transmission is therefore 50%, regardless of gender, and shows an autosomal dominant mode of transmission.

Classification of variants (ACMG classification):

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    - Class 5: Pathogenic

    - Class 4: Likely pathogenic
    - Class 3: Uncertain significance
    - Class 2: Likely benign
    - Class 1: Benign

If a genetic predisposition is identified, there are:

- Individual challenges requiring management and monitoring tailored to the patient (renal: MRI +++, pancreatic, multi-organ).
- Family challenges, with the possibility of (targeted) predictive genetic testing, which will help:

- Reassure relatives who are not carriers
- Propose appropriate monitoring for relatives who are carriers

It should be noted that the family has an obligation to inform other family members.

Obstacles in oncogenetic consultations include:

1. Family conflicts
2. "Secrecy" in families and filiation
3. Relevance in the absence of offspring
4. Discouragement in drawing up a family tree
5. Disease outlook

Recommendations: indications for genetic testing for melanoma

There are:

- Formal indications, i.e.
    - Melanoma before the age of 75
    - Affecting the same person or two first- or second-degree relatives
    - At least two cases of histologically verified invasive cutaneous melanoma
    - An invasive cutaneous melanoma can be replaced with: an ocular melanoma, pancreatic cancer, kidney cancer, mesothelioma or a central nervous system tumour
- Questionable indications, i.e.
    - Sporadic melanoma in a young patient (under the age of 18)
    - Melanoma associated with another cancer not mentioned above (rare, unusually early, or multiple)

Comparative views of a dermatologist and genetic oncologist

The genetic panel for melanoma is as follows: CDKN2A - CDK4 - BAP1 - MITF - MC1R - ACD - POT1 - TERT and TERF2IP

CDKN2A

- Rare variant (2% of familial forms of melanoma)
- Major predisposition gene for cutaneous melanoma
    - Cumulative risk at age 80: 58% (Europe) and 90% in Australia
    - Median age: 33-45 years
    - Risk of pancreatic cancer (adenocarcinoma)
    - Other risk?
- Monitoring from age 18, with dermatological examinations every six months

(+ initial digital video-dermoscopy at M0, M3, M12 and then half-yearly, and annual whole-body imaging)

- Smoking cessation and strict photoprotection
- From the age of 40: pancreatic monitoring alternating between endoscopic ultrasound and annual pancreatic MRI.

MC1R

- Frequent variant: 66% of patients from large cohorts of sporadic melanoma cases are carriers. It is therefore a weak-effect variant/"susceptibility gene".
- Its genotype determines the ratio of eumelanin (dark) to pheomelanin (light), responsible for phenotype.
- OR of 1.2 to 4 with additive effects of variants
- Monitoring: No particular recommendations

BAP1

Rare variant

Leading tumour spectrum

- Choroidal melanoma (28%)
- Mesothelioma (22%)
- Cutaneous melanoma (18%)
- Kidney cancer
- Median age of 43 years
- High prevalence of multiple BAP1-inactivated flesh-coloured or reddish-brown naevi, median age of 31, specific histology (epithelioid features) → Loss of BAP1 protein expression in immunohistochemistry

Monitoring from the age of 18:

- Annual fundus examination
- Lifelong half-yearly dermatological examinations (+ initial digital video-dermoscopy at M0, M3, M12 and then half-yearly, and annual whole-body imaging)
- No consensus on mesothelioma screening
- Renal monitoring: Alternating annual MRI and ultrasound
- Photoprotection and smoking cessation

Sebaceous carcinoma

- Cases of sebaceous carcinoma after the age of 60 and history of uterine and colon cancer → Need to investigate the Muir-Torre variant of Lynch syndrome.
- Constitutional mutations in the following mismatch repair system genes: MLH1 - MSH2- MSH6 - PMS2
- Predisposition for colorectal and endometrial cancer and for ovarian, urinary tract, and biliary tract cancer
- Tumour lesions can be analysed with an anatomopathological examination by looking for protein expression using immunohistochemistry.

Monitoring:

- Colorectal risk: from the age of 20, perform a complete colorectal endoscopy
- Endometrial and ovarian risk: from the age of 30, perform at least one endovaginal ultrasound every two years in addition to endometrial sampling (preferably using Pipelle de Cornier)

Tumour suppressor gene diseases

Cowden syndrome

- Multiple hamartoma syndrome
- Mutation in the PTEN tumour suppressor gene
- Very low prevalence: 1/200,000

- Variable phenotype: intra- and inter-familial variability

Clinical signs:

Mucocutaneous lesions (>95%)

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  - Gingival papillomatosis
  - Trichilemmomas: well-limited dermal epithelial proliferation
  - Storiform fibroma: bundles of collagen with scattered cells, arranged in a lamellar pattern
  - Acrokeratosis (edges of feet and fingers), often mistaken for flat warts
  - Genital lentiginosis

Thyroid involvement >70%

- Heterogeneous multinodular goitre
- Follicular carcinoma

Digestive involvement

Mammary involvement (>65%)

- Adenocarcinoma (60%)

Urogenital involvement

Neurological involvement (40%)

- Macrocephaly
- Epilepsy, meningioma
- Vascular abnormalities
- Lhermitte-Duclos disease
- Impaired social cognition (80%)
- Impaired fine dexterity (93%)

Tuberous sclerosis complex

Incidence: 8-9/100,000

Genes coding for TSC1 and TSC2, autosomal dominant transmission

Reduced life expectancy

Clinical manifestations:

- Hypochromic ash-leaf macules
- Facial angiofibromas
- Fibrous plaques on the scalp
- Koenen's tumour, nail fibromas
- Shagreen skin patches
- Juvenile xanthogranuloma
- Tooth enamel pitting
- Intraoral fibromas
- Iris hamartomas or retinal achromic patches
- Tubers and white matter abnormalities

- Cardiac rhabdomyoma: present *in utero*
- Lymphangioleiomyomatosis
- Renal angiomyolipomas: high haemorrhagic risk

Good genotype/phenotype correlation but possibility of a mosaic form of tuberous sclerosis complex.

Monitoring should include an annual dermatological examination.

As regards drug treatments, prescription of:

- Sirolimus to reduce renal angiomyolipomas, although better results have been observed with everolimus.
- Topical sirolimus for facial angiofibromas.

Neurofibromatosis type 1 (NF1)

1/3,000 births

Complete penetrance at eight years of age; children have almost all (97%) the diagnostic criteria.

Highly variable phenotype.

Mutation in a tumour suppressor gene: NF1 acts in the MAP-kinase pathway, enabling cells to survive and proliferate.

Neurofibromin negatively regulates the RAS pathway by converting active RAS-GTP into inactive RAS-GDP.

Kinetics of the lesions

Before one year: characteristic bone lesions and café au lait spots

Three years: Lisch nodules

Four to six years: optic pathway glioma or lentigines

Investigation of complications during:

- Early childhood
    - Optic pathway glioma: affects 15% of patients around the age of four years. Has a good prognosis.
        - Low-grade pilocytic astrocytoma.
        - Generally not very symptomatic.
        - Recommendation: perform a fundus examination once a year
        - To be considered in the presence of visual disturbance (loss of visual acuity, ptosis, strabismus) or endocrinopathy (glioma of the chiasma): early puberty (before the age of nine), abnormal growth, etc.
    - Plexiform NF accounts for 30% of NF1 cases; it is congenital or occurs before five years of age
    - Bone dysplasia: found in less than 10% of cases
- Childhood
    - Attention deficit disorder
    - Scoliosis
    - Plexiform NF
- Adolescence
    - Retarded growth
    - Early puberty
    - Neurocognitive disorders
- Adulthood

    - Cancer, gastrointestinal stromal tumours (GISTs), sarcomatous degeneration
    - Breast cancer: 10% risk at age 50. 25% risk of the cancer becoming bilateral over 20 years
        - Perform an annual breast MRI and examination.
    - Pheochromocytoma/hypertension: triad of sweating, headaches, palpitations/anxiety
    - Vascular dysplasia/hypertension

Paediatric dermatological emergencies

Kawasaki disease

- Acute vasculitis of medium-sized vessels, with particular tropism for the coronary arteries.
- Affects children aged between six months and five years and is more common in boys.
- Unknown pathophysiology
- Mere suspicion of the disease is sufficient to initiate treatment, provided that other causes have been reasonably ruled out in the time available.
- Clinical presentation: maculopapular exanthema, with perineal exanthema, strawberry tongue, fissural cheilitis, conjunctivitis, involvement of the extremities, erythema, oedema and desquamation.

The presence of vesicles or bullae is rare in Kawasaki disease and should lead to the consideration of other diagnoses.

This means we should **watch out** for the polymorphism of mucocutaneous eruptions in Kawasaki disease.

Incontinentia pigmenti

- Case: mosaic NEMO mutation identified in a boy.
- Syndromic multisystem ectodermal dysplasia.
- X-linked dominant genodermatosis, NEMO gene mutation.
- Neonatal period: urgent ophthalmological and neurological assessment as there is a risk of retinal detachment, which can cause blindness.
- In boys: lethal unless there is a 47 XXY chromosomal abnormality, somatic mosaicism, or a hypomorphic NEMO mutation.
- The severity is comparable to that in girls and monitoring is the same.
- Consider a diagnosis of IP in a male newborn.

Hodgkin's disease

- 15-30% of malignant lymphomas in children
- 17-35% of patients present with skin lesions, but these are often non-specific as part of a paraneoplastic syndrome.
- Non-specific lesions are variable and include urticaria, eczema, erythema nodosum, acquired ichthyosis, linear IgA dermatosis and annular erythema.
- Pruritus in 10-15% of cases.
- Never minimise an unexplained ordinary sign.

Toxic shock syndrome

- 38°C fever
- Diffuse, macular, scarlatiniform exanthema
- Desquamation one to two weeks later
- Hypotension or orthostatic hypotension
- Involvement of three or more organs
- With Staphylococcus: there is often an increase in temperature, diarrhoea, and vomiting
- With Streptococcus: there is no prodromal phase and diarrhoea is uncommon
- No signs are trivial: take all signs into account

CONNECTIVE TISSUE DISORDERS IN CHILDREN: DERMATOLOGICAL WARNING SIGNS AND PATHOPHYSIOLOGICAL AND THERAPEUTIC ADVANCES

Speakers: Dr. Anne Welfringer-Morin, Dr. Laura Polivka and Prof. Christine Bodemer

Report written by Dr. Deborah Salik

Morphea

Localised cutaneous morphea is not associated with a vascular disorder or the presence of autoantibodies. There may be a triggering factor.

The clinical evaluation can be difficult, as morphea "en coup de sabre" can resemble vitiligo.

There are various types of morphea: linear, limited, generalised, deep, mixed, and eosinophilic fasciitis.

Linear morphea:

- Mainly affects the extremities (83%) and more particularly the lower limbs (rather than the upper limbs), then the head (17%) and lastly, the trunk.

Limited morphea:

- Plaque form (more common in adults), sometimes with a purplish "lilac ring" border, showing the activity of the plaque.
- Guttate.
- Atrophoderma of Pasini and Pierini.

Generalised morphea:

- If there are more than four plaques of over 3 cm affecting two anatomical sites.

Pan-sclerotic morphea:

- Extending from the skin to the fascia and then the bone.

What examinations are necessary for morphea "en coup de sabre"?

1. Biological: CBC, kidney and liver function, CRP, ESR, ANA, pre-therapy,
2. Ophthalmological consultation,
3. Dental consultation,
4. MRI of the face + brain with injection and EEG?

Treatment:

- If extensive morphea or deep involvement:

Prescription of general corticosteroid therapy: IV *methylprednisolone*, 30 mg/kg (max 1,000 mg), three days/month for three to six months, or oral prednisolone, 0.5 to 1 mg/kg for two to four weeks, then tapering off over three to six months.

+ Combined with *methotrexate* at a dose of 15 mg/m2/week for at least 12 months.

- If localised morphea with superficial involvement (dermis):

Prescription of topical corticosteroids:

- A potent topical corticosteroid such as clobetasol for one month.
- Followed by a potent corticosteroid for three months.

Alternative:

- Topical calcipotriol: one or two applications/day.

- Calcineurin inhibitor: one or two applications/day.
- PUVA therapy: two to four sessions/week for a total of 30 sessions.
- UVA1 therapy: three to five sessions/week for a total of 30 sessions.

For the 30% of patients who do not respond to *methotrexate*, there are various alternatives:

- *Mycophenolate mofetil*, *ciclosporin*,
- *Abatacept*, *tocilizumab*,
- *Hydroxychloroquine*,
- *Imatinib* (a tyrosine kinase inhibitor),
- JAK inhibitors (*ruxolitinib*).

Complications of morphea:

- Aesthetic: fibrosis, atrophy, post-inflammatory pigmentation/dyschromia
- Functional with deep involvement: contractures, myositis, significant joint retraction, shortening of limbs
- Increased incidence of autoimmune diseases (diabetes, vitiligo or thyroiditis)
- Sometimes associated with mucosal lichen sclerosus et atrophicus

Specific complications of linear facial morphea

- Epilepsy: 13-21% of cases
- Migraines
- Vascular abnormalities
- Trigeminal neuralgia

Morphea progresses unpredictably; recurrences are not uncommon and can sometimes occur 20 years later. Plaque morphea progresses over three to five years, while linear forms stabilise within two to three years.

Around 20-25% of recurrences occur within 20 months of stopping treatment.

Progression to the systemic form is exceptional, and a work-up should only be carried out if a warning sign appears.

Generalised pan-sclerotic morphea

- 60 patients currently described.
- Morphea extending deep down to the bone, sometimes leading to diffuse ulceration.
- Progression to squamous cell carcinoma.
- STAT4 variants discovered and relevance of treatment with *ruxolitinib*.

Diffuse cutaneous systemic sclerosis

This is rare and accounts for 3% of patients with systemic sclerosis.

The average age is 9.9 years and the female-to-male ratio is 9:1 after eight years.

It is characterised by:

- Cutaneous involvement: Raynaud's phenomenon (90%), cutaneous sclerosis, digital ulcers, calcinosis, bands of hypopigmented skin, capillaroscopic abnormalities (enlarged capillaries).
- Digestive involvement: anorexia, gastro-oesophageal reflux, gastroparesis.
- Lung involvement: restrictive lung disease.
- Muscle and joint involvement.
- Exceptional renal involvement: <5% of patients.
- Cardiac involvement: 8.4% at disease onset and 24% over the course of the disease. Is a major cause of mortality. Annual monitoring is necessary.
- Autoimmunity: high ANA titre, especially for anti-Scl-70 antibodies.

Inflammatory myopathies in children

Inflammatory myopathies in children include dermatomyositis (DM) (pure, amyopathic, overlap) and polymyositis.

Myositis antibodies:

- The following are mutually exclusive: AntiTIF1, Anti-Mi-2, Anti-MJ, Anti-MDA5 and Anti-NXP2 antibodies.
- Present in 60-95% of cases.
- At diagnosis or during follow-up.
- Produce clinical-prognostic phenotypes in adults.

Dermatological signs:
These often occur at a very early stage, in particular gottron papules and facial erythema (including chin involvement which is characteristic in DM). There is also thickening of the cuticles associated with an abnormal periungual capillary network.

Capillary dilation can be seen on the gums (a sign of enlarged capillaries).

Facial oedema may be indicative of dermatomyositis or else of a viral infection, which could itself be a trigger for DM.

There may also be pigmentation disorders or areas of calcinosis.

Lipodystrophy is more likely to be seen in the course of DM; it is less commonly a telltale sign.

Clinical diagnosis is based on:

- Muscular signs:
    - Proximal weakness.
    - Elevated levels of at least one muscle enzyme: LDH, ALT, AST, etc.
- Pulmonary involvement: interstitial lung disease
- Cardiac involvement: conduction disorder
- Gastrointestinal involvement: digestive vasculopathy is a sign of severity

- Biological: thrombocytopenia, lymphopenia, anaemia, hypoalbuminemia with capillary leak syndrome.

Treatment:
Corticosteroids 1 to 2 mg/kg/day, oral or IV

- Concerning bolus injections, there is no proven benefit and they promote digestive perforation.

- Rapid tapering: 0.5 mg/kg/day after three months
- Start *methotrexate* at 15-20 mg/m²/week, one year after stopping corticosteroids (European recommendation).

For the skin:

- Photoprotection.
- Topical corticosteroids: *Protopic (tacrolimus), Plaquenil.* Intensify systemic treatment if necessary and in some cases, use IV immunoglobulins (Ig).

Prevention of osteoporosis, photoprotection, monitoring of growth retardation, ophthalmological monitoring.

There is no effective treatment for calcinosis.

If the patient does not tolerate *methotrexate* or if this treatment is not effective after 12 weeks:

- *Mycophenolate mofetil*: 600 mg/m2 twice a day.
- Intravenous Ig.
- *Rituximab*: effective after two months.
- *Cyclophosphamide (Endoxan)*.

Plasma exchange/immunoadsorption for patients with vasculopathy.

Relevance of JAK inhibitors in the management of DM.

Raynaud's phenomenon

This is where the cold triggers spasms in small blood vessels of the extremities.

We should look for signs of secondary Raynaud's by carrying out a work-up including: CBC - ESR - CRP - ANA - Capillaroscopy.

Possible diagnoses:

- Systemic lupus erythematosus,
- Mixed connective tissue disease,
- Dermatomyositis,
- Systemic sclerosis,
- Antiphospholipid syndrome,
- Drug-related cause: beta-blockers, treatment of attention deficit disorder (ADD) with or without hyperactivity in children,
- Less common: cryoglobulinaemia, local disease, paraneoplastic syndrome.

What is the follow-up?
Progresses to disease for 23.6% of children with Raynaud's phenomenon (median time to disease onset of 2.4 years)

Frostbite/pseudo-frostbite
Abnormal prolonged vasoconstriction triggered by cold due to hypoxia, generating a local inflammatory reaction in predisposed individuals.

- Typical frostbite: around 13 years of age, thin girl, hyperhidrosis, acrocyanosis, dorsal surface of toes more than fingers, pain, burning, cold 8°C weather.
- Pseudo-frostbite: continues in summer, affecting the ears and nose as well.

What examinations are required?

- For a first or atypical episode.
- CBC, ESR, ANA, Anti-DNA, Anti-ENA, APL, cryoglobulinaemia, cold agglutinin disease.

Juvenile lupus

- 15-20% of cases before the age of 16.
- Severe disease: mortality rate of 3% to 18% in adults.
- 1 to 4% monogenic.
- Manifestations:
    - Central nervous system: mood disorder, difficulty concentrating.
    - Renal impairment.
    - Haematological involvement.

Interferonopathies (IFNs)

- Role of type 1 IFNs: immune response against viruses and pathogens.
- Inappropriate and excessive secretion of IFN1 either by activation of the IFN1 pathway or by a defect in its feedback mechanism.
- Thirty-eight genes described, phenotypic variability, including for the same genotype or within the same family.

E.g. Aicardi–Goutières syndrome.

Quality of life and stigma in vitiligo patients

The first descriptions of vitiligo date back 3,500 years. This condition was often mistaken for leprosy. Its worldwide prevalence is 0.5 to 1%.

The skin plays an important role in our interactions with the world; this is particularly true for skin colour. Half of patients surveyed say that vitiligo affects their quality of life, and if it occurs on visible areas such as the face or more than 5% of body surface area, they are even more stigmatised.

Patients report rude remarks and being stared at. A negative impact on patients' sexuality has also been attributed to the condition.

It is estimated that patients with vitiligo are five times more likely to suffer from depression.

These patients present with anxiety and low self-esteem; they often experience depression, stigma and somatisation, all of which have a major impact on their quality of life.

Vitiligo patients also experience workplace discrimination.

Sixty-five percent of patients in Europe have been told their vitiligo could not be treated.

The key points of the international expert group's recommendations

1. Diagnose the disease.
2. Importance of shared medical decision-making: what is the objective and what are the different treatment options, sites to be treated, etc.?

- Acknowledge the severity of the disease,
- Inform the patient of the psychological support that is available,
- Provide the patient with information about associations,
- Provide clear information.

Objectives

- Assess disease activity, manage progressive forms rapidly (systemic treatment), and stabilise the disease,
- Achieve and maintain repigmentation,
- Or sometimes depigmentation if there are no other options (*monobenzone*, cryotherapy or laser therapy).

The combination of an immunomodulator and phototherapy is the most effective.

Patients should be assessed every six months (or every three months if they are undergoing phototherapy).

3. Repigmentation of vitiligo

With current treatments, complete repigmentation is achieved:

- On the face in 70-80% of cases,
- On the body in 50% of cases,
- On bony prominences in 25-30% of cases,
- It remains exceptional on the extremities of the hands and feet.

It is necessary to wait six to 24 months before the response can be assessed.

Benefits of combined treatments

- There are benefits of combining calcineurin inhibitors or topical corticosteroids with the sun or UVB rays. This combination has been confirmed in meta-analyses.
- Face and sensitive areas: *Tacrolimus* 0.1% (including for children and eyelids) twice a day for off-label use
- Rest of the body: Strong topical corticosteroids once a day, five days a week
- In combination with UV rays:

- Either with sun exposure (April to October),
- Without sunscreen, until the skin turns pink,
- Three or four times a week,
- Or with phototherapy (UVB booths, excimer lamps and lasers, home lamps (but these are very expensive: €200-400)).

Preventing recurrences

- 40 to 50% of vitiligo lesions recur during the first year after repigmentation.
- If the recurrence is limited: application of *tacrolimus* twice a week (no sun exposure is necessary); reduces the risk of recurrence by 40%.
- For vitiligo on the body: Topical corticosteroids
- For diffuse vitiligo: UVB rays two to four times a week

Ruxolitinib *cream (OPZELURA 15 mg/g)*
JAK1/2 inhibitor constituting the first treatment for non-segmental vitiligo in adults and children aged 12 and over; used as monotherapy twice a day.

It is also effective on the body, but less so than on the face.

After one year, patients no longer see their vitiligo and do not experience hyperpigmentation with repigmentation.

This treatment is well tolerated, although a moderate and transient acneiform reaction and mild local pruritus may occur.

Tolerance at two years is excellent.

Outlook

- The combination of *ruxolitinib* and UVB rays enables repigmentation to be achieved in patients who have not responded to the treatment used as monotherapy.

- Topical BET inhibitor
    - Immunosuppressive action
    - MMP9 inhibition
    - Phase 2 study in 2024
- Topical MMP9 inhibitor to prevent recurrences
- Topical agonists of the Wnt signalling pathway
    - Stimulate the differentiation of melanocyte stem cells to repigment all the most difficult areas.

How to prescribe and manage phototherapy

Recurrence for optimum results: three times a week, although twice a week remains acceptable.

The maximum dose is 1,500 mJ/cm2 for the face and 30,000 mJ/cm2 for the body.

- The initial dose is 200 mJ/cm2 for all phototypes.
- If no erythema: 10-20% dose escalation.
- If erythema is pink and asymptomatic: maintain the dose until the erythema disappears, then increase by 10-20%.
- If erythema is red and asymptomatic: stop phototherapy until the erythema turns pink, then resume at the last tolerated dose.
- If erythema is symptomatic (pain or bullae): stop phototherapy until healing and pink erythema, then resume at the last tolerated dose.
- Assessment after 18 to 36 sessions.
- Wait for 48 sessions before declaring failure.

Post-treatment recommendations:

- Apply sunscreen,
- No intentional sun exposure.

Do not apply any products for four hours before phototherapy (except mineral oils on hyperkeratotic areas of elbows and knees).

How to stop phototherapy:

- Reduce the frequency to twice a week for the first month,
- Then to once a week for the second month,
- Decrease to once every two weeks for the third and fourth months.
- Completely stop the sessions after four months.

Minimum age:
hen the child is able to remain in the booth and keep the protective shells on, i.e. around the age of 7-10 years, depending on the child's level of maturity.

Treating eyelids:
Can be exposed if the eyes are kept closed and the face is covered during the session.

Combined treatments:

- Topical treatments

- Corticosteroids at weekends if vitiligo is active

Cancer risk and phototherapy with vitiligo
Patients with vitiligo have protective properties against melanoma and are four times less likely to develop it. No increased risk of Bowen's disease with phototherapy. The risk of melanoma is not increased. The risk of actinic keratosis (AK) may be increased after 200 sessions.

Association between lymphoma and tacrolimus and phototherapy: No increased risk of any cancer.

Systemic treatments:
For active vitiligo:

- How can we tell if vitiligo is active?

- Koebner phenomenon,
- Blurred edges,
- Confetti-like depigmentation shows it is extremely active.

Active vitiligo should be treated urgently:

- Low dose of *prednisolone* (0.3 mg/kg/day) for two months
- IV bolus of *methylprednisolone* (8 mg/kg) for three days

- Mini-pulses of *betamethasone* or *dexamethasone* twice a week on two consecutive days for three to six months.

These treatments halt progression in 85% of cases.

For example: an adult patient treated with *Medrol* (*methylprednisolone*) 16 mg twice weekly (8 mg for older children, 4 mg for younger children, equivalent to 2 mg drops for very young children) but with side effects: weight gain, insomnia, adolescent growth (maximum three months because of impact on growth).

The other possible treatments are as follows:

- *Methotrexate,*
- *Ciclosporin,*
- *Minocycline,*
- *Simvastatin*: no demonstrated efficacy,
- Combination of gastro-protected superoxide dismutase (SOD) and UVB rays.

Systemic treatments: oral JAK inhibitors as monotherapy

Upadacitinib, baricitinib, povorcitinib

PSORIASIS IN CHILDREN - MANAGEMENT APPROACHES IN 2023

Speakers: Dr. Emmanuel Mahé and Prof. Anne-Claire Bursztejn

Report written by Dr. Déborah Salik

Clinical features of psoriasis

The clinical features of psoriasis progress differently according to age.

In infants, the appearance of plaques is rare. Napkin and inverse psoriasis are more common.

In older children, scalp involvement, palmoplantar forms and guttate psoriasis predominate. Balanitis or inverse psoriasis, sometimes with fissures, may also be observed.

Children may present with facial psoriasis, around the eyes or mouth or on the cheeks.

Psoriasis of the scalp may be seen in the form of pityriasis amiantace, seborrhoeic dermatitis, or plaque psoriasis.

Palmoplantar forms are often difficult and fissured.

There is also linear psoriasis, which is highly resistant to treatment.

Severity of psoriasis

The Psoriasis Area Severity Index (PASI) has never been evaluated in children, even though it is the US Food and Drug Administration's (FDA) benchmark score for studies.

In terms of quality of life, the Dermatology Life Quality Index (DLQI) is the main score used in studies. It is essential to listen to children and how they feel from day to day, and put them in situations (for example, holding a pen with psoriasis with fissures, going to the swimming pool, etc.).

American paediatric recommendations for assessing severity:

- They are the same as for adults
- Adapt the rule of nines
- Children's DLQI
- PASI, but there is not enough literature to apply it to children.

Psoriatic arthritis

There are various forms:

- Peripheral,
- Axial,
- Enthesitis,
- Dactylitis.

Diagnostic criteria:

- Arthritis + psoriasis,
- Arthritis + two other signs,

- Onycholysis or pitting of the nails,
- Dactylitis.

The prevalence ranges from 1 to 15% and is highly dependent on the type of study, recruitment, and the age of the population.

Psoriatic arthritis can be associated with:

- Onychopathy
- Overweight

Is systemic screening necessary? What is the therapeutic impact? What are the benefits of ultrasound imaging of the joints?

Fate of children with psoriasis

The co-morbidities of psoriasis can cause anxiety in parents.

What about the risks of depression, smoking, alcoholism, myocardial infarction, and the progression of the psoriasis itself?

The form of psoriasis is stable (pustular or plaque form) and persists over time.

In terms of severity, there is no difference in adulthood.

There is no evidence that the earlier the disease appears, the more severe it will be.

What co-morbidities are observed in adults?

Age at onset has no impact on the frequency of co-morbidities in adulthood.

Age at onset also has no influence on the occurrence of psoriatic arthritis in adulthood.

Age at onset of psoriasis does not affect the risk of consuming alcohol or tobacco, the level of education, age at marriage, etc.

Psoriasis can be aggravated by

- The Koebner phenomenon.
- Stress (arrival of a brother or sister, for example).

- Infections in children
    - Streptococcus: sore throat, anusitis, vulvitis, impetigo,
    - Staphylococcus,
    - Respiratory viruses,
    - COVID: 11/152 children with de novo psoriasis and 25/152 had post-COVID flare-ups. What would be the benefits of vaccination in these children?

Treating psoriasis in children

- Treatment with *betamethasone/calcipotriol*: one application seven days a week for four weeks, then four days a week.
- Few, if any, side effects of vitamin D derivatives in children.

Guttate form:

- Often eruptive.
- Regresses within a few months.
- Look for streptococcal infection.

- Phototherapy: contraindicated before the age of eight, and risk of cancer.
- *Acitretin*: dyslipidaemia, hepatic cytolysis, kidney failure, pregnancy, and risks to growth.
- *Methotrexate*: haematological disorders, hepatic cytolysis, kidney failure, pregnancy, and pulmonary risks (off-label use).
- *Ciclosporin*: high blood pressure and kidney failure with renal and cancer risk and increased hair growth.

Geographic tongue

Is it psoriasis? How should it be treated? How does it progress?
Present in 1 to 2.5% of the general population and 0.37 to 14% of the paediatric population.

There are many associations, so it is not necessarily psoriasis. There are also familial forms, probably of genetic origin.

What treatments are available for palmoplantar psoriasis of the hands?

- *Adalimumab,*
- *Etanercept,*
- *Ustekinumab,*
- *Secukinumab,*
- *Ixekizumab.*

Pre-therapy assessment for biologics:

- Same as for adults,
- Blood tests for sexually transmitted infections (STIs) to be discussed,
- Vaccination.

Child abuse

What is a child at risk?
When a child is faced with difficulties endangering their health or safety...

Child abuse is not just about physical or sexual violence. It encompasses actions, or a lack thereof, that cause major disruptions to a child's life or that hinder their physical, mental or sexual development.

No forms of child abuse are harmless.

The figures have been rising since the COVID pandemic, linked to an increase in domestic violence and lifestyle changes (teleworking).

Various types of abuse:

- Physical,
- Sexual abuse or solicitations,
- Psychological,
- Neglect, or failure to meet a child's basic needs.

Perpetrators:
The perpetrators of abuse are mainly adults, but they can also be adolescents or children. They are most often close family members, in 95% of cases.

A legal obligation to report child abuse:
The protection of children is everyone's business.

A doctor must act as a child's advocate if they consider that the child's health interests have been misunderstood or are being inadequately protected by those around them.

What are the warning signs?

- Cuts, burns or fractures before the age of one year, repeated domestic accidents,
- Any bruises/haematomas before the age of nine months,
- Any drug intoxication before the age of nine months,

- Behavioural problems:
    - Violence, aggression, silence, inhibition, withdrawal, unexplained fears,
    - A child who appears submissive or secretive about what is going on at home,
    - Systematic attention-seeking or excessive fear of adults,
    - Repeated running away, risk-taking,
    - Eating disorder (anorexia, bulimia, frequent vomiting),
    - Difficulties at school (absenteeism, lack of investment or over-investment in school, religion or sport).

Attention should be paid to any:

- Absent, incoherent or inconsistent clinical history,
- History incompatible with the child's age or development,
- Delayed access to care, lack of medical follow-up, or medical nomadism,
- Lack of interest in a child's injuries.

Many people who have been victims of maltreatment or sexual abuse do not show any specific signs. More often than not, the accumulation of mild signs will provide grounds for suspicion.

The carer's perspective is important:
Identify warning signs, assess the overall situation, and write to the relevant authorities

TEN ESSENTIAL META-ANALYSES FOR MY PRACTICE

Speakers: Dr. Patricia Senet, Prof. Émilie Sbidian and Prof. Laurence Le Cleach

Report written by Dr. Joséfina Marco-Bonnet

1. Efficacy of various pre-treatments combined with photodynamic therapy (PDT) in actinic keratosis

5FU or laser therapy before PDT is superior to PDT alone.

2. Monitoring of patients with squamous cell carcinoma (SCC) or basal cell carcinoma (BCC)

The guidelines are very heterogeneous.

For BCC, monitoring every six to 12 months for five years.

For high-risk SCC, monitoring every three months for two years, then every six to 12 months for three to five years.

3. Meta-analysis on the bidirectional association between lichen planus and hepatitis C (HCV)

HCV is four times more common in lichen planus (LP) patients and LP is three times more common in HCV-positive patients. However, the results vary depending on the:

- Continent (more common in Africa and South-East Asia),
- Country (more common in Egypt, Iraq, Thailand and Japan),
- Region (more common in southern Italy),
- Location (skin +/- mucosal (OR 6)> mouth (OR3)> genital (OR?) involvement).

4. Efficacy and safety of high-dose antihistamines in chronic urticaria

There is no significant difference in acute side effects or anticholinergic effects between the H1 antihistamines tested.

Bilastine 20 mg has the fewest neurological effects. *Ebastine* 10 mg, *levocetirizine* 5 mg, *mizolastine* 10 mg and *rupatadine* 20 mg also have few neurological effects. Those with the most adverse events, particularly neurological adverse events, are *mizolastine* 10 mg and *cetirizine* 10 mg.

5. Cochrane review on the treatment of bullous pemphigoid (BP)

Clobetasol 40g/day is superior to *prednisone* (0.5 to 1 mg/kg/day) in terms of healing after 21 days and mortality after one year.

Clobetasol 10-30 g/day is as effective as *clobetasol* 40 g/day.

Doxycycline 200 mg/day is not as good as *prednisolone* 0.5 mg/kg/day for healing after 21 days but this is not true for mortality after one year.

6. There is an established link between atopic dermatitis (AD) and psoriasis on the one hand and anxiety, depression and mental illness on the other. What are the associated factors?

No studies have been conducted for AD.

For psoriasis, depression is associated with female gender and psoriatic arthritis but not with age, severity, or systemic treatment. Anxiety is associated with female gender, severity, and psoriatic arthritis, but not with age or systemic treatment. Based on a single study for each of the following factors, there is no association with place of residence, occupation, genital or facial involvement, psoriasis phenotype, or co-morbidities (bipolar disorder, cardiovascular disease, diabetes, schizophrenia). The results are contradictory for level of education, age at onset, ethnicity, and history of depression.

7. Review of the perceptions, opinions and satisfaction of AD patients

AD patients fear the long-term side effects of topical corticosteroids (TCs) in terms of skin atrophy (moderate level of certainty).

They are concerned that TCs will become ineffective if used over a long period of time (low level of certainty).

They prefer:

- A treatment that rapidly relieves pruritus and burning sensations (low level of certainty).
- A natural treatment to start with (high level of certainty).
- A systemic treatment that does not affect their quality of life or daily activities (low level of certainty).
- Therapeutic education sessions with a doctor or nurse (low level of certainty).

8. Feedback from the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC), which has issued several recommendations.

These are aimed at reducing the risk of serious side effects (cardiovascular disorders, blood clots, serious infections, cancer) associated with JAK inhibitors when used to treat chronic inflammatory diseases.

JAK inhibitors should only be used in the absence of appropriate therapeutic alternatives in patients:

- over the age of 65,

- with risk factors for major cardiovascular events (such as heart attack or stroke),
- with risk factors for cancer,
- who currently smoke or have smoked in the past.

Moreover, they should be used with caution in patients with risk factors for blood clots in the lungs or deep veins.

The dose should be reduced for certain groups of patients at risk of venous thromboembolism, cancer, or major cardiovascular events.

The JAK inhibitors covered by these recommendations are *baricitinib*, *tofacitinib*, *upadacitinib*, *filgotinib,* and *abrocitinib*.

9. Adalimumab is an alternative treatment for acne refractory to well-managed conventional therapies.

10. Comparison of biomedicines for palmoplantar psoriasis.

Not all drugs have been compared with each other. *Adalimumab* is superior to *apremilast* and *etanercept*. *Guselkumab* is superior to *ixekizumab*. The three drugs that work best are *guselkumab*, *adalimumab,* and *bimzelx*.

In palmoplantar pustulosis, studies show no difference between the various drugs.

CLINICAL CASES INVOLVING THE SCALP

Speakers: Dr Bruno Matard (Croissy-sur-Seine), Dr Philippe Assouly (Malakoff) et Dr Pascal Reygagne (Paris)

Report written by Dr. Joséfina Marco-Bonnet

Scalp folliculitis in infants

It is important to consider:

- Staphylococcal follicular impetigo: It disappears with antibiotics and does not recur unless immunosuppression is present,
- Scabies,
- Langerhans cell histiocytosis,
- Ringworm: **always perform a mycological examination** for pustular lesions on the scalp of a child or adult.
- Eosinophilic pustulosis: This is a benign, rare and itchy disease characterised by flare-ups and remissions. It resolves around the age of 5.

It is diagnosed by cytodiagnosis and CBC. It is treated with Class II *topical corticosteroids*.

Non-scarring folliculitis in adults

It can be caused by pyogenic bacteria, C. *acnes*, yeasts of the *Malassezia* genus, or gram-negative and other bacteria. It can also be idiopathic.

The usual bacteriological samples should therefore be taken, and an anaerobic culture for C. *acnes* as well as mycological samples should be requested. Treatment is usually empirical.

It is important to explain to the patient that there is follicular dysbiosis and that the goal of zero pustules is impossible, but that we are aiming for an acceptable situation where the length of exposure to systemic treatments is minimised.

Treatment includes:

1. Stopping daily shampooing. Local treatment of pustules with *erythromycin* or *clindamycin*, with reassessment after two or three months.
2. *Ketoconazole* shampoo twice a week for one month, then once a week + Local treatment of pustules with *erythromycin* or *clindamycin*, with reassessment after two or three months.
3. *Doxycycline* 100 mg/day or *lymecycline* 300 mg/day for several months + Local treatment of pustules with *erythromycin* or *clindamycin*.
4. Oral *isotretinoin* 0.25 to 10 mg/24 hrs for several months + Local treatment of pustules with *erythromycin* or *clindamycin*.

Dissecting cellulitis of the scalp

A mycological sample should always be taken to rule out a kerion.

Prescribe a course of oral antibiotics for forms with secondary infection, before and/or during treatment with *isotretinoin*.

The benchmark treatment is *isotretinoin* 0.5 to 1 mg/kg for several months.

Fluctuating cysts should also be drained with a needle and injected with triamcinolone acetonide (10 to 20 mg/ml).

If this fails, excision surgery is required. This is a treatment of last resort for patients who have been warned of the risk of scarring and keloids.

Early treatment is necessary to avoid scars, which are difficult to manage.

Lichen-type folliculitis decalvans

It can affect the entire scalp. In the early stage, histology shows neutrophils, while in the late stage, there are lymphocytes, plasma cells, and a few perifollicular granulomas. No evident lichen-type lymphocytic infiltrate is found.

Clinically, it resembles lichen planopilaris, but with outbreaks of pustules and scabs as it progresses. Adult ringworm should always be ruled out.

There are some other tricky forms:

- Hyperkeratotic forms mimicking psoriasis,
- Inflammatory forms mimicking lupus,
- Stable, non-progressive forms mimicking lichen (the most common diagnostic problem).

Androgenetic alopecia (AGA)

In women
An ovarian tumour should be considered in the presence of male-pattern AGA (receding hairline) of recent onset.

In men and women

The new treatment in 2023 is oral *minoxidil* (Lonoten®) 0.5 to 1 mg in women and 2.5 to 5 mg in men.

Patients should be informed of the risks of hypertrichosis (15%), dizziness (2%), headaches (0.5%), oedema (1%), and tachycardia (1%).

This is an off-label treatment whose efficacy should be assessed after around six months.

It can even be used if there is an allergy to minoxidil lotion. It should be used with caution in brown-haired female patients from the Mediterranean region and in patients who are taking more than three blood pressure medicines.

Lipedematous alopecia

This is alopecia associated with an increase in the skin's thickness to 9 to 15 mm (it is usually 4.5 to 6 mm). This occurs because the hypodermis is thickened (x2). This produces an elastic, spongy "cotton wool-like" consistency.

It affects women (9/10) with black skin. There is no treatment.

An underlying cause should always be sought so it can be treated (trauma, inflammatory disease, etc.).

Pressure-induced alopecia

Of sudden onset (postoperative > 4 hrs, coma, lack of nursing care, forceps, hairdressing equipment, EEG electrodes) with pain and oedematous pink patches.

Dermoscopy shows initial inflammation, black dots, broken hairs, dystrophic hairs, and vellus hairs.

The risk factors are intubation > 24 hrs, operation time > 10 hrs + Trendelenburg positioning, hypoxia, hypotension, hypothermia, diabetes, and war.

Hair loss occurs within three to 30 days. It spontaneously resolves within a few months.

Twenty percent of cases progress to scarring alopecia.

Chronic lupus erythematosus

Clinically, this is characterised by well-defined patches, diffuse erythema, diffuse scales, no significant central atrophy, central recurrences, dilated ostia, dyschromia, and telangiectasias. It is important to look for involvement of the face and ears, which is common.

Dermoscopy shows:

- Scarring alopecia,
- Fairly specific red dots corresponding to dilated follicular ostia with horny plugs and vessels around them,
- Arborising telangiectasias,
- Mega comedo-like dots.

Treatment is as follows:

- First line: photoprotection and *hydroxychloroquine* 400 mg/day for at least six months + very strong topical +/- intralesional corticosteroid therapy.
- Second line: prednisone 3-4 mg/day for two weeks, then tapering off over three months.

- Third line: *Cellcept*, *thalidomide* or *dapsone*.

Complications such as ulceration and SCC can occur.

Lichen planopilaris (LPP)

Based on the experience of the Sabouraud team, in cases of LPP refractory to conventional treatments, *ciclosporin* may be an option at a dose of 4 to 5 mg/kg/day for four months. The success rate is 77%, but this is only a suspensive treatment, with a 12-month relapse rate of 80%.

LPP treatments in 2023

- *Clobetasol propionate (Dermoval)* gel twice a day for one month, then once a day for one month, then once every other day for four months.
- *Clobetasol propionate* **(**Clobex®) shampoo three times a week,
- Triamcinolone acetonide (Kenacort®) *in situ* once a month for three months (5 to 10 mg/ml),
- *Doxycycline* 100 to 200 mg/day for 12 months,
- Oral *prednisone* 1 mg/kg for 15 days, then tapering for four to six months,
- *Methotrexate* 15 to 20 mg/month over a long period,
- *Ciclosporin* 4 to 5 mg/kg for four months,
- *Mycophenolate mofetil* (Cellcept®) 2 g/day for 12 months,
- Low-dose oral *minoxidil*.

Dermoscopy in ringworm

Dermoscopy is reliable for diagnosing ringworm.

For trichophytic ringworm, comma and corkscrew hairs are visible.

For microsporic ringworm, Morse code-like and zigzag hairs are observed

VITILIGO: WHAT ROLE SHOULD JAK INHIBITORS PLAY? WHAT OTHER OPTIONS ARE AVAILABLE?

Speaker: Prof. Thierry Passeron

Report written by Dr. Josefina Marco Bonnet

The VIOLIN study showed that vitiligo is a condition that affects quality of life and is associated with co-morbidities such as depression in addition to autoimmune diseases such as autoimmune thyroiditis (x2), alopecia (x2), psoriasis, and atopic dermatitis (AD).

No treatment had been prescribed for 83.8% of patients.

The objectives of treating vitiligo are to:

1. Stop melanocyte destruction,
2. Induce melanocyte differentiation and proliferation (a long process requiring six to 24 months of treatment),
3. Prevent recurrences.

The patient should always be asked for their treatment objectives, and medical decision-making should be shared.

When faced with vitiligo, it is important to recognise the active forms, as these require urgent treatment!

The treatment that blocks flare-ups in over 90% of cases is UVB therapy (two or three times a week) combined with mini-pulses of *cortisone* (twice a week for three to six months).

For example: *methylprednisolone* (Medrol®) 16 mg twice weekly in adults, 8 mg in older children, 4 mg in younger children, 2 mg drops in very young children.

During puberty, treat for a maximum of three months.

Combination treatments are the gold standard for the repigmentation of vitiligo.

For the face and sensitive areas: *tacrolimus* 0.1% twice a day (off-label use).

For the rest of the body: strong topical corticosteroids (TCs) once a day, five days a week.

These treatments should be combined with either:

- The sun (from April to October without sunscreen, until the skin turns pink),
- Or phototherapy (UVB booths, excimer lamps and lasers, home lamps).

Prevention is important as 40 to 50% of vitiligo lesions recur during the first year after repigmentation.

If the depigmentation is limited: *tacrolimus* 0.1% twice a week, with no need for sun exposure. It reduces the risk of recurrence to 9.7%. TCs are probably just as effective, but the effect has not been demonstrated.

If the depigmentation is diffuse, UVB therapy two to four times a month as maintenance treatment (expert opinion).

Management of vitiligo in 2024

***Ruxolitinib* cream** is recommended for non-segmental vitiligo with facial involvement in adults and adolescents over the age of 12. Long-term treatment is required.

Four percent of patients achieve F-VASI90 at Week 104.

It does not work as well on the body and hands. Forty percent of patients are satisfied.

Treatment must be continued, otherwise 60% of patients relapse. However, a response is obtained again when treatment is resumed.

For patients showing the least response, if treatment is continued, they continue to improve.

Tolerance is good. "Acne" and mild pruritus are the main adverse events.

Oral *JAK inhibitors* should be used for diffuse vitiligo. They represent real therapeutic progress. It takes several months to achieve satisfactory repigmentation. The studies carried out have focused on these medicines used as monotherapy. There is:

- *Ritlecitinib* (a JAK3/TEC inhibitor), currently undergoing a Phase 2b study. 205 improvement after six months on the face, with improvement continuing after one year. It does not appear to be very effective on the body.
- *Povorcitinib*. The results are more promising, although improvement is slow. Tolerance is good, with a few acneiform reactions and an increase in CPK.

- *Upadacitinib*. 60 to 68% repigmentation of the face after one year and 45 to 49% repigmentation of the body. Tolerance is good.

Only a combined approach can achieve fully satisfactory results.

- ***Afamelanotide*** (an MC1R agonist) **and *UVB therapy*** were evaluated in a prospective study. Potential benefits, but only in patients with high phototypes, because in 7% of cases, there is hyperpigmentation of healthy skin.
- The combination of ***oral gliadin-protected superoxide dismutase (GP-SOD) and UVB therapy*** produces good results with very good tolerance.
- ***Ruxolitinib* and UVB therapy**. The combination improves results, with good tolerance.
- **Baricitinib and UVB therapy.** The combination improves results, with good tolerance.

There are other avenues to explore:

- Intrinsic cutaneous abnormalities: abnormalities in melanocytes, keratinocytes and fibroblasts. They are more susceptible to oxidative stress with increased production of reactive oxygen species (ROS), mitochondrial damage (link with the mother?), a SAPS secretome, and an abnormality in the extracellular matrix.
- Melanocytorrhagy secondary to altered e-cadherin levels and distribution. IFNg and TNFa also induce melanocyte detachment through e-cadherin degradation secondary to MMP9 production.
- Triggering factors such as stress (PAMPs and DAMPs).
- Digestive (increase in the Firmicutes/Bacteroidetes ratio) and cutaneous (dysbiosis, especially deep down, Bifidobacterium depletion, mitochondrial damage, and immune activation) dysbiosis.
- Stress activates the innate immune system, which activates the adaptive immune system. There are also memory T cells (the memory of vitiligo), which may be why vitiligo always recurs in the same place.
- Target the Wnt pathway, by applying Wnt agonists to repigment the skin.
- How can the distribution of lesions be explained? Depending on their location, certain fibroblasts attract immune system cells to a greater or lesser extent.

AUTOINFLAMMATORY DISEASES (AIDS)

Speaker: Dr. S. Georgin-Lavialle

Report written by Dr. Josefina Marco Bonnet

The findings in favour of an AID include:

- Onset more than six months ago (in adults), often with initiation in childhood,
- Recurrent episodes, often with fever,
- Periodic fever (skin, mucous membrane, musculoskeletal, and digestive tract involvement),
- Inflammatory syndrome during attacks,
- Negative work-ups (no infection, no neoplasia, no antibodies, no immune deficiency). It should be considered for patients who are unclassifiable.

There are three main pathways:

1. Interleukin-1 pathway: inflammasome abnormalities

- Familial Mediterranean fever (FMF),
- Cryopyrin-associated autoinflammatory syndromes,
- Tumour necrosis factor receptor-associated periodic syndrome (TRAPS),
- Mevalonate kinase deficiency (MKD).

2. NF-KB pathway: downstream of the TNF receptor, protein ubiquitination system

- Haploinsufficiency of A20,
- VEXAS syndrome.

2. Interferon pathway: activates pathways or leads to interferon production

- Aicardi-Goutières syndrome,
- SAVI,
- COPA syndrome.

Inflammasome diseases include hereditary periodic fever syndromes, cryopyrin-associated autoinflammatory syndromes (CAPS), TRAPS, and MKD.

In **Familial Mediterranean fever (FMF)**, the pathognomonic sign is pseudo-erysipelas of the ankle; it is complicated by amyloidosis. It can be associated with psoriasis and Verneuil's disease.

In **CAPS**, the dermatological sign is cold-induced urticaria. It is important to investigate a family history of deafness, aphthosis, clubbing of the fingernails and toenails, and a permanent increase in CRP in adults (between 20 and 50 years of age).

In TRAPS, which is a rare disease, there is a rash during bouts of fever, periorbital oedema, and CRP of 400 during flare-ups, which returns to normal between flare-ups.

What do we need to know about **haploinsufficiency of A20 (HA20)**, a disease of the NF-NK pathway?

It is a cosmopolitan autosomal dominant disease that begins in childhood (before the age of 10 in 94% of cases, often in the first year of life). It should be considered in the presence of oral or bipolar (Behçet-like) aphthosis, abdominal pain, bloody diarrhoea, an inflammatory context (permanently elevated CRP), onset in childhood, or a family context.

An AID of the NF-NK pathway should be considered when there is:

- Recurring inflammatory aphthosis,
- *Pyoderma gangrenosum* and inflammation,
- Neutrophilic dermatoses,
- Aseptic pustulosis.

In the presence of stroke, an AID should be considered in the event of livedo, recurrent ulcers, necrosis, or inflammation (increased CRP). This starts before the age of 10. Protein electrophoresis should be ordered. It is secondary to ADA2 deficiency (DADA2).

Diseases of the interferon pathway correspond to the JAK pathway. There are loss-of-function as well as gain-of-function mutations associated with inflammation that can go as far as autoimmunity. These are STAT diseases.

Dermatologically, STAT3 (gain-of-function) mutations result in alopecia, eczema, and psoriasis.

Dermatologically, STAT6 (gain-of-function) mutations produce severe and resistant atopy, food allergies, asthma, chronic diarrhoea, serosal calcifications, hyper IgE syndrome, and hypereosinophilia.

Early onset, inflammation (of mucous membranes+++), severe and recurrent infections, cytopenia and sometimes eczema and cutaneous vasculitis should suggest actinopathy.

Monogenic AIDs that begin in adulthood include VEXAS, CAPS, and systemic inflammatory trunk recurrent acute macular eruption (SITRAME).

SITRAME is probably an interferonopathy that causes an erythematous-macular rash on the trunk with fever. Blood IgE and IL-18 levels should be measured.

In conclusion, there are many new monogenic AIDs, so they should be kept in mind. It is important to measure CRP, perform a CBC and protein electrophoresis test, draw up a family tree, and discuss a genetic analysis using next-generation sequencing.

FROM MINOR TO SEVERE ACNE: CLINICAL CASES FROM A MULTIDISCIPLINARY DERMATOLOGY/GYNECO-ENDOCRINOLOGY CONSULTATION

Speakers: Dr. F. Ballanger, Dr. O. Cogrel and Dr V. Bernard

Report written by Dr. Joséfina Marco-Bonnet

Adult female acne (AFA)

This is usually moderate but chronic acne that recurs and responds slowly to treatment. It is a peripheral hormonal condition with a major impact on quality of life. AFA patients have reactive skin and a tendency to pick at their acne, which can leave scars.

This is a therapeutic challenge.

One treatment option is *spironolactone* (off-label use) at a dose of 50 to 200 mg per day. Peak efficacy is reached within three to five months. No work-up is required.

No association has been found between spironolactone use and cancer (breast, ovarian, bladder cancer). There is no increased risk of thromboembolism with spironolactone.

Certain drugs interact with spironolactone:

- Potassium-sparing *trimethoprim-sulfamethoxazole* and *ACE inhibitors*.
- Lithium, whose clearance is reduced by *spironolactone*.

Several questions still remain:

- Contraception is recommended as there is a risk of feminisation of male foetuses. The risk of teratogenicity is lower than with *cyclins*. A synergistic effect has been demonstrated between *combined contraceptives* and *spironolactone*.
- What about the dose and duration? It seems that 100 mg is a sufficient dose and that a prolonged effect is achieved if treatment has lasted more than two years.
- What is the optimum protocol? *Spironolactone* and combined contraceptives? *Spironolactone* and *isotretinoin*?
- What is the profile of responding patients? Patients with moderate, chronic, predominantly inflammatory acne and premenstrual flare-ups.

Recommendation:

In cases of moderate hirsutism and/or acne in non-menopausal women, treat with:

- 1st line: *Combined contraceptive,*
- 2nd line: *Combined contraceptive + spironolactone,*
- 3rd line: *Spironolactone* alone, with effective contraception that can be prescribed if there are side effects, contraindications (CIs) and/or a lack of efficacy with *combined contraception*.

Combined contraceptives:

In the absence of CIs, a *combined contraceptive* containing *levonorgestrel* or *norgestimate* (the only one with the same relative risk of thrombosis as *combined contraceptive*s containing *levonorgestrel*) should be prescribed as first-line treatment.
In practice, there are no proven benefits of one *combined contraceptive* over another for acne or hirsutism.

Vascular risk factors should systematically be investigated before prescribing any medication.

Endometriosis is currently treated with *dienogest* administered continuously at a dose of 2 mg/day, but this does not have MA for contraception.

Contraindications:

- For *combined oral contraceptives*, they are the same as for patches and vaginal rings.
- If there are CIs for *combined contraceptives*, *copper intrauterine devices* or oral (*levonorgestrel*, *desogestrel*, *drospirenone*) or non-oral (subcutaneous implants and injectables) progestin-only contraception can be proposed, although these can aggravate acne.
- There is a lack of studies comparing the effects of different progestin-only pills on acne.

In conclusion, in cases of moderate to severe AFA:

- If hyperseborrhoea and premenstrual flare-ups: *spironolactone*.
- If risk of scarring: *isotretinoin*.
- Discuss the most suitable contraception.
- Systematically follow with a topical maintenance treatment or *spironolactone* as there is a high risk of recurrence.

For moderate to severe acne + hyperandrogenism:

- Carry out a hormone test,
- Consider the differential diagnosis of PCOS,
- Discuss the most suitable contraception,
- Treat with *spironolactone*.

For very severe acne with major repercussions:

- Combination of low-dose *isotretinoin* + *spironolactone* (faster improvement),
- Continue maintenance treatment with *spironolactone*,
- Relevance of multidisciplinary management,
- Very close monitoring and psychological support.

Future topical treatment: *Clascoterone*

This is the first topical anti-androgen medication; it was approved by the FDA in August 2020. This 1% cream should be applied twice a day for 12 weeks. It is indicated for moderate to severe facial acne in patients over the age of 12 (both boys and girls).

It is not available in France.

Polycystic ovary syndrome (PCOS)

To diagnose PCOS, two of the three Rotterdam criteria must be met and other causes of hyperandrogenism (non-classic 21-hydroxylase deficiency, Cushing syndrome, adrenal or ovarian androgen-secreting tumours)

and menstrual cycle disorders (hyperprolactinaemia, functional hypothalamic amenorrhoea, other gonadotropin deficiency) must be ruled out.

Rotterdam criteria:

1. Oligo/anovulation (spanio/amenorrhoea),
2. Clinical and/or biological hyperandrogenism,
3. Multifollicular ovaries on ultrasound.

The hormone test to be carried out after three months off hormonal contraception, between D2 and D15 of a spontaneous cycle or one triggered by *duphaston*, in the morning, includes:

- Beta-HCG
- E2, LH, FSH
- Total testosterone (+ SHBG if overweight patient)
- Prolactin
- TSH
- 17-OH progesterone (normal if <2 ng/ml in early follicular phase)
- Do not include other androgens initially
- Dexamethasone suppression test with serum cortisol or 24-hour urine free cortisol with creatinine, if clinical suspicion of Cushing syndrome

Pelvic ultrasound should not be performed before eight years post-menarche. It is not essential if two other Rotterdam criteria are present. PCOS is diagnosed if there are more than 20 x 2-9 mm follicles per ovary or if ovarian volume is greater than 10 cm3.

Pelvic ultrasound can be replaced with an AMH test for the diagnosis of multifollicular ovaries. This test is difficult to interpret and should only be performed at the request of an endocrinologist or gynaecologist.

Acne cosmetica

Described in 1972 by Kligman and Mills, this is acne worsened by unsuitable cosmetics (products that are too greasy or too oily, make-up powders, harsh cleansers, hair products that affect the temples and forehead, topical corticosteroids); it mainly affects patients with pigmented skin. It is moderate, polymorphic acne. When acne occurs due to friction, it is known as acne mechanica.

The treatment of acne on pigmented skin is different. The need to use photoprotection and manage hyperpigmentation should be emphasised.

For very mild acne: topical *retinoids* +/- *benzoyl peroxide* (BPO); if erythema: *topical corticosteroids* for two to three days.

For mild acne: topical *retinoids* +/- BPO; if this fails: *cyclins*.

For moderate acne: *cyclins* or *isotretinoin* 0.2 mg/kg/day or *spironolactone*.

For severe acne: *cyclins* for one month, then *isotretinoin* **0.2 mg/kg/day**.

For very severe acne: *isotretinoin* + general *corticosteroid therapy*.

Acne-induced macular hyperpigmentation (AMH)

This is acquired pigmentation resulting from inflammation that can take the form of scarring. It can affect all skin types. The risk factors are phototype III/IV, a high degree of inflammation, delayed treatment, and a tendency to pick at and rub the skin.

Treatment varies depending on acne activity. For active acne and AMH:

- First-line treatment: topical *retinoid* +/- *benzoyl peroxide* (BPO) and oral treatment if moderate to severe acne.
- Second-line treatment: chemical peel, IPL, non-ablative fractional laser or tranexamic acid.

If there is no active acne:

- First-line treatment: azelaic acid, hydroquinone, topical *retinoid* alone.

- Second-line treatment: kojic acid, arbutin, vitamin C.

The whole face should be treated over a long period of time, suitable cosmetics should be used, SPF50 photoprotection should be applied, scrubs and rubbing should be avoided, and the role of make-up should be optimised.

Acne conglobata
There is a probable clinical spectrum between acne conglobata and Verneuil's disease.

Isotretinoin should be used with caution as there is a risk of aggravation, especially if the patient is male and has a BMI>25.

Facial abscesses can be treated with *long-acting corticosteroid injections* (10 mg/ml), sometimes combined with oral corticosteroid therapy.

If the acne is resistant to *isotretinoin*, it can be treated as hidradenitis suppurativa with biotherapy.

Scar management is difficult, which is why early treatment is essential.

Post-acne keloid scars can be treated with:

1. Intra-lesional injections of long-acting *corticosteroids* or *Dermojet*
2. Vascular lasers (PDL/long-pulse YAG/IPL)
3. Hair removal lasers if the keloid scars are on hairy areas; intra-keloid folliculitis
4. Focused continuous CO2 laser wells or fractional CO2 or microneedling + topical corticosteroids.

Atrophic scars on the trunk are impossible to treat.

Atrophic scars on the face are difficult to manage because they are deep and irregular and have a sclerotic base. The degree of sclerosis should be assessed by a stretch test and based on the appearance of the scar base. The more severe the sclerosis, the more difficult it is to correct.

Treatment:

Ice pick scars should be treated by punch excision, TCA Cross, radiofrequency therapy, or laser resurfacing.

Shallow U-shaped scars should be treated by punch excision, dermabrasion, microneedling, radiofrequency therapy, or laser resurfacing. Deep U-shaped scars should be treated by subcision, TCA Cross, punch excision/elevation, or laser resurfacing.

Slightly sloping U-shaped scars should be treated by subcision, fillers, dermabrasion, microneedling, radiofrequency therapy, or laser resurfacing.

Inflammatory scars should be treated early with vascular laser, IPL, or LED light therapy.

Lasers can even be used under *isotretinoin*.

CLINICAL CASES, BLACK SKIN

Speakers: Prof. Antoine Mahé, Prof. Antoine Petit and Dr Emilie Baubian

Report written by Dr. Joséfina Marco-Bonnet

Photodermatoses in patients with dark phototypes

According to the data in the literature, they are not exceptional.

They are common among African Americans and in Asia (Thailand, Singapore, India) but are much rarer in Sub-Saharan Africa.

Clinical forms vary depending on the phototype and geographical location:

- In Europe: contact/systemic/drug-induced photoallergies/phytophotodermatoses/benign summer light eruption (BSLE)/polymorphous light eruption (PLE).
- In the USA: pinpoint dermatitis variant of light eruption +++, PLE and BSLE.
- In Asia: actinic prurigo (South America), photoallergies (solar filters).
- In the UK: 1/3 of cases of chronic actinic dermatitis (CAD) are diagnosed in patients with dark phototypes.

Management includes photoprotection and tolerance induction in CAD.

Post-inflammatory hyperpigmentation (PIH) on dark skin

It is more frequent on black skin (prevalence of 65% vs 25% on white skin). It is a frequent reason for consulting because it has a major impact on quality of life. Treatment is difficult, with a risk of worsening the PIH.

SPF30+ photoprotection with an anti-visible light filter and good UVA protection is necessary.

Start with a hydroquinone-corticosteroid-retinoid combination for three months.

- If intolerance: vitamin C, *thiamidol*, *cysteamine* 5% or depigmenting dermocosmetics (niacinamide, ascorbic acid) can be used.

Local treatments should be tested behind the ear. These are the same treatments used for melasma.

- If local treatments are insufficient: superficial chemical peels (salicylic acid+++, glycolic acid and Jessner's solution) can be proposed. They should be tested on a small area as there is a risk of secondary PIH.

Preparation is necessary: sunscreen for two months before the peel and for three months afterwards; start *tretinoin* six weeks and stop two to three weeks before the peel.

If *tretinoin* is poorly tolerated, depigmenting dermocosmetic cream for six weeks before the peel, continuing afterwards.

- As third-line treatment, lasers can be proposed (low-fluence Q-switched Nd:YAG +++, erbium, thulium fibre laser, picosecond laser?).

There are also alternative treatments: PRP, bakuchiol, or oral or local tranexamic acid.

Discoid lupus

It is more common on black skin. There are more severe lesions and sequelae (alopecia, pigmentation disorders) that affect quality of life. The risk of scarring is also increased, as is the prevalence of severe depression (x2), anxiety disorders, panic disorders, suicidal risk, alcohol addiction, and agoraphobia.

In terms of treatment, photoprotection against UV rays should be put in place, and an inducing drug should be sought out and discontinued.

First-line treatment: apply topical corticosteroids and if there is resistance, use local *tacrolimus* 0.1% (off-label use).

If there is resistance to local treatment, prescribe *hydroxychloroquine* (6.5 mg/kg/day), which leads to clinical improvement in 80% of cases.

In the event of failure, it is important to ensure that the drug is being taken correctly by measuring *hydroxychloroquine* levels in the blood, and check that there are no inducing factors such as sun exposure or smoking.

After failure of or resistance to synthetic antimalarial drugs, try *thalidomide* or *methotrexate* (off-label use). As third-line treatment, combine *belimumab* (MA) with standard therapy

THERAPEUTIC ALTERNATIVES AND PERSONALISED TREATMENTS FOR ACNE

Speakers: Prof. Marie-Thérèse Leccia, Prof. Brigitte Dréno, Dr. Jean-Paul Claudel and Dr. Fabienne Ballanger-Desolneux

Report written by Dr. Laura Bouchard

Professor Leccia spoke about the role of **hormone treatments** in the management of acne.

Second-generation combined oral contraceptives (COCs, ethinylestradiol + progestin) containing *norgestrel* or *levonorgestrel* ("androgenic" progestin) are **preferred** to third- and fourth-generation pills containing *desogestrel*, *gestodene* or *norgestimate* ("non-androgenic" progestin) because of a lower thrombotic risk.

Following a campaign undertaken in 2012-2014 by the French National Agency for Medicines and Health Products Safety (ANSM) on the thromboembolic risk associated with third- and fourth-generation pills, a health survey conducted in France in 2016 revealed a **decline in the use of the pill as a method of contraception**, particularly among young **women aged 20-29**.

In the **contraception study** published by the ANSM in conjunction with the Epi-Phare Scientific Interest Group (GIS Epi-Phare) covering a 10-year period from **2012-2022**, **oral contraception** containing **oestrogen and progestin** had **sharply decreased (-36%)**, while the use of **progestin-only pills** had **increased** by **50%**.

Sales of *levonorgestrel* intrauterine devices (IUDs), used mainly by women over the age of 35, had remained stable, and copper IUDs accounted *for more than half* of all *IUD* sales in France.

The ANSM conducted an information campaign for professionals to ensure that **first-** and **second-generation** pills are systematically **favoured**, and that the use of **third-** and **fourth-generation** pills is the **exception** rather than the rule.

Second-generation pills are preferred for patients with an oestrogenic profile (**heavy, painful periods, mastopathy**), and **third- or fourth-generation** pills for patients with an androgenic profile (**acne, hirsutism**).

A **study** by Barbieri *et al*. (Obstet Gynecol 2020):

- **Influence** of **contraception class** on the **incidence** and **severity** of **acne** in the first year after the initiation of contraception.
- Retrospective study using a US national database, conducted among 336,738 women aged 12-40 years.
- There was an **increase** in the **incidence** and **severity** of **acne** in users of **IUDs** (*levonorgestrel* and *copper*) **compared with COCs**.

Indications for cyproterone acetate + ethinylestradiol (**Diane 35**®) (third generation)

- Only acne and hirsutism,
- **No MA for contraception,**
- In a Danish cohort (1995-2009) of 1.2 million women (Lidegaard *et al*., BMJ 2011), **thromboembolic risk** in women:
    - Without oral contraception: 3.7 cases/10,000 women over one year
    - **Cyproterone acetate + ethinylestradiol (Diane® 35)** and other third-/fourth-generation COCs: **risk x 4!**
    - Second-generation COCs: risk ~ x 2

Cyproterone acetate (Androcur® and generics)

- Polycystic ovary syndrome (PCOS), major hirsutism, gender transition
- Risk of **meningioma** at doses ≥ 25 mg/day
    - x 7 after six months of treatment,
    - x 20 after five years of treatment,
    - **MRI** before starting treatment.
- Start with an **endocrinologist**

Spironolactone and **acne:**

- Potassium-sparing diuretic,
- **Anti-androgenic** action,
- Well tolerated.

Review by Layton *et al.* (Am J Clin Dermatol 2017): **efficacy** of spironolactone in **acne**

- Literature: clinical case reports and small-scale studies
- **No MA** for acne
- No proof of efficacy < **100 mg/day**

Study: Santer *et al.* (BMJ 2023):

- ***Randomised***, ***double-blind***, ***placebo-controlled*** study
- *410 women; age > 18 years: 176 cases vs 166 controls*
- *facial acne > 6 months*
- *average age: 29 years*
- *severity of acne requiring systemic antibiotics*
- *spironolactone 50 mg/day for six weeks, 100 mg/day up to week 24*
- *outcome measure:*
    - *Acne-Specific Quality of Life (Acne-QoL) questionnaire at weeks 12 and 24*
    - Cases improved at week 12 (Investigator's Global Assessment (IGA)): intervention vs control
    - Patient-assessed improvement at weeks 12 and 24
- **Acne QoL:**

1. Minor effect at week 12
2. **Significant difference** at **week 24**

- **Patient-assessed improvement**: significant difference at **week 24**
- **Treatment success** at **week 12**
    - significant difference: cases 31 (19%) placebo 9 (6%)
- Conclusion: *spironolactone* is a good alternative to systemic antibiotics for the treatment of acne in women.
- Alternative to *cyclins*, for moderate acne in women and adolescents,
- Recommended **dose** of **50-100 mg/day**,
- No need to monitor renal function or potassium < 45 ml/min/1.73 m^2
- Very weak teratogenic effect,
- Very good tolerance (headaches, menstrual disorders)

DERMOSCOPY NEWS

Speaker: Dr. Jacques Savary

Report written by Dr. Laura Bouchard

There are some cases of melanoma associated with pregnancy: they are diagnosed during pregnancy or in the year following childbirth.

Is the risk of melanoma increased by pregnancy? The results are very contradictory.

Melanoma is the **most common** form of **cancer** in **pregnant women** (31%).

1% of melanoma cases are **diagnosed** in women during **pregnancy**.

1/3 of women with melanoma are of childbearing age.

- Influence of pregnancy on melanoma (Carter *et al.*, Eur J Cancer, 2022)
    - **Time** to diagnosis.
    - **Lymphangiogenesis**: increased metastatic spread?
    - **Immunological** changes: foetal immune tolerance mechanisms – increased tumorigenesis during pregnancy?
    - **Hormonal** effects: oestrogen may modulate tumorigenesis
    - **Hyperpigmentation**: increased melanocytic activity and hyperpigmentation during pregnancy – changes in pigmentation due to pregnancy make it more difficult to distinguish between benign and malignant lesions?
    - Influence on **prognosis:**
        - Greater Breslow thickness at diagnosis
        - Prognosis linked to Breslow thickness or negative influence of pregnancy?
        - Pooled analysis of 10 case-control studies with 5,000 women: no definitive association between pregnancy and the risk of developing melanoma or more aggressive diseases (Karagas *et al.*, Cancer Causes & Control, 2006)
- **Increase** in naevus **size** in certain areas (abdomen, chest)
- Appearance of **new naevi**? Only one study supporting this appearance. Martins-Costa *et al.* Dermatol Pract Concept 2019
- **Dermoscopic** changes:
    - **Increase** in the **Total Dermoscopy Score in the 3rd** vs 1st**trimester** (Akturk *et al.* Eur J Acad Dermatol Venereol 2007, Zampino *et al.* Dermatol Surg 2006, Gunduz *et al.* Eur J Acad Dermatol Venereol 2003) – return to baseline six months post-partum.
    - Change of **colour**: hyperpigmentation, variable according to anatomical location, as reported by Cosgarea *et al.*, Front Med, 2021.

- Modification of **structures** supported by Zelin *et al.* Melanoma Manag 2020, Martins-Costa *et al.*, Dermatol Pract Concept, 2019.
  - Increase in **network irregularities** with mesh thickening,
  - Increase in the **number** of **dots**,
  - Increase in the number of **peripheral globules** (sign of growth?),
  - Appearance of **striae** in the **periphery**: thinning of the epidermis due to skin distension (fair skin) supported by Martins-Costa *et al.*, Dermatol Pract Concept, 2019.
  - New **vascular structures** (neovascularisation).

ROLE OF LASERS IN THE TREATMENT OF PROGRESSIVE ACNE: CURRENT SITUATION AND VERY NEAR FUTURE

Speakers: Dr. Gerard Toubel, Dr. Jean-Michel Mazer and Dr. François Will

Report written by Dr. Laura Bouchard

Is there a miracle wavelength for treating acne?

For more than 10 years, Rox Anderson's research group in Boston has been trying to find a wavelength that would **selectively** treat the **sebaceous glands**. The success of laser hair removal has shown that selective photothermolysis of the **stem cells** around hairs is effective.

The group used a **free electron laser** (choice of wavelength and power) to develop a laser that would selectively target sebum. They found three wavelengths that were selectively absorbed, but only the **~1700 nm** wavelength penetrated deeply enough.

Tests on scalp biopsies showed that laser-induced heating of the **sebaceous glands** caused **atrophy** of the gland **without any necrosis** around it (Sakamoto et al, Lasers Surg Med 2012).

In 2011, Jeffrey Orringer's research group in Ann Arbor published a study with a **1708 nm** laser that destroyed lipid-rich targets such as sebaceous glands down to a depth of 1.65 mm in the skin. Ex vivo tests on human skin nevertheless caused epidermal and dermal burns when no cooling method was used, but contact **cooling** effectively protected the skin's surface (Alexander et al, Lasers Surg Med 2011).

At the 2019 Annual Conference of the American Society for Laser Medicine and Surgery (ASLMS), the first oral presentation addressed the results of treatments with the 1726 nm laser on **patients** (Tanghetti et al, oral presentation ASLMS 2019).

The authors achieved **selective photothermolysis** of **sebaceous glands** on the face and back. They subsequently developed an integrated cooling system and in March 2022, Cutera launched the first commercial laser using the **AviClear© 1726 nm** wavelength.

In November of the same year, Accure launched a laser using the **same wavelength** but a slightly different technology: **Accure Laser System©**. The Accure laser is precisely driven by **skin temperature** and relies on air cooling, whereas AviClear operates at a certain **fluence** and uses contact cooling. Accure is sold to dermatologists and plastic surgeons, while AviClear also targets the medical spa market and other non-medical users.

The **AviClear clinical trial** included **104 patients** with moderate to severe acne (https://www.accessdata.fda.gov/cdrh_docs/pdf21/K213461.pdf).

- 304 treatments, two to five weeks apart, to facial skin (one to three split-face, split-back treatments)

- Follow-up four and **12** weeks after the final treatment
- Late follow-up after **26** and **52** weeks
- Treatment was considered **effective** if it showed **>50%** improvement in **inflammatory lesions** at the 12-week follow-up visit.

Treatment response rate by sub-group 12 weeks after the final treatment

- The response rate after **six months** was **88%**. There was a reduction in inflammatory and comedonal lesions, although the reduction was greater for inflammatory lesions.
- **Side effects** were **mild** and **transient** (oedema and redness); the most significant was **acne purging** a few days after the laser session (which could last three weeks).
- Treatment was well tolerated with an average **pain** score of **5.2 out of 10**. Cooling was the only pain management method used.
- **No pigmentation disorders** despite the high phototypes (no problems up to phototype V).
- Even nodules and **comedonal lesions** decreased over time.

Open-label study with 17 patients aged 18 to 36 treated with AviClear (Goldberg et al, J Cosmet Dermatol 2023)

Another **open-label study**, conducted by David Goldberg using the same laser, showed statistically significant **reduction**s in **inflammatory lesions** of 52% and **56%** after four and **12 weeks**. However, **24 months** post-treatment, there was a **97%** reduction. There was also a **high level of satisfaction** among the treated subjects (70%).

The AviClear protocol consists of **three treatments** one month apart and Accure consists of **four treatments**.

These lasers are not yet available in Europe and the **price** is not known, as the machine is rented in the United States.

The price of three treatments with AviClear is around $3,000 in the United States.

These lasers are an **alternative to *isotretinoin*** for patients who are unable or unwilling to take medication. As with *isotretinoin*, there is an initial flare-up of acne and it takes some time to see a result.

LICHEN PLANUS AND LICHENOID DERMATOSES IN 10 ANATOMOCLINICAL OBSERVATIONS

Speakers: Dr. Marie-Sylvie Doutre and Prof. Bernard Cribier

Report written by Dr. Laura Bouchard

Lichen planopilaris (LPP)

Diagnosis

The differential diagnosis should be made with lupus erythematosus and Pseudopelade of Brocq.

To differentiate between lichen and lupus, we need:

-
  - A "good" interview (history, associated symptoms)
  - A "good" clinical examination
    - Observation of the lesions on the scalp (the edges are a little less clear than for lupus, a little more purple) and any other lesions on the skin, mucus membranes or nails.
- **In dermoscopy, we observe**:

    - Lichen: **hyperkeratosis** around the follicles, pinkish peripilar inflammation (jam-like appearance around the peripilar orifice), erythema and peri-follicular vessels, loss of vellus follicles.
    - **Lupus**: "mega" yellow or brownish papules or spikes (follicular hyperkeratosis), thick, tortuous branching vessels, follicular red spots and blue-grey or grey-brown speckled spots.
- **Biopsy:** Biopsy a **recent lesion** in an **inflamed area; do not overlook horizontal cuts** which are useful.

Therapeutic
Treating lichen planopilaris is difficult.

It is a **scarring** alopecia so **do not wait** to start therapy.

Prescribe:

- Powerful or very powerful corticosteroids (shampoos, foams, local application, intra-lesional injections)
- Systemic corticosteroid therapy
- As secondline: *ciclosporin*, *methotrexate*, *mycophenolate mofetil*, *dapsone*, *thalidomide*, etc., *hydroxychloroquine*?
- Anti-JAK?

Monitor evolution as objectively as possible by

- **LPP Assessment Index** (functional and physical signs)
- Comparative **photos**
- A **pull test**
- **Counting hairs** in an identifiable, inflamed, evolving area.

Pseudo-frontal fibrosing alopecia

A specific form of lichen planopilaris that is particularly prevalent in **postmenopausal women**, and sometimes younger men and women. We are seeing increasing numbers of **familial cases. Potential role** of **environmental factors** and solar filters?

It is mainly seen on the forehead, but it can also affect the retroauricular area and the neck. The **eyebrows** are often affected too, sometimes initially. It can also impact the eyelashes, axillary hair, pubic hair and hair on the limbs.

In 20–25% of cases, there are small **facial papules** that are the same colour as the patient's skin or slightly pinkish, on the forehead, temporal area and sometimes on the cheeks.

The **histology** is similar to that of sebaceous hyperplasia, BUT **only sebaceous glands remain once the vellus follicles have disappeared.**

LICHEN PLANUS AND LICHENOID DERMATOSES IN 10 ANATOMOCLINICAL OBSERVATIONS

Dr M.S. Doutre (Bordeaux, France) and Prof. B. Cribier (Strasbourg)

Lichen planus of the skin – What's new

Physiopathological level

- A new **meta-analysis** evaluated **lichen planus's** (LP) association with **hepatitis C** (Garcia-Pola et al., J Clin Med 2023).
- In the 143 studies analysed, hepatitis C (HCV) was prevalent overall in 9.4% of patients with LP.

- In 84 studies, the results showed that patients with LP were 4 times more likely to be infected with HCV than the other subjects.
- HCV is not very prevalent in France and, in treated patients, the virus has a negative reaction in almost 100% of cases.
- **Serology** of hepatitis C only in **specific cases** with typical lichen planus.
- **Associated** with various **comorbidities**:
    - Neuropsychic (depression, anxiety)
    - Autoimmune diseases
    - Cardiovascular involvement

Therapeutic level
Carried out based on:

- Affected area
- Mucs membrane and/or appendages affected
- Age, associated pathologies:
    - Local treatment
    - Systemic treatment

Local treatments:

- Very powerful corticosteroids (local application, intralesional injections).
- Calcineurin inhibitors.

Study on the **safety** and **efficacy** of high doses of ***clobetasol propionate*** 0.05% to treat lichen planus (Melin et al., J Dermatol 2023). The study was carried out on 57 patients with an average affected surface area of 27% (10–40) and pruritus (55/57 patients). Prescription of:

- Complete remission (surface area < 5%): 25/57 in W6, 16/57 in W16 and 41/57 in all (72%).
- Good tolerance: 1 case of folliculitis, 2 cases of hypopigmentation.

JAK inhibitors (Motarnad-Sanaye et al., J Dermatol Treat 2022, Abduelmula et al., J Cutan Med Surg 2023):

- Mucus membrane and/or appendages affected
- Local JAK inhibitor, ***ruxolitinib*** cream is somewhat effective (Brumfiel et al., J invest Dermatol 2022)

Lichen planus pigmentosus

Presents as grey-blue or brown-black macular lesions, without a prior erythematous phase. They are usually seen on the face and neck, and are often slightly itchy. They evolve over months or years.

Most often seen in females, with a dark phototype.

This pathology has bothersome negative aesthetic impacts.

Lichen planus pigmentosus-inversus

Seen in axillary, inguinal and inframammary folds. Lichen planus pigmentosus is difficult to treat.

Therapeutic level
Local treatments:

- Powerful or very powerful corticosteroids
- Topical calcineurin inhibitors (TCI)
- Combination of corticosteroids and TCI simultaneously or sequentially

Systemic treatments:

- *Hydroxychloroquine*
- *Isotretinoin*
- *Mycophenolate mofetil*
- *Tranexamic acid* 250–500 mg/day.

Laser treatment:

Often **2 or 3 lines of treatment**, often for patients who are **not satisfied** aesthetically.

Differential diagnosis

- **Ashy dermatosis** (*Erythema dyschromicum perstans*):

Seen in phototype IV or V patients with macules or pigmented plaques which are erythematous to begin with (sometimes forgotten) and progress to slate grey, "ashy" lesions. Usually found on the torso and limbs, possibly on the neck and face.

- **Riehl's melanosis:**

Heterogeneous pigmented lesions in patients with dark phototypes, located in exposed areas. It is considered to be a contact photodermatosis.

New disorder with pigmented lesions on the face and neck

Melanotic lupus erythematosus

A recently described pathology (Litaiem et al., Clinics in Dermatology 2022).

It affects phototype III–V patients and appears in the form of brown plaques or diffuse reticulate hyperpigmentation. In the cases described, there are no scales, no atrophy, no telangiectasias and no immunological anomalies.

THE SKIN MICROBIOME: A FORGOTTEN PLAYER IN HEALING

Speaker: Prof. Brigitte Dréno

Report written by Dr. Laura Bouchard

Prof. Brigitte Dréno spoke about the importance of the **microbiome** for the **healing** of wounds.

A **rupture** in the **skin barrier** destroys the **microbiome** that exists on the skin and creates an area rich in skin nutrients that favours the growth of opportunistic commensal or pathogenic microbes (Tomic-Canic et al., Am. J. Clinical Dermatol. 2020).

This leads to dysbiosis or a **loss of diversity in the microbiome**.

The **dysbiosis** caused by a wound can differ according to its **origin**: diabetic ulcer, pressure ulcer, burn, etc. This is found when analysing microbiota using bacterial cultures or ribosomal RNA testing (White & Grice, Cold Spring Harbor Perspect. Biol. 2023).

The profile of the skin microbiome differs between the upper layers and deeper layers of the epidermis, and there is a **dermal microbiome** (Nakatsuji et al., Nat. Commun. 2013).

The new microbiome appears two weeks after the formation of a wound and resembles that of the deeper layers of the epidermis and of the dermis. This suggests that the bacteria in the deeper layers of the skin colonize the healing wound on the surface.

Additionally, the skin microbiome blocks the penetration of pathogenic bacteria.

Pathogenic microbes adhere to corneocytes using their membrane proteins, which bind to specific receptors on the corneocytes (pattern-recognition receptor (PRR) proteins).

The commensal bacteria produce **antimicrobial peptides** (AMPs), with two types:

- Bacteriocins, which are AMPs released directly by the bacteria,
- AMPs released from precursors via proteases.

The stratum corneum is covered in antimicrobial peptides called "**antibiotic-like peptides**" and thus forms an antimicrobial barrier.

If the pathogenic microbe **crosses** the **stratum corneum**, the epidermis develops a new strategy to block the invasion of the skin (Timar et al., Mol. Immunol. 2006; Chehouad et al., Proc. Natl. Acad. Sci. 2013; Ersanli et al., Biology 2023)

- It activates a greater number of PRRs on the keratinocytes and sebocytes, which **increases** the production of **PAMs**.
- It activates the **innate immune system**: cytokines, MMPs, recruitment of neutrophils.
- The keratinocytes express **factors inhibiting bacterial adhesion**, such as CD46 (*Streptococcus pyogenes*).

The skin microbiome has **three targets** for **healing** wounds (Canchy et al., Eur. J. Acad. Venereol. 2023). Commensal bacteria:

- Help **prevent** a pathogenic **invasion** by producing **AMPs**,
- **Accelerate healing** by **limiting** the duration of **inflammation** via the innate immune system,
- Induce the production of **T-cells** specific to the commensal microbes, which encourage **tissue repair**:
    - The immune system distinguishes pathogenic microbes to favour the tolerance of commensal microbes.

The microbiome:

- Induces the activation of adaptive T-cell immune responses with the production of lymphocytes against *S. epidermidis*,
- Stimulates the formation of granulation tissue and re-epithelialisation of the wound,
- Induces the production of AMPs by the keratinocytes, which protect the skin against other pathogenic microbes.

Each commensal bacterium has a protective function in the barrier.

If its **activity** becomes **excessive**, the skin microbiome can have a **negative impact**:

- Excessive production of proteases, reactive oxygen species, and other bioactive substances, causing excessive inflammation.
- Certain **external factors** can alter the activity of the skin microbiome: age, nutrition, coexisting illnesses, genetic factors, etc.
- Inducing **chronic inflammation**: tissue alteration and increased permeability of vessels.
- It may participate in the formation of a bacterial **biofilm**.

If a person has **chronic inflammation** that is not prevented by the skin microbiome, in **60%** of wounds, bacteria will develop a **biofilm** in the bed of the wound and make it harder to heal.

The **profile** of the commensal bacteria may be to **help** in antimicrobial defence, improve the skin barrier, boost the immune response, and recruit T-cells. However, in **another environment**, it can have the **opposite effect** and favour chronic inflammation.

Stress controls the skin microbiome, inducing chronic inflammation.

Stress mediators (cortisol, catecholamines, acetylcholine, neuropeptides, etc.) influence the wound's microbiome (Holmes et al., Adv. Wound Care 2015):

- Altering the profile of the skin microbiome,
- Altering the host's innate immune response,
- Stimulating the formation of a biofilm.

Stress can be physiological or psychological and controls the skin microbiome via **neurogenic inflammation**.

Stress → signals from the brain → production of **substance P** by nerve endings near the sebaceous glands → activation of **substance P receptors** on the sebaceous glands → increased production of **sebum** → induced **alterations** of the **microbiome** (notably *S. aureus* and *S. epidermidis*).

Substance P (N'Diaye et al., Front. Microbiol. 2016):

- Increases the **adhesion** of bacteria to keratinocytes,
- Increases the **secretion** of the **enterotoxin** C2 by *S. aureus*,
- Increases the formation of biofilm by *S. aureus* and *S. epidermidis*.

The healed wound never returns to a normal microbiome. As such, a therapeutic approach is required.

Therapeutic approaches for **restoring balance** to the skin microbiome in the healed area of the wound:

- **Bacteriophages** (reduce resistance to macrolides), used topically on the skin.
- **Bacteriotherapy** (topical and oral):
    - Bacterial transplants,
    - Probiotics (live bacteria),
    - Prebiotics (bacterial extracts),
    - Combinations of pre- and probiotics,
    - Postbiotics: AMPs.

Probiotics – **new prototypes** from **lactic acid bacteria.**

- Plantaricin A (AMP):

- Induces the migration and differentiation of keratinocytes and fibroblasts,
- The formation of collagen,
- Reduces the inflammatory phase,
- Accelerates total healing in Wistar rats.

- Nisin
    - Was electrospun into nanofibres that were used to significantly reduce *S. aureus* infections in animal test subjects. The nanofibres also helped accelerate the wound healing process.

Key messages

- Human skin has a complex and symbiotic relationship with the microbiome.
- The skin microbiome is involved at every stage of healing.
- Recent advancements in genomics and bioinformatics have enabled the discovery of a dermal microbiome with distinct characteristics whose role in healing remains unclear.
- By altering the skin microbiome, stress increased the risk of altered healing.
- The microbiome of healed skin is not the same as that of normal skin.
- Bacteriotherapy to stimulate wound healing is a new, essential target for therapy.

WHAT'S NEW IN PHOTOPROTECTION

Speaker: Prof. J.C. Béani

Report written by Dr. Laura Bouchard

Sun protection products (SPP)

Answers to questions: Doubts, polemics, controversies

Should we discourage use of SPPs because they are harmful to health?
The allergic reactions caused by SPPs are above all photoallergies. They are particularly due to **oxybenzone** or **benzophenone-3** (BP-3) and **octocrylene** (OCT) (allergies which are more common in children). This is because impurities from benzophenone (BP) remain when OCT is synthesised, and **OCT** produces **BP** when it **breaks down**

SPPs containing OCT should therefore be discarded after a certain period of time

Certain solar filters have systemic toxicity as they **penetrate the skin.** This is the case with **oxybenzone**, which penetrates the skin **to a significant extent** and which was found in plasma levels that were much higher than the other filters in all the studies. It is also found in **urine**, **amniotic fluid** and **breast milk.**

We must also be careful with endocrine disruptors:

- In vitro studies in rats and fish showed that certain filters such as Benzophenones, 3- and 4-methylbenzylidene camphor and octyl methoxycinnamate may be potential endocrine disruptors (ED), but not all.
- Barbaud and Lafforgue (Ann Dermatol Venereol 2021) published an article containing a list of solar filters that are not ED.
- None of the studies applied the products topically, the filters were given **orally** in addition to **topically**.
- Matta et al. (JAMA 2020) measured the concentration of six **solar filters** in **plasma** in 48 subjects after the **maximum application** of SPP in the form of an aerosol spray, non-aerosol spray, pump and lotion on 75% of the body 4 times a day for 4 days.
- The **concentration** of the **six filters** (avobenzone, oxybenzone, octocrylene, homosalate, octisalate and octinoxate) exceeded the FDA's concern limit of **0.5 ng/ml** after the **first application** of solar product.

Certain solar filters are found in the environment:

- **Oxybenzone** is found in **water sources** across the world, and lower concentrations of camphor and octocrylene derivatives are present in **fish** in Switzerland, Norway, Spain and China. Filters can therefore **contaminate the food chain**.
- According to a study in Hong Kong, **benzophenone** was present in the urine of **53 children** aged **4 to 6**, only 2 of whom had applied a SPP.
- Benzophenone is found in **100% of water samples** from tap or bottled water.
- Benzophenone is seen in lots of **cosmetic products** (moisturisers, shampoos, hair treatments, nail varnishes) and countless **industrial products** (plastic materials, dental composites, paints, varnishes).

Conclusion:

Solar filters are just one small source of the filters we are exposed to.

The cosmetics industry should:

-
  - Limit filters in products that are not SPPs
  - Limit the number and concentration of filters used in SPPs
  - Choose filters that don't have a proven effect on the environment, and exclude BP-3, ethylhexyl methoxycinnamate, methylbenzylidene camphor
  - Test the **finished product,** not just the filter. 192 sun products of the 661 products tested contained a concentration of **carcinogenic benzene** that was classed as worrying by the FDA (Hudspeth et al., Environmental Health Perspectives 2022). The contamination originates in the manufacturing process

No studies recommended avoiding using SPPs.

VITILIGO: LOOKING BEYOND APPEARANCES… A NEW ERA IN CARE

Speaker: Prof. Thierry Passeron

Report written by Dr. Laura Bouchard

Prospective therapies

Prof Thierry Passeron gave a presentation on **care** for **vitiligo**, along with the results of local treatment with the **JAK-1 and -2 inhibitor *ruxolitinib,*** which will soon be available in France.

The goals of therapy *are to* halt depigmentation, induce repigmentation (between 6 and 24 months), and prevent recurrences.

Care according to the Worldwide expert recommendations for the diagnosis and management of vitiligo: Position statement from the International Vitiligo Task Force Part 1: towards a new management algorithm. Van Geel et al., J. Eur. Acad. Dermatol. Venereol. 2023.

- Recognising an **active form** – **urgent need for therapy** (van Geel et al., Br. J. Dermatol. 2020),
  - Koebner phenomenon,
  - Hypochromic borders,
  - Confetti-like depigmentation.
- **Stopping progression** (Tovar-Garza, Br. J. Dermatol. 2019)
  - Using mini-pulses (= low dose) of **cortisone** twice/week for 3 to 6 months
    - Example: methylprednisolone at 16 mg twice a week in an adult (for a child, 4-8 mg twice a week, depending on the age)

- Narrowband **UVB** phototherapy (*TL01*) 2 to 3 times a week (also helps induce repigmentation),
- Useful to **combine UVB** and oral mini-pulse therapy (**OMP**) for very active forms as doing so can **halt** progression in over **90%** of cases!

- Inducing **repigmentation:**
  - Useful to **combine calcineurin inhibitors** or **topical corticosteroids** with **sunlight** or **UVB** rays (Dang et al., Dermatol. Ther. 2016; Li et al., Photodermatol. Photoimmunol. Photomed. 2017; Lee at al., JAMA Dermatology 2019),
  - Combined treatments are the reference treatments,
  - Better results on the face,
  - Optimum repigmentation after 12-24 months,

    - Current treatments insufficient.
- Preventing **recurrences:**
    - **40% to 50%** of vitiligo lesions recur during the first year after repigmentation.
    - If the affected area is limited:
        - ***Tacrolimus*** 0.1% twice a week (without the need for sun exposure) – decreases the risk from 40% to 9.7%
        - Topical corticosteroids are probably just as effective, but this has not been proven.
    - For diffuse patterns:
        - **UVB** 2 to 4 times a month as maintenance therapy (opinion of experts, but no studies on it).
- Effectiveness and tolerance of ***ruxolitinib* cream** (Janus kinase 1 (JAK1) and 2 (JAK2) inhibitor)
    - *Ruxolitinib* cream (Opzelura®) is indicated for the treatment of non-segmental vitiligo **affecting the face** in adults and adolescents over 12 years old.
    - The **treated area** must not exceed **10%** of the **body's surface area.**
    - Effectiveness on the **face:**
        - Approximately **half** of patients who applied *ruxolitinib* cream twice a day from day 1 achieved F-VASI75 (Facial Vitiligo Area Scoring Index, **improvement** of at least **75%**) at week **52** compared to a control group (Rosmarin et al., N. Engl. J. Med. 2022).
    - Effectiveness on the **body:**
        - Approximately **half** of patients who applied *ruxolitinib* cream twice a day from day 1 achieved **T-VASI50** (Total Vitiligo Area Scoring Index) at week **52.**
    - **Tolerance:**
        - Adverse effects (AE) appeared in the course of treatment:
            - Reactions at the application site, including acne, are the most common AEs (mild to moderate),
            - **No severe AEs.**
    - Data on the **long term** (Harris et al., AAD 2023):
        - **69%** of patients who **continued** application maintained a **F-VASI75** response at **week 104.**
        - Among patients who **stopped** treatment, **39%** maintained a **F-VASI75** response at **week 104.**
        - Continued application was associated with a reduced risk of losing a F-VASI90 response compared to the control group. After stoppage of treatment, the median time for which an F-VASI90 response was maintained was 6.5 months.
        - Recovery of a **response** after **retreatment** (n=16, Harris et al., AAD 2023)
            - **75%** of patients recovered their **F-VASI75** response (median time of 12 weeks) after restarting ruxolitinib treatment
            - **70%** of patients recovered their **F-VASI90** response (median time of 15 weeks)

- **Continued improvement** in patients < F-VASI90 at week 52: 33.9% F-VASI90 at **week 104** (Rosmarin et al., AAD 2023)

- *Ruxolitinib* cream + UVB:
    - Phase II open-label trial.
    - Improvement in the small number of patients.

Conclusions

- Therapeutic objectives: stop depigmentation, stimulate repigmentation, and prevent recurrences.
- *Ruxolitinib* cream has been proven effective as a monotherapy, with high-quality repigmentation.
- *Ruxolitinib* cream has a good tolerance profile.
- New therapeutic strategies with *ruxolitinib* should be considered in the future, particularly its combination with UVB phototherapy.
- Many formulations of oral JAK inhibitors are being developed.

PRACTICAL NEWSFLASH – PAEDIATRICS

Speakers: Dr. Olivia Boccara, Dr. Stéphanie Mallet, Dr. Thomas Hubiche, Dr. Sophie Leducq, Prof. Sébastien Barbarot, and Dr. Christine Léauté-Labrèze

Report written by Dr. Joël Claveau

This very clinical session was split into five sections: naevi in children, warts and molluscum contagiosum, scalp pathologies in children, atopic dermatitis and infantile haemangiomas. Each speaker reviewed recent publications and some of the treatment algorithms that had the greatest impact on everyday practice.

Should we monitor naevi in children?

In the first section which covered naevi in children, a large study in the Journal of the American Academy of Dermatology revealed that melanomas before the age of 12 are extremely rare. There are just 5 to 10 cases of paediatric melanomas in France each year in under 18s. In children under 10, there were no recorded deaths, melanomas are non-spreading and do not resemble naevi. This supports the idea that this population should not be considered "young adults", as they are two entirely different cases. As such, the diagnostic criteria for adult melanomas do not apply to children. The situation only becomes similar to that of adults in adolescence (superficial spreading melanoma (SSM) with ABCD criteria). To conclude, the speakers mentioned that a melanoma together with (even giant) congenital naevi is exceptional and that a Spitz naevus is often clinically concerning but biologically benign.

How should we treat a wart or molluscum in children?

In the second section on warts and molluscum contagiosum, we were reminded that there are a number of therapeutic options. This includes, first of all, abstention from therapy since 52% of cases resolve themselves in 15 months, cryotherapy, salicylic acid, localised chemotherapy and immunotherapy. However, high-quality meta-analyses have shown that each of them is only slightly more effective than a placebo. There is a slight increase in efficacy when the methods are combined. It is therefore important to correctly choose the patients who require treatment, i.e. those with bothersome, painful and visible lesions. We should choose the therapeutic option that is the least traumatising. Lastly, in cases of anal or genital condylomas, we should check for sexual abuse, maternal-foetal transmission in the very young and transmission within the family.

Scalp disorders in children: finding your way and selecting treatment

When it came to childhood pathologies of the scalp, we were shown a very interesting classification algorithm to help identify pathologies in our surgeries. Firstly, you must distinguish congenital or early-onset alopecia from acquired forms. The first category can be further split into scarring disorders including aplasia cutis congenita, which requires swift treatment, as opposed to non-scarring alopecia such as neonatal occipital alopecia and congenital triangular alopecia. On the other hand, acquired forms include alopecia areata, ringworm and induced pathologies such as trichotillomania and traction alopecia. Next, hair shaft abnormalities are rarer pathologies that require specialist treatment. In terms of pathologies that change the colour of the hair, there is greying or premature loss of hair colour associated with a number of aetiologies to be investigated with blood tests, and Green hair syndrome resulting from deposits of copper sulphate crystals in pool water. Lastly, the category for tumour lesions includes sebaceous naevi and congenital naevi.

How should we treat eczema in children?

Similarly to the previous section, the speakers presented a very clear decision-making algorithm to help clinicians faced with atopic dermatitis. First of all, remember that it is important to consider differential diagnoses such as newborn rash, scabies, psoriasis and mycosis fungoides as well as specific phenotypes in patients with darker skin who present with follicular hyperkeratosis. Secondly, we should assess the severity of the atopic dermatitis using global assessment and quality of life scores such as the Atopic Dermatitis Control Tool (ADCT) and the Investigator Global Assessment (IGA). Alongside this, we must assess the associated comorbidities of asthma and food allergies, which can be reduced with early treatment of atopic dermatitis. All these prior assessments help define a personalised, 3-part treatment covering patient education, local

treatment and systemic treatment. Education is based on local treatments, understanding the disease and regular cleansing. Local treatment comprises corticosteroids during the initial treatment phase, and calcineurin inhibitors as maintenance therapy. As for systemic treatment, it is constantly evolving and involves numerous biological agents such as *dupilumab*, *tralokinumab* and JAK inhibitors which replace older first-line molecules such as *methotrexate* and *ciclosporine*.

When and how should we treat infantile haemangiomas?

The final session covered the treatment of infantile haemangiomas and, unsurprisingly, focused on systemic beta-blockers. The speakers mentioned that *propranolol* is the only treatment authorised for sale in France (AMM) and that it is essential that this treatment begins as early as possible. The haemangioma regresses entirely or almost entirely in 60% of cases at 3 mg/kg/day when treatment begins within 3 months of birth. It is also effective in 76% of cases of severe forms if treatment continues up to 12 months, though recurrence is possible when treatment stops. *Atenolol* is also offered as an alternative although the molecule has not been authorised for sale in France (AMM). If this fails or in case of contraindications for *propranolol*, we can suggest *rapamycin*. Corticosteroids are now only suggested as a second- or third-linetreatment. Surprisingly, *timolol*, a topical beta-blocker, was not more effective than the placebo and is therefore a secondary option which should not delay initiation of *propranolol* when necessary.

ONE IMAGE, THE RIGHT QUESTION, THE RIGHT DIAGNOSIS

Speakers: Dr. Emmanuelle Amsler, Dr. Brigitte Milpied, and Prof. Marie-Sylvie Doutre

Report written by Dr. Joël Claveau

This practical session was informative and interactive and mainly consisted of overviews of clinical cases. After the initial presentation of each case, there was an educational questionnaire linked to the diagnosis, the investigations or the therapy. The right answer was then presented during case feedback, together with a description of the pathology and a quick review of the relevant literature.

The first case covered a chronic, recurring eczematous rash on the face and hands. It was a photoallergy induced by contact with *chlorpromazine* after repeatedly preparing this antipsychotic medication. The key here was sufficient case history, enabling us to identify that this medication had been handled.

The second case was the sudden appearance of a unilateral erythema on an upper limb, affecting the elbow, back of the hand and periungual areas on the fingers. The right answer to the quiz was carrying out a blood test for Lyme borreliosis, which would have strong positive results. The issue was therefore acrodermatitis chronica atrophicans, presenting with purplish acral inflammation followed by an atrophic, fibrosing phase. Treatment with *doxycycline* was necessary.

The third case looked at a recurring exanthema on the trunk with infection, with no other related symptoms. The correct response was measuring CRP, which is always high in acute cases of this stereotypical rash. The disorder in question is called SITRAME (systemic inflammatory trunk recurrent acute macular eruption), which is a recently described autoinflammatory syndrome that always affects the trunk and sometimes the arms.

The fourth case was that of a middle-aged male presenting with a well-delineated pruriginous papulopustular eruption on his back, which appeared after facial surgery. It was a case of allergic contact eczema caused by betadine, the product used for preoperative disinfection. It was diagnosed with a positive patch test.

The fifth case covered the recurrent appearance of papulovesicular lesions on the upper limbs and hands after taking *paracetamol*. For this case, the examination to be requested was a skin biopsy, which would reveal pseudo-bullous lesions with neutrophilic infiltration. This result enabled a diagnosis of Sweet syndrome, or

neutrophilic dermatosis. We were reminded that this syndrome has numerous histological subtypes. The literature only reported a single case like this patient's linked to taking *paracetamol*.

The sixth case was recurrent periorbital swelling followed by significant facial oedema in a young female patient. The correct response was allergic contact eczema caused by epoxy resin. This is a common allergen in professional environments, but apparently it is becoming increasingly common in non-professional cases as it is used for crafting projects. As such, this dermatosis is becoming increasingly prevalent.

The seventh case tackled pruritic nodules on the outer arms which had been progressing for several years. The questionnaire should cover vaccination history and other injections in the location of the lesions. The additional investigation should include a deep biopsy, which would reveal nodular infiltration and lymphocytic hyperplasia. The diagnosis was reactive pseudolymphoma caused by vaccination. *Tetracyclines* are suitable asfirst-line treatment, but *thalidomide* is often more effective.

The eighthcase saw a patient being treated with *nivolumab* for metastatic melanoma, presenting with fixed, recurring pseudo-bullous lesions which appeared after around 3 months. The diagnosis made was fixed pigmented erythema following the periodic injection of the iodinated contrast products used in imaging to monitor melanoma. The diagnosis was confirmed with a patch test on damaged skin. We were reminded that these new contrast agents cause delayed reactions compared with the immediate reactions of older-generation products.

The ninth case was a middle-aged man with a fungated lesion on the head of his penis, which his GP believed was a carcinoma. The key to diagnosis was a complete cutaneous examination which revealed a palmoplantar keratoderma. This led to a blood test for syphilis, which gave a strong positive and revealed a primary syphilis infection.

The tenth case involved a young girl with papules where a mosquito spray had been applied. The patient was referred with a suspected contact allergy. However, additional history revealed that she had been experiencing cold-induced urticaria for several years. The key to diagnosing this case was listing the ingredients in the mosquito spray, since it contained menthol. The product had a cooling effect which was triggering the reaction.

Lastly, the eleventh case looked at a patient who had undergone a thyroidectomy and whose scar became very inflamed a few days after the procedure. The key here was to look at the different products used during the surgery. The culprit was in fact the wound adhesive, containing the allergen 2-octyl cyanoacrylate. During the allergological investigation, the patient had a significant positive reaction to the product in the patch test. The speakers mentioned that this issue is growing rapidly, particularly among paediatric patients, as wound adhesive is increasingly used due to its cosmetic advantages compared to conventional sutures.

CUTANEOUS TOXICITY OF CANCER TREATMENTS

Speakers: Dr Candice Lesage (Montpellier, France), Dr Laetitia Visseaux (Reims, France), Prof. Florent Grange (Besançon, France), Prof. Olivier Dereure (Montpellier, France)
Report written by Dr. Joël Claveau

This session was highly relevant given that the indications for new cancer therapies are constantly increasing. The three main classes of systemic agents used in oncology are chemotherapy, targeted therapy and immunotherapy. Regardless of their type of practice, clinicians will encounter various types of dermatoses since these skin toxicities are highly prevalent. From the outset, we were told that the dermatologist's role is to assess and manage the toxicity, to enable the agent to continue to be used where possible and, finally, to be able to recognise severe presentations. The key to good patient management is assessing the patient quickly and maintaining good relations with oncological, allergological and pharmaceutical colleagues. It is important to

inform patients of the expected effects as part of a preventive approach, i.e. the importance of skin care, moisturising and providing information leaflets. When a rash appears, drug investigation is crucial in determining the causal agent.

For the 3 types of treatment, being able to recognise severe reactions is essential. They may occur immediately (IgE-mediated type), such as anaphylaxis, urticaria and angioedema. *Cetuximab* is the prototype of this reaction, but several other agents, such as taxanes, can cause it. In some cases (e.g. *cetuximab*), the infusion rate may be slowed for prophylaxis. Shock is treated with adrenaline and injectable corticosteroids. Other delayed severe toxidermias include toxic epidermal necrosis (TEN/Lyell), Stevens-Johnson syndrome, DRESS (drug reaction with eosinophilia and systemic symptoms) and AGEP (acute generalised exanthematous pustulosis). We should look for signs of severity such as facial oedema, mucosal involvement, the presence of vesicles or bullae, Nikolsky's sign, purpura, skin pain and fever. Biological tests are used to identify haematological, hepatic or renal disorders. Toxicity must be graded in order to adapt treatment and follow-up. Anti-BRAF agents are associated with complete or incomplete DRESS (without eosinophilia). The delay is generally shorter than with other agents, and corticosteroid therapy very often ensures rapid and complete remission. The therapy cannot always be reintroduced. Contrary to typical Lyell's syndrome, systemic steroids are usually recommended in cases secondary to anti-cancer immunotherapy.

Chemotherapy causes skin toxicities secondary to damage to rapidly renewing cells such as keratinocytes. Firstly, there is hand-foot syndrome, which is more inflammatory. We can try to prevent it with suitable shoes and insoles, avoiding rubbing and consulting a podiatrist if necessary. Emollients and very strong topical corticosteroid therapy under occlusion are recommended as treatment. More rarely, capecitabine-associated adermatoglyphia may also be encountered. In terms of pigmentation disorders, we most often see diffuse or localised hyperpigmentation which may have a coppery-brown pseudo-Addisonian appearance. It can also affect appendages such as the hair *(methotrexate*), nails *(5FU*, taxanes) and mucous membranes. *Bleomycin* flagellate dermatitis may also be encountered. Reticular hyperpigmentation has been described with *paclitaxel*. Toxic erythema is a bilateral inflammatory condition affecting the acral regions after 2 to 4 weeks of treatment. Late-onset cutaneous porphyria can also occur with *tamoxifen* and *cyclophosphamide*.

The class of targeted therapies (anti-EGFR, anti-BRAF, anti-MEK, etc.) present frequent and very specific cutaneous toxicities depending on their target. With anti-EGFR treatments, we very frequently observe acneiform eruptions and paronychia. They are also known to cause hand-foot syndromes, which are initially inflammatory, sometimes bullous and finally hyperkeratotic. They present differently from chemotherapy-related hand-foot syndrome. *Encorafenib* is most often responsible here, but it can also be observed with various targeted therapies. With melanoma, anti-BRAF agents are often used in combination with anti-MEK agents. Adding in anti-MEK reduces cutaneous effects to around 25%. However, certain pathologies or situations require the use of anti-BRAF monotherapy, resulting in various manifestations of hyperkeratosis ranging from keratosis pilaris to keratoacanthoma and multiple acrochordons. The mechanism is linked to overactivation of the MAP kinase pathway. There may also be various eruptive pigmented lesions. The induction of wild-type BRAF melanomas has even been reported. Cystic acne can also occur. However, certain dermatoses occur even with the addition of anti-MEK, such as photosensitivity associated with *Vemurafenib* (induced by UVA). Strict, broad-spectrum photoprotection is recommended. Certain reactions are due to the use of anti-MEK monotherapy (affecting up to 60% of patients), such as folliculitis similar to that seen with anti-EGFR treated with cyclins, topical corticosteroids and photoprotection. Finally, in high-grade squamous cell carcinomas treated with *Cetuximab* or *Panitumumab*, a very significant inflammatory reaction may be observed at the site of actinic keratoses and may even cause sterile erosive and pustular dermatoses.

The final section dealt with the cutaneous toxicities of immunotherapy. There are three groups of molecules: anti-CTLA4, anti-PD1 and anti-PDL1. These different agents can provoke numerous reactions via an immune mechanism. The toxicity spectra are quite similar regardless of the indication. The main signs are maculopapular, eczematous and lichenoid eruptions, psoriasis and vitiligo. The cutaneous effects

of *Pembrolizumab* and *Nivolumab* are almost identical. Reaction intensity is usually grade 1–2 and permanent discontinuation of treatment is rare (5%). Rash and pruritus are often the first immunological reactions to occur, before any other non-dermatological reactions. Rash is the most common reaction (20–25%), it occurs early and is often self-limiting. The appropriate use of sufficient quantities of topical steroids, together with good skin hydration, usually prevents the need for systemic steroids. It is generally quite rare for therapy to have to be stopped. There is also the appearance of vitiligo (2–10% of cases), which is usually delayed, after a few months of treatment, and is almost exclusively associated with melanoma immunotherapy. Its occurrence is associated with a better anti-cancer response. However, rashes are more frequent and often more severe with dual immunotherapy (*Ipilimumab* + *Nivolumab*). Finally, numerous rarer dermatoses have also been described with immunotherapy: pemphigoid, panniculitis, mucositis, sarcoidosis, cutaneous lupus, Grover's disease, etc.

SKIN CANCERS IN THE ELDERLY: HOW FAR SHOULD WE GO?

Speakers: Dr O. Zehou (Créteil, France), Dr M.S. Gautier (Créteil, France), N.H. To (France), Dr O. Hermeziu (Créteil, France), Dr A. Ostojic (Créteil, France), Dr P. Caillet (Issy-les-Moulineaux)
Report written by Dr. Joël Claveau

The forum addressed the problem of the increasing incidence (mainly of skin carcinomas) and complexity of skin cancers in the elderly. Increasingly frequently, dermatologists are having to deal with very elderly patients or those suffering from reduced independence. The benefit/risk ratio of treatment can be difficult to assess, and a multidisciplinary approach is very often desirable.
Oncogeriatric assessment is based on screening for frailty, the patient's general prognosis, and tumours. The following factors must be taken into account: autonomy, nutritional status, mobility, cognition, psychological state and any comorbidities. Dermatologists can carry out summary screenings (*G8 Score*) and then request a more in-depth oncogeriatric assessment for more problematic patients.
When making therapeutic decisions, life expectancy must be taken into account, in terms of both age and state of health. For example, a frail 70-year-old patient has a life expectancy of 6.7 years, compared with 8 years for an 85-year-old patient in good overall shape. This is particularly relevant when deciding on adjuvant treatment for melanoma.
In multidisciplinary management, the various alternatives must be considered: surgery, topical treatment if indicated (e.g. *imiquimod* for carcinoma), radiotherapy, systemic treatment, or no treatment at all.
We frequently see communication problems, especially in patients with deafness or dementia. Insufficient family support, difficulties in taking action, economic considerations and other factors contribute to the complexity of these cases and often lead to ethical debates. We want to offer our patients the best care, without being relentless.
During this interactive session, the various speakers presented a series of clinical cases for discussion: a reticent 95-year-old woman with several cutaneous carcinomas; some had been operated on, some treated with *imiquimod* and some left in place. A peaceable 91-year-old woman with Alzheimer's and a large Dubreuil-type melanoma in situ who underwent simple surgery (1 cm margin and purse-string closure), which ultimately produced an acceptable aesthetic result. An agitated, visually impaired 90-year-old woman with hearing loss and a large basal cell carcinoma on her nasal root and internal canthus, who finally agreed to plastic surgery after much hesitation. An 87-year-old man with basal cell carcinoma of the lower eyelid treated with contact radiotherapy instead of complex surgery. Finally, an 86-year-old man with moderate cognitive impairment, operated with a 1 cm margin for a thick, ulcerated melanoma of the face – the sentinel node technique and adjuvant treatment were not offered. These cases required a multidisciplinary approach and were presented at consensus meetings.

PRURITUS: HOW TO GET OUT OF THE TRAP?

Chairman: Prof. Laurent Misery
Speakers: Prof. Joachim Fluhr (Berlin, Germany), Dr Emilie Brenaut (Brest, France), and Dr Christelle Le Gall-Ianotto (Brest, France)
Report written by Dr Ibrahim Fayez

Prof. Joachim Fluhr

Classification:

The classification of the impact of pruritus (itch) on quality of life, considering factors such as pain, desquamation, psychological effects, and even suicidal ideation, is often addressed in the context of the International Forum for the Study of Itch (IFSI).

Category	Diseases
I. Dermatological	Arising from "diseases of the skin", such as psoriasis, atopic dermatitis, dry skin, scabies and urticaria
II. Systemic	Arising from "diseases of organs" other than the skin, such as liver (e.g. primary biliary cirrhosis), kidney (e.g. chronic renal failure), blood (e g. Hodgkin's disease), and certain multifactorial (e.g. metabolic) states or drugs
III. Neurological	Arising from "diseases or disorders of the central or peripheral nervous system", e.g. nerve damage, nerve compression, nerve irritation
IV. Psychogenic/ Psychosomatic	Somatoform pruritus with co-morbidity of "psychiatric and psychosomatic diseases"
V. Mixed	Overlapping and coexistence of several diseases
VI. Other	Undetermined origin

Classification
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New pathogenic type of chronic pruritus: Pluriplastic pruritus.

	Pruriceptive	Neuropathic	Pruriplastic
Origin	Pruriceptor	Lesions of peripheral or central nervous system	Dysfunctions of itch processing (central sensitization, loss of downstream controls)
Characteristics	Variables	Associated with other unpleasant sensations (paraesthesia, dysesthesia)	Atypical*
Localization	Locoregional or diffuse	According to involved nervous system	Local or diffuse
Neurological examination	Normal	Abnormal	Normal
Evolution	Acute or chronic	Chronic	Chronic
Treatment	Etiological	Gabapentinoids	Antidepressants**
	Symptomatic	Antidepressants**	

New pathogenic type of chronic pruritus: Pluriplastic pruritus
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***There is a need for confirmation by clinical trials.*
**Examples: association with extra-cutaneous sensory or other disorders.*

Assessment of the pruritus:

- Pruritus history
- Location on body
- Onset, course, durations
- Character: pain, burning, itch
- Associated symptoms and effect on sleep
- Evolution of cold, hot, or intensifying factor
- Verbal rating scale 0-10
- Numeric scale: 0-3

The development of pruritus can be attributed to various factors:

- Skin origin: atopic dermatitis, psoriasis, etc.
- Liver or kidney involvement: auto-toxins, xerosis, medications
- Haematological and thyroid diseases
- Neurogenic-like notalgia

Clinical case: 27-year-old individual presenting with pruritus, the final diagnosis being Hodgkin disease with pulmonary lesions.
Lab studies: routine blood tests, urine analysis, abdominal ultrasound, total Ige. We can also add: ANA, immunofluorescence, HIV and hepatitis serology, skin biopsy, tryptase, and allergy testing.

Dr Emilie Brenaut

Intractable pruritus is a persistent and uncontrollable itching sensation, serves as a primary complaint across various dermatological conditions such as psoriasis, atopic dermatitis, lichen planus, and Sezary syndrome. Pruritus, being the predominant symptom in numerous skin disorders, has far-reaching implications affecting different aspects of an individual's life. The consequences of pruritus and the subsequent scratching behaviour extend beyond the physical discomfort, impacting social dynamics through stigma and isolation. Furthermore, the effects encompass mental and emotional well-being, creating a profound influence on the quality of life for affected individuals.

The impact of pruritus is multifaceted, imposing financial burdens due to the necessity of creams and treatments. Social aspects are also affected, contributing to feelings of isolation and potentially influencing relationships. The repercussions extend to sleep disturbances, affecting both the patient and their partner.
In the evaluation of pruritus, clinicians consider various aspects, including its quality, intensity, frequency, and duration. Moreover, the secondary effects of scratching are assessed, recognizing its implications on physical health, mental health, and overall social well-being.
To gauge pruritus accurately, different assessment tools are employed. These range from simple and linear scales, such as visual and numerical rating scales, to more intricate measures like the Multi-Dimensional Scale or the Daily Life Quality Index. The latter options provide a comprehensive evaluation by considering various factors contributing to the complexity of the condition.

Dr Christelle Le Gall-Ianotto

Mechanism of Pruritus: through histaminergic or non-histaminergic pathways

1. *Chemical pruritus*

Histaminic and non-histaminic pathways play a crucial role in activating nerve receptors that release neuropeptides like substance P and CGRP. These substances subsequently induce vasodilatation and enhance the upregulation and migration of immune cells to the dermis. This immune cell influx results in the release of more inflammatory mediators, intensifying pruritus.
Pruritus involves various mechanisms and mediators, including histamine, endorphins, neuromediators, substance P, CGRP (a vasodilator), and TRP (activated by temperature and capsaicin, involving around 30 chemicals). The transmission of the pruritus signal later occurs through the spinal cord to the brain.
To inhibit pruritus at the spinal cord level, afferent receptors and neurotransmitters such as CGRP, substance P, MDMA, and morphine receptors can be targeted, often using agents like naloxone. Additionally, inhibition at the brain level involves areas such as the frontal, prefrontal, and motor areas, treating pruritus and rubbing as reflex-like responses.

2. *Mechanical touch*

Pruriceptor in the skin:
In terms of mechanical touch, pruriceptors in the skin, including Merkel cells, keratinocytes, and specific AB and C-AD fibres, play a role in perceiving light touch as pruritus through a phenomenon called allokinesis. As individuals age, there is an increase in Merkel cells in conditions like prurigo nodularis and psoriasis.
Typically, a descending pathway from the brain activates mechanisms and mediators to reduce pruritus. However, in cases of dysregulated pathways, as seen in atopic dermatitis, benefits can be obtained by using treatments that target specific cytokines like IL-4, IL-13, IL-31, and Janus kinase (JAK) inhibitors. These interventions help modulate the dysregulated immune responses, alleviating the symptoms of pruritus associated with certain dermatological conditions.

Prof. Laurent Misery

Get out of the trap:
Finally, pharmaceuticals are interested in treatments for pruritus.
European guideline: Advances in dermatology and venereology Acta Dermato-Venereologica Acta Derm Venereol 2019; 99: 469–506
Link to online article: https://medicaljournalssweden.se/actadv/article/view/3172/4985

1. Treat causes: skin, liver, renal, psychological, other.
2. General rules: avoid rubbing, moisturization, clothing, technique to stop excoriation.
3. Placebo effect: 30-70% improvement.
4. In case of inflammatory conditions: Topical steroid preparation, calcineurin inhibitors, local anaesthetics, capsaicin.
5. Antihistamines: 10-20% of cases related to histamine, so placebo effect.
6. Naltrexone (U-receptor agonist).
7. Gabapentin and Lyrica. Can increase dose. Usually well tolerated.
8. SSRI (*Prozac*® and *Zoloft*®).
9. SNRI (*Cymbalta*®) Rare SE, well tolerated.

10. Anticholinergics: *Hydroxyzine*, *Doxepin*.
11. Antidepressants.
12. Anti-anxiety, sedatives, opioids.
13. Psychotherapy, CBT, meditation, hypnosis, music therapy, acupuncture, other.
14. Immuno-modulators: *Cyclosporine*.
15. Phototherapy.
16. Biologics*: anti IL-4, anti IL-13, anti IL-31, NK1 inhibitors*.
17. PDE4 inhibitors.
18. NEW STUDIES: Chronic pruritus and prurigo including prurigo nodularis: duration of prurigo more than 6 weeks *Dupilumab* (anti IL-4 and 13), *nemolizumab* and *vixarelimab* (anti IL-31).
19. Uremic pruritus: associated with chronic renal insufficiency and renal dialysis.

Nalbuphine: Kappa agonists: *difelikefalin* given with renal dialysis solution also available in oral form (also trials for use in notalgia paraesthetica and atopic dermatitis).

ACUTE URTICARIA, CHRONIC URTICARIA, CONTACT URTICARIA: WHAT'S THE DIFFERENCE?

Speakers: Prof. F. Tétart (Rouen, France), Dr F. Hacard (Lyon, France), Dr R. Boussaid (Alger, Algerie), and Dr P. Mathelier-Fusade (Paris, France)
Report written by Dr Ibrahim Fayez

Acute urticaria

Clinical cases presented by Dr Hacard and Dr Mathelier Fusade
Viral rashes and other causes

1. Acute allergic urticaria

A 25-year-old female with a history of environmental allergies is currently taking Amoxicillin for bronchitis. Following a dinner with friends, she experienced angioedema and an urticarial eruption. Upon presentation to the emergency room, the symptoms rapidly resolved with intravenous antihistamines and systemic steroids. Given the likely connection to a chest infection, no further treatment or investigations are deemed necessary. The challenge lies in distinguishing whether the reaction is immunological (IGE mediated) or non-immunological, with potential triggers including infections, viruses (such as COVID), hormonal factors, complement issues, neuropeptides, etc. Both scenarios can manifest with similar clinical presentations.
Key points related to the case:

- Allergic urticaria, typically IgE mediated, involves prior sensitization/exposure, with reactions occurring within 1-4 hours upon re-exposure.
- Anaphylaxis symptoms encompass angioedema, palmar and plantar pruritus, swelling, laryngeal swelling, pruritus, chest congestion, cough, and dyspnoea.
- Acute urticaria is clinically diagnosed based on a history compatible with allergy and negative serum tryptase levels.
- An allergist's workup may include prick tests and serum IgE assessments. If allergy testing is positive, considerations include education and avoidance, an allergy kit containing *antihistamines*, a Ventolin inhaler, and *adrenaline* auto-injectors. Note: Steroids are generally avoided due to the risk of rebound reactions after 4 hours (10-15%).

The mention of facial oedema and desquamation after applying shampoo to the scalp suggests a potential skin sensitivity or allergic reaction.

2. 13-year-old with recurrent urticaria and facial oedema

A 13-year-old with recurrent urticaria and facial oedema experienced symptoms starting 15-20 minutes into a soccer game. The episode included itchiness on the body, palms, and soles. The trigger appears to be related to the consumption of bread just before playing, particularly involving the omega gliadin protein in wheat and physical exertion. This reaction is largely IgE mediated and rechallenge is likely to reproduce symptoms.

Management recommendations include not necessitating complete avoidance of wheat but advising against physical exertion within four hours after consuming it.

3. From Japan: allergic contact urticaria from facial cosmetics, bio-soaps containing wheat protein causing eyelid angioedema

4. Allergic reaction to Cetuximab *after first exposure which is not typical of IgE mediated reactions*

A patient experienced an allergic reaction to *Cetuximab* after the first exposure, a reaction not typical of IgE-mediated responses. The reaction is attributed to a monoclonal antibody with a fragment antigen-binding (Fab) component.

The individual has a history of previous urticarial reactions and abdominal pain. As a butcher and hunting enthusiast, it was discovered that the allergic response is linked to a sugar called galactose alpha 1,3, found in edible red meat from animals and in some medications containing gelatine, such as *Cetuximab*. This allergic reaction is IgE mediated and acquired, with tick bites being a potential inducer.

Primary symptoms associated with this allergy include urticaria, abdominal pain, and the potential for anaphylaxis.

5. Quincke's oedema in the context of a 55-year-old female experiencing facial swelling in relation to NSAIDs:

4 scenarios:

1. Five days after starting low-dose NSAIDs: Skin only symptoms.
Recommendation: Reassurance and add antihistamines.
2. One hour after starting different types of NSAIDs, resolves rapidly with antihistamines, patient is atopic: NSAIDs induced urticaria, reassurance, take with antihistamine.
3. Immediately after the first dose, severe reaction, needs ICU admission: NSAID-exacerbated respiratory disease or Vidal syndrome. Not IGE mediated. Recommendation: Prevent future NSAIDs
4. Severe symptoms and shock one hour after the second dose of NSAID: This is an allergic reaction. Allergy tests will be positive.

NSAIDs through COX-1 inhibition will cause overproduction of leukotrienes and inhibit prostaglandin 2 production and increased mastocyte degranulation.

Classification or NSAIDs reactions

Onset of reaction	Clinical manifestation	Mechanism	Allergy testing
Acute	Cutaneous	Pharmacological	No. Can take NSAIDs
		(COX-1)	Add antihistamines
Acute	Cutaneous and systemic	IgE	Yes
Delayed	Cutaneous and/or systemic	T lymphocyte	Yes

Classification or NSAIDs reactions
DOWNLOAD

Take home message: In case of isolated acute urticaria.

- Ensure absence of systemic symptoms.
- Consider the type of reaction: onset, course, duration.
- Allergy tests are not needed in most cases.
- Rule out atopic dermatitis and chronic spontaneous urticaria.
- Premedication with antihistamines is advisable.

Chronic urticaria

Clinical cases presented by Dr Boussaid (paediatric allergy dermatology specialist)

1. 3-year-old, generalized eruption 4 days post starting antibiotic: maculopapular reaction
2. 4-year-old male, eruption post ibuprofen taken for fever, otherwise well: viral urticaria
3. 6-year-old female, atopic, pruritic skin eruption after a sleepover with candies, chips, strawberry milkshake, and chocolate mousse: non-allergic urticaria, spontaneous, histamine release.
4. Recurrent urticaria in a 10-year-old.

Started 2 months ago, recurrent, and better with antihistamine.
Perianal pruritus has ascariasis and clears with antiparasitic treatment.
Acute urticaria: remains challenging to diagnose, main causes are infections, food and medicines.

5. A 12-year-old girl presents with multiple recurrent urticarial rashes with specific triggers and a family history of Hashimoto's (mother and grandmother).

Rash disappears with prednisolone but recurs, now almost daily.
Triggers: activity, stress, *ibuprofen* and certain histamine-rich foods.
She is otherwise healthy and normal.
Chronic urticaria (inducible physical urticaria, dermographism)
No test is necessary, but if the situation does not improve, a test may be performed.
Administer oral antihistamines and adjust dosage.
Usually resolves itself.

Contact urticaria

Clinical case presented by Prof. Francoise Tetart

Definition: Erythematous urticarial papules arising 30 min after contact with allergen and resolving after a few hours.

Stages:

1. Localised
2. Generalized
3. Systemic (including asthma, rhino-conjunctivitis, GI symptoms)
4. Anaphylactic reaction

Types:

- Immunologic contact urticaria (IgE mediated)

Characteristics: Requires previous sensitization.
Testing: Can be diagnosed using prick tests and IgE testing.
Possible Causes: Allergens from animal or plant ingredients, or oils.

- Non-immunologic contact urticaria (non-histamine-mediated), due to contact with chemicals and systemics. Antihistamines non efficient here.

Testing: Prick tests may be negative.
Diagnosis: Positive open test or rechallenge confirms the diagnosis.
Possible causes: Contact with chemicals and systemic factors.
Note: Antihistamines may not be effective for non-immunologic contact urticaria.