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Acne

Microbiota and acne

We are learning more and more about the importance of microorganisms that live with us (making up our microbiota), and in relation to skin, among the most studied microorganisms are acne bacteria. In the case of acne, both the skin and intestinal microbiota are altered. In the skin microbiome, IA-type *Cutibacterium acnes* feeds off of sebum and is more inflammatory than other types of acne bacteria. Biodiversity is lost in the microbiome in favour of this bacterium. In addition, the involvement of *Malasezzia* has been found in some cases. With regard to the intestinal microbiome, acne has been associated with cases of intestinal permeability and excessive bacterial growth. There are studies suggesting it can be beneficial to give probiotics in these cases.

Acne in adult women

Above all, adult acne predominates among women, representing 82.1% of cases, with men only making up 17.9% of cases. It is unknown if cases of adult acne are actually increasing or if patients are just now consulting dermatologists more often. It appears that the pathogenesis of adult acne is different from that of adolescent acne: multiple factors are involved, including stress, diet, changes in sebaceous secretion, medication, smoking, endocrine disorders, and more, in addition to a genetic predisposition.

With regard to associated endocrine disorders, polycystic ovary syndrome is the most common in women of reproductive age: 6 to 10% of women live with this condition, and among those women, 42% have acne. It is more common for acne to recur in these cases after dermatological treatment and it typically affects the lower portion of the face. In all of these patients, we must investigate if there is any hormonal alteration associated with acne fulminans, characterised by ulceronecrotic lesions, scabs, and scarring.

Severe forms of acne

Acne fulminans is a severe form of acne with several differences in comparison to acne conglobata. Acne fulminans occurs more suddenly and mainly during adolescence, while acne conglobata occurs more often in adults and does not begin as abruptly. Both are associated with androgens. These conditions should be treated with corticosteroids and isotretinoin. However, isotretinoin has been associated with the appearance of acne fulminans, in which case isotretinoin treatment should cease

and be replaced with corticosteroids. Once the patient is stabilised, isotretinoin treatment can start again at low doses. This type of pathology can be associated with systemic symptoms such as fever, arthralgia, and leukocytosis, but not in all cases.
Other types of severe acne are associated with autoinflammatory diseases, such as PAPA, PAPASH, PASH, PASS, and SAPHO. Such severe cases are treated with biologics such as anakinra, ustekinumab, and secukinumab.

Advancements in the treatment of acne
New treatments for acne are emerging.
- Minocycline topical foam 4% showed improvement for 30% of patients, versus 19% for the foam vehicle group in the study.
- Microencapsulated benzoyl peroxide 3% + tretinoin 0.1%: with silica-based gel that enables deferred release. Thanks to the formulation and vehicle, there are virtually no side effects.
- Clascoterone 1%: first new mechanism in many years. It is an androgen receptor inhibitor, thus blocking the release of sebum and proinflammatory cytokines such as IL-1, IL-6, and TNF-alpha. However, the results are not very compelling, with improvement for 20% of patients, versus 8.8% for the vehicle group in studies. It is being sold in the United States, but it is not yet available in Europe.
- Spironolactone is used not only for treatment of acne, but also for HS and androgenetic alopecia. It is particularly used for women aged 19 years and older. What's new is topical spironolactone. In studies, it diminished comedones and inflammatory lesions. (In one study of topical spironolactone 2% versus topical clindamycin 1.5%, the spironolactone demonstrated greater efficacy. Other concentrations go up to 5%. More studies are needed.)
- Additionally, spironolactone has anti-acne effects up to months after its use has ended.
- N-Acetyl-GED-0507-34-LEVO gel in patients with moderate to severe acne: The first topical combination of three products: clindamycin, benzoyl peroxide, and adapalene. Available soon. In studies, over 50% of patients (52.5%) achieved satisfactory results at 12 weeks. It appears to be the most effective topical treatment (current topical treatments achieve efficacy in at most 40% of cases).
- Probiotics in the treatment of acne: for treatment of *C. acnes*, taken both orally, with lactobacillus, and topically to regulate sebaceous secretion from the sebaceous glands. More studies are needed.

Latest developments in cosmetic dermatology

What's new with lasers and light devices?
There are more and more lasers available for treating pigment, both endogenous and exogenous, such as tattoo ink. Tattoos remain in the skin within macrophages, and when we treat them with a laser, the pigment is transferred to the lymphatic ganglia.
The pigment can be treated with Q-switched nanosecond laser (ruby, alexandrite, or KTP-Nd:YAG) or picosecond laser. The picosecond laser is very useful for resistant pigments or difficult colours such as yellow, green, or turquoise. Additionally, it does not cause the paradoxical darkening that occurs with some other lasers.
The combination of ablative fractional CO2 laser with a Q-switched Nd:YAG laser is very effective in resistant cases, producing better results than with the Nd:YAG laser alone, with statistically significant differences.
You can also use Nd:YAG laser, KTP laser, or both for patients with hyperpigmentation caused by extravasation of intravenous iron, with good results, although multiple sessions are required.
Use caution with lactic acid injections to remove tattoos as they can cause skin necrosis. This product is being sold online and some patients are injecting it into themselves at home. As dermatologists, we should be informing patients of the risks of these procedures.

For vascular lasers, there are two main wavelengths used: the 595 nm wavelength has greater affinity for haemoglobin, while the 532 nm wavelength can be used to treat red and brown pigments.

Fillers

Fillers have been used since 1893, when the first fat transplant was performed. Since then, many different products have emerged, including collagen, polylactic acid, calcium hydroxyapatite, and hyaluronic acid.

These products are used because with age, collagen breaks down, bone is reabsorbed, and fat diminishes. We can treat these issues with fillers, but we can also use multiple therapies and combinations. In fact, patients are increasingly asking for minimally invasive procedures.

A multi-step treatment has been proposed: first, botulinum toxin is applied; then, hyaluronic acid or collagen inducers, until the desired effect is achieved. That said, we already have hybrid products that combine hyaluronic acid and a collagen inducer in the same vial.

Botulinum toxin

Until very recently, we've had three forms of botulinum toxin available. Botulinum toxin has been approved for medical use since 1989.

· The most common form: Botox or Vistabel, for which we have more studies and more scientific evidence.

· Bocouture does not require a cold chain and is the least immunogenic (it does not generate resistance).

· In a few studies, Azzalure appears to demonstrate longer lasting effects. Additionally, using the same molecule as Azzalure is Alluzience, the first liquid form of botulinum toxin. In studies, it appears to last longer, but the product is more concentrated.

Greater concentrations of the botulinum toxin produce longer lasting effects. However, there is no major difference between administering 40 IU versus 80 IU. Where we do see major differences in duration is between injecting 20 IU versus 40 IU.

The new forms of botulinum toxin are:

· Jeauveau: prabotulinumtoxin A (South Korean)

· Daxxify: daxibotulinum A, 150 kDA and a stabilising protein (RTP004). According to studies, it likely has the greatest duration of effects.

· Botulax: Letibotulinum A (South Korean)

All of these are type-A botulinum toxin. However, the new BoNT-E botulinum toxin has also emerged: it starts working fast, but lasts two to four weeks (approval is expected in 2024). It will be an option for when the patient is in a hurry, if a patient is unsure and wants to give botulinum toxin a try, or if the patient doesn't want the effects to last long.

To summarise, the new forms of botulinum toxin may change the landscape, and what patients are most often looking for is the duration of the effects.

Another important aspect is how studies are conducted: they are no longer conducted in animals. Before, the products were tested in animals, and each test required six to 16 mice, all of which would die. That is no longer justified: today, other types of laboratory studies are conducted, some of which do not use animals. However, these other studies are less accurate.

Treatments for improving skin slackness

Patients are increasingly seeking out procedures without "downtime." People want the best version of themselves, but don't want to change. They also seek body treatments, also known as "body contouring": these treatments aim to do things like diminish volume, improve slackness, and eliminate cellulite. There are multiple devices available for such treatments: CoolSculpting, radio-frequency devices, HIFU, ultrasound, laser, etc. None of these is 100% effective. Thus, a combination of treatments is used.

Sexually transmitted infections

Sexually transmitted infections (STIs) in adolescents

Adolescents are becoming sexually active earlier and earlier. As such, we need to provide them with high-quality sex education, vaccinate them against HPV, and give them access to health care for diagnosis and treatment. Adolescents who are sexually active are at the highest risk of contracting an STI among all age groups.

Chlamydia trachomatis is the most common STI among adolescents. Gonorrhoea is particularly common among women and girls ages 15 to 19 years old. HPV is also most prevalent among adolescents.

Herpes simplex is increasing in prevalence for type 1 due to the types of sexual activities. It is also a risk factor for contracting HIV. We also can't forget pelvic inflammatory disease (PID) caused by gonorrhoea and chlamydia.

We need to provide more information to sexually active adolescents, including women who have sex with women, as many of them have never used a barrier method.

The widespread use of the human papillomavirus (HPV) vaccine has decreased the number of patients with genital warts. The vaccine is also effective in men and boys. As such, they should also get vaccinated. A study was conducted on the side effects of the vaccine and no significant side effects were found. The study also found no increase in autoimmune diseases.

What's new with antibiotic resistance in STIs?

Antibiotic-resistant gonorrhoea is increasing, while syphilis is resistant to macrolides… All of this is occurring because many patients have received incomplete treatment or short courses of treatment. Gonorrhoea in women is more likely to be asymptomatic than it is in men and it can cause pelvic inflammatory disease, ectopic pregnancy, and transmission from mother to foetus.

Since 2016, the WHO has been warning about the increase of resistance in gonorrhoea to antibiotics such as azithromycin and ciprofloxacin. The most effective antibiotics are penicillin derivatives applied intramuscularly (e.g., ceftriaxone).

Mycoplasma genitalium shows resistance to macrolides. As such, the treatment should be a course of doxycycline, followed by azithromycin or moxifloxacin.

Shigella sonnei: A lesser-known bacterium that produces symptoms including fever, diarrhoea, abdominal pain, and tenesmus with pus or bloody diarrhoea. Its transmission is faecal-oral or sexual. For sexual transmission, it is particularly linked to anal or oral sex. It can also be contracted via indirect contact. It is treated with fluoroquinolones, cephalosporins, or beta-lactams as a second-line treatment.

However, its antibiotic resistance is increasing. For an antibiotic-resistant infection, there aren't many treatment alternatives: you can use nanoparticles, phage therapy, or vaccines, although currently none of these treatments are approved.

We need to raise awareness about the increase of antibiotic resistance, optimise the use of antibiotics, and have rapid tests available to prevent the spread of diseases.

Mycoplasma: to test or not to test

Mycoplasma genitalium has a prevalence of 1%. Many people have an asymptomatic form of the infection. The microorganism has the shortest known genome (580 Kbp).

It plays a key role in non-gonococcal urethritis. It can cause pelvic inflammation. However, we don't know what favours its spread to some people but not others. It is also associated with risk during pregnancy and problems during delivery.

Should we be testing for Mycoplasma? No. You only need to test for it when there is clinical suspicion. There is an issue with at-home tests and incomplete treatments that are encouraging antibiotic

resistance. The infection should not be treated with a single dose of azithromycin because while it may cure 86% of cases, 14% of cases develop resistance. It should be treated with azithromycin at a dose of 1 g per day for five days. Resistance to moxifloxacin has been stable over time.
However, macrolide resistance in Europe is up by 50%, reaching as high as 90% in some countries.
Among men who have sex with men, test if the patient does not respond to antibiotics and look out for epididymo-orchitis and proctitis. Among women, test for it if they have a pelvic infection, abnormal bleeding after sexual activity, or if they have had contact with an infected person.

Has HIV become a chronic disease?
The human immunodeficiency virus was discovered in 1981 and since then, we have made numerous advancements in its treatment. Currently, in many patients, the virus can be controlled with a single pill taken once daily or even an injection given every two months, which will soon be available.
If the viral load is undetectable, the person is not contagious: this is important to note. And if the patient follows their treatment regimen, they can maintain an undetectable viral load for a long time.
We should raise awareness about early detection of HIV given that when it is diagnosed with a diminished CD4 count (AIDS stage) it can decrease the life expectancy of the patient by as much as 20 years.
Dermatologists can play a key role in early diagnosis, for example, when diagnosing STIs that are sometimes associated with HIV infection or skin conditions that lead us to suspect HIV infection, such as persistent pruritus, oral aphthous ulcers, psoriasis that doesn't improve, severe seborrhoeic dermatitis, Kaposi sarcoma, etc.

Pigmentation disorders

The challenges of hyperpigmentation in patients with dark skin
Dark skin offers natural protection against solar radiation compared to light skin; however, it also has a greater amount of melanin. Inflammation and proinflammatory growth factors can stimulate melanocytes, which can cause the appearance of hyperpigmentation.
The melanocytes can move into the dermis due to gaps in the basal layer, alteration of keratinocytes, an increase in prostaglandins, and other inflammatory signalling pathways, such as NF-kB and microRNA.
We are learning more and more about the importance of mesenchymal stem cells and inflammation in the appearance of hyperpigmentation.
With regard to treatment, Kligman's triple-combination formula is effective for all skin phototypes. However, the best option is a combination of treatments.
Patients should always use sun protection of at least SPF 30 that also protects against visible light. For this, there are tinted creams that are very effective and better at protecting against visible light.
There are also other depigmenting agents like retinoids, alpha hydroxy acids, corticosteroids, thiamidol, niacinamide, and plant derivatives. Many of these have anti-inflammatory activity, like azelaic acid, which reduces IL-1, IL-6, and TNF-alpha; or kojic acid and calycosin, which inhibit NF-kB. Most inhibit tyrosine kinase.
You can also apply laser or chemical peel treatments. You should always avoid inflammation, which can be counterproductive.
Some oral treatments for hyperpigmentation have shown efficacy:
Niacinamide at 200 to 1500 mg a day, tranexamic acid at 500 mg a day, melatonin at 3 mg a day, and carotenoids: 800 mg per day.

New developments in the treatment of melasma
It is very important for patients to use broad-spectrum sun protection that includes visible light.

The best treatments for melasma are tyrosine kinase inhibitors. It is very important to consider epidermal-dermal interactions. In patients, dermal vascularisation is altered, with an increase in blood vessels and VEGF. Melasma occurs more often in women, at an average age of 34 years old, with a hormonal factor involved (linea nigra during pregnancy, colouration of the areolas, etc.).

It also occurs more often in areas with a high concentration of sebaceous glands. Sebocytes can produce growth factors, proinflammatory ILs, and hyperpigmentation.
The best therapies for melasma are ones that combine the inhibition of pigment formation with a strengthening of the skin barrier and dermis (combination of treatments).

Vitiligo: Stem cell transplant and PRP
In vitiligo, the body produces antibodies against melanocytes. To repigment the areas that have lost melanocytes, there are strategies using MUSE-type stem cells (mesenchymal stem cells) or adipose-derived stem cells. There is also treatment using platelet-rich plasma (PRP).
The PRP should be prepared using the double spin method. The first spin is to separate out the red blood cells and the second spin releases growth factors. The combination of PRP with narrowband UVB phototherapy, with three PRP treatments monthly combined with three NB-UVB treatments weekly, has shown good results.
Whether using PRP or stem cells for treatment, we should use phototherapy to stimulate repigmentation, whether it be narrowband UVB therapy or excimer laser therapy.

Will Janus kinase inhibitors revolutionise vitiligo treatment?
Recently, topical ruxolitinib (a JAK inhibitor) was approved for the treatment of vitiligo affecting the face. The medicine shows good results, with repigmentation in up to 40% of patients. For the treatment to be truly effective, it should be combined with a source of UVB light.
Other topical JAK inhibitors, such as tofacitinib, are being researched, with similar results.
Oral JAK inhibitors have shown efficacy in studies. Interestingly, an oral drug such as methotrexate at moderate doses has produced results similar to those of JAK inhibitors, with improvement for 40% of patients, and up to 80% when combined with phototherapy.
With systemic Janus kinase inhibitors, we need to keep in mind the risks, which are similar to those of anti-TNF drugs, with infections and thromboembolic events. However, they also present a greater risk for the development of cancer in these patients.
Other promising future treatments include biologics, like the IL-15 inhibitor.
What's clear is that new treatment options for vitiligo are emerging, but all of them should be combined with phototherapy to be truly effective.

Allergology and reactions to drugs

Contact allergens

With contact allergies, frequency varies from country to country due to the fact that people in each place don't have the same exposure to the same allergens. As such, the batteries of tests change from one country to the next. Methylisothiazolinone (MI) is an allergen that is associated with allergic response to other allergens. It is present in many things: tattoos, fabric softener, ironing water, etc., but it is sometimes difficult to know where the patient may have been sensitised.
Another common allergen is decyl glucoside, which is found in textile and photography products.
Another new allergen to test for is octylisothiazolinone (OIT), which may have cross-reactivity with MI. OIT was found in 55% of leather products coming from Switzerland.

With contact allergy to limonene and linalool, the clinical manifestations can include eczema on the eyelids caused by shampoo, on the fingertips due to contact while working, or on the body caused by shower gel. Sensitivity in the population has been found to be between 1% and 8%. There are pros and cons of routinely testing for this allergy since its concentration is low in some products. You only need to test for it when you suspect a fragrance allergy.
There has also been an increase in contact dermatitis caused by acrylates among nail technicians and among people who use semi-permanent gels. In one study, it occurred in 0.75% of people. Interestingly, **hairdressers and beauticians are at nine times greater risk of developing contact dermatitis compared to the general population**.
Another contact dermatitis that is emerging is related to glucose monitors and insulin pumps worn by diabetic patients. The allergens that have been linked to this contact dermatitis are colophony, formaldehyde, butyl acrylate and other acrylates, and isopropyl alcohol.
Doctors have also described contact dermatitis caused by an acrylate found in a mobile phone screen protector.
A pathology that is increasing in frequency is frontal fibrosing alopecia, and it may be linked to a contact dermatitis caused by sunscreen. However, more studies of this are required.
An article was published on all forms of occupational contact dermatitis recorded during the COVID-19 pandemic among healthcare personnel, particularly caused by masks.

Adverse effects of new oncological therapies

There are five grades of side effects caused by oncology drugs, from 1 to 5, with 1 being the mildest and 5 causing the patient's death. This grade determines if we should cease treating the patient with the drug.
Adverse effects related to immunotherapy: we should know these and, particularly, know at what point in the treatment they may appear.
For example, ipilimumab can cause rash/pruritus from the second to the tenth week; it can also cause diarrhoea or colitis from the fifth to the tenth week. Meanwhile, hypophysitis and hepatitis can appear from the fifth or sixth week and last for a longer duration.
It is important to know when adverse effects might appear and whether or not they will improve so that we can determine if we should continue or discontinue treatment with the drug.
For mild reactions (grades 1-2), we can use topical corticosteroids, have the patient avoid irritants, and combine the treatment with antihistamines. For more severe reactions (3-4), we can give oral corticosteroids and seriously consider discontinuing treatment with the drug, especially if the patient develops SJS.
For other toxicities, such as hepatic or gastric, initiate treatment with steroids.
For pneumonia, rule out the possibility of an infection, and if there is none, treat it with corticosteroids.
Other rarer reactions may be neurological, such as meningitis, encephalitis, myasthenia, etc.
We are gaining access to more and more PD-1 inhibitors. These include relatlimab, nivolumab, and even the combination of both, which of course causes more adverse effects.
The patient's microbiota should be evaluated before treatment as they can help predict the response to the treatment or the possibility of adverse effects from the cancer treatment, such as colitis, but also others.
With CTLA-4 inhibitors, we expect to have a 21% rate of adverse effects, and with PD-1 inhibitors, a rate of 34%.
Targeted therapy: against mutation of the BRAF gene. It can cause arthralgia, QT prolongation, and nausea. In the skin, it can cause squamous cell carcinoma, erythema nodosum, photosensitivity, dry skin, folliculitis, or cysts. In these patients, we always need to do periodic dermatological checks.
One option is to decrease the dose of the drug down to a minimum level where it's no longer effective, and then end its use.

There are currently many emerging advancements in the treatment of melanoma. There are two studies in progress on a combination of treatments and the sequencing thereof.

- Phase 3 trial: Dabrafenib and trametinib, followed by ipilimumab and nivolumab, or vice versa. In this study, the toxicity was greater.
- Phase 2 trial

Prospects for the treatment of severe drug reactions

There are several types of severe drug reactions: Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN): mortality rate of 10% to 30%, with significant morbidity; DRESS: Mortality rate of 10% with some morbidity; Acute generalised exanthematous pustulosis (AGEP): Significant morbidity

With these pathologies, it is important to have both supportive care and active therapies.

Supportive therapies:

· Dressings and direct therapy on the skin:
o Daily thorough cleaning (with diluted chlorhexidine)
o Stay well-hydrated
o Dressings with silicone or paraffin
o Replace bedding soiled by exudate
o Topical antibacterial products should be microbiology-oriented
· Oral mucosa:
o Lip balm
o Maintain oral hygiene with mouthwash
o Corticosteroids for inflammation
· Genital mucosa:
o Moisturisers
o Catheterisation to prevent urinary tract obstruction
o Silicone dressing
· Ophthalmology:
o It is essential in the first 24 hours
o Antiseptic and lubricating drops
o Amniotic membrane
· Airway:
o Bronchoscopy
o Intubation if necessary, especially if the patient's oxygen saturation falls or if there are bronchial secretions or tachypnoea
o Be aware that X-ray images may appear normal
· Fluid balance:
o Change the line and cannulas every 48 hours
o The Parkland formula, which is used in burn patients, can overestimate fluid needs. You need to individualise care for each patient.
· Temperature:
o Between 25 and 28 degrees centigrade
· Pain management:
o Visual analogue scale (VAS, a scale for assessing pain)
o Paracetamol combined with tramadol or codeine
o Infusion with an opiate, benzodiazepine, or ketamine
o Entonox is used specifically during interventions (dressings, cleanings, etc.), with 0.1 mg/kg in a bolus
o Local analgesia:
§ Mouthwash with sodium bicarbonate

§ Lignocaine gel
§ Paraffin-based emollients
· Nutrition:
o Should be enteral, not parenteral
o 20-25 kcal/kg for early catabolic phase and 25-30 for anabolic phase
· Psychological care:
o Nurses
o Involve the family
o Provide psychological support and intervention as early as possible

With regard to active therapies, corticosteroids or cyclosporine are the classic treatment.
For SJS or TEN, treatment with 25-50 mg of etanercept twice a week, versus 1-1.5 mg/kg of prednisone, has been shown to be more effective as it decreases mortality and complications. In another study, it was shown that if etanercept is combined with corticosteroids, the improvement is even better. (Etanercept decreases granulysin and TNF in the skin and plasma. With the corticosteroid, IL-15 and IL-6 are decreased.)
DRESS: To avoid this condition, we can do HLA testing before giving certain drugs, such as abacavir, allopurinol, carbamazepine, or phenytoin.
In such cases, we need to identify the drug responsible and provide supportive care and treatment. For the first line of treatment, you can use systemic and topical corticosteroids. Other treatments can include cyclosporine, especially for patients with “prolonged DRESS” (more than 6-8 weeks of treatment with corticosteroids). There is not much evidence for intravenous immunoglobulin therapy, and as a new treatment, benralizumab (IL-5 inhibitor) prevents the activation of eosinophils and can play a role in DRESS.

New treatments for chronic urticaria

Treatment guidelines: first, give a standard dose of a second-generation antihistamine. If there is no improvement, increase the dosage up to four times the standard dose. If there is still no improvement, you can prescribe omalizumab, for which you can increase the dose or decrease the interval. If that doesn’t work, you can prescribe cyclosporine.
Keep in mind that chronic urticaria is a disease of mastocytes. As such, therapeutically, we can directly or indirectly inhibit the activity of the mastocytes. Some patients respond to omalizumab from the first week of treatment, while others need up to eight weeks.
Those who respond quickly are BAT (basophil activation test) negative; those who respond to the treatment late are BAT-positive and present type II or autoimmune (IgG) urticaria.
Type I - autoallergy: Autoantigen against IgE
Type II: IgG against IgE
New drugs are in clinical trials to treat urticaria:
o Tezepelumab (phase 2): Inhibition of TSLP
o Inhibition of the histamine 4 receptor (H4R): LEO 152020 (phase 2)
o Lirentelimab (siglec-8 antibody) is effective in treating chronic urticaria, including in patients who did not respond to omalizumab.
o BTKi (Bruton’s tyrosine kinase inhibitors) can be used to treat urticaria type I (autoallergy) or type II (autoimmune).
o Remibrutinib can be used for treatment-naive patients and those who did not respond to omalizumab.
o Barzolvolimab (currently in a phase 2 trial). Depletes mastocytes. Rapidly decreases serum tryptase at four weeks and maintains this effect up to week 12. Single IV dose of 3 mg/kg. Side effects: Change of hair colour (76%) and change in taste (38%), particularly for the umami flavour.
In the near future, not only will be have omalizumab to treat chronic urticaria, but also BTK inhibitors, anti-cytokine monoclonal antibodies, and MRGPRX2 inhibitors, and for patients who don’t respond to

any of them, we will be able to treat the condition by depleting mastocytes.

Hidradenitis suppurativa and acne inversa

Hidradenitis suppurativa (HS): recent advancements relating to physiopathology

Hidradenitis suppurative (HS) is a pathology for which, thankfully, new treatments have emerged in recent years. It is strongly linked to smoking and an elevated BMI, especially appearing in patients who are obese and who have metabolic syndrome.
Is HS a disease of the epithelium? Yes, and also of hair follicles that don't produce proper epithelialisation. Immunologically, all inflammatory markers will be at elevated levels ("the most inflammatory of inflammatory diseases"). Researchers have identified genetic mutations in the 19p13 chromosome. Mutations of gamma secretase result in activation of inflammatory pathways involved in the proliferation and differentiation of keratinocytes.
A study sequenced the full exomes of patients with syndromic HS and found that the metabolism of vitamin D was altered. Additionally, the study also found altered immunity accelerated by bacterial colonisation. There are many anaerobic bacteria linked to the area of the body and BMI.
To summarise, HS is an inflammatory disease of keratinocytes with systemic manifestations; as such, we must treat the disease accordingly.

HS: Diagnosis and treatment based on phenotype

There are no identified genotypes or biological markers for HS; it is diagnosed by the phenotype.
The affected areas include the underarms, the inframammary fold, the groin, and the gluteal region.
Early diagnosis, focussed on the phenotype, can help us identify targeted therapies for each patient.
There are three different phenotypes that will determine the type of treatment:

- Type I, or follicular
- Type II, or mixed
- Type III, or inflammatory

Comorbidities with HS

How common is HS? In Europe, it affects between 1% and 4%. In the UK, 0.77%, and in the US, 0.1%. When it occurs, the environmental factors that most influence the disease are obesity and smoking: not only does smoking increase the chances of developing the condition by 3.4 to 18 times, but also, having been a smoker increases the likelihood by 2.1 times compared to people who have never been smokers. Obesity is another important factor.
HS decreases life expectancy. In one study in Finland, researchers compared a control group of patients with nevi to patients with HS: the control group lived to an average of 75 years old while the HS group lived to an average age of 60.
HS patients have increased rates of cancer of the respiratory tract (due to tobacco use?), as well as of diabetes, cardiovascular disease, and cerebrovascular disease. They also have increased rates of accidents, violence, and death by suicide. This can be attributed to the fact that HS is a disease that strongly affects patients: pain, inflammation, bandaging, etc. Many patients suffer from depression and anxiety, and some even go as far as to commit suicide. In a meta-analysis, it was shown that HS patients are at a two-times greater risk of suicide compared to the general population.
Obviously, it is also associated with other chronic inflammatory diseases, such as Crohn's disease, ulcerative colitis, inflammatory arthritis, and psoriasis. Other associations include pilonidal sinus, acne vulgaris, PCOS, Down's syndrome, and obstructive sleep apnoea.

Additionally, it can be associated with other inflammatory diseases such as PASH, PAPASH, and PASS.
To summarise, HS more often affects smokers, people with obesity, women in their 40s and 50s, and people with a genetic predisposition, and it is associated with other diseases. Potential consequences include squamous cell carcinoma and increased mortality related to cardiovascular disease and suicide.
As such, when talking with patients, we should offer measures for quitting smoking and for losing weight if needed, and we should assess their cardiovascular risk, as well as the possible association with depression and anxiety.

Combined treatment approaches for HS

How should we treat patients with hidradenitis suppurativa? We have both medical and surgical options, but we need to know when each is better.
With regard to medical treatments, we should absolutely treat:
- Inflammation: oral zinc, immunosuppressants, biologics, colchicine plus dapsone, apremilast, and intralesional corticosteroids
- Dysbiosis: antiseptics, tetracyclines, clindamycin, rifampicin, metronidazole, dapsone, or ertapenem
- Hormones: contraceptives, spironolactone, cyproterone, or finasteride
- Follicular occlusion: topical resorcinol, acitretin, isotretinoin, and laser hair removal
- Metabolic disorder: metformin and GLP-1 analogues
- Avoid friction or irritation: loose clothing, weight loss, botulinum toxin injections

Surgical treatments include incisions and draining, flaps, and wide excision with closure by secondary intention.
As such, we have multiple treatment targets: we can treat obesity and metabolic syndrome, inflammation, and other comorbidities. Additionally, we need to manage the pain and both dynamic and static lesions.
It is important to treat obesity: to do so, liraglutide is a drug that can help these patients lose weight.
It is also important to measure zinc levels. If the patient has low zinc levels, they will need a supplement. If this occurs post-surgery, the patient should take zinc gluconate at 90 mg/day.
Women of childbearing age can take contraceptives, while women in menopause can take cyproterone. Spironolactone can be prescribed for women with varicose veins or fluid retention and finasteride can be prescribed for androgenic alopecia.
In the future, epigenetics will allow us to develop personalised treatments and better understand the physiopathology of the disease. In cases of inflammatory HS, it is better to use biologics, and doing so early produces better results. Finally, ultrasound scans are very useful for defining the disease type.

Atopic dermatitis

New drugs are emerging for atopic dermatitis, opening up new treatment pathways. These can be divided into two major groups: biologic drugs (IL-4 inhibitors like dupilumab and the IL-13 inhibitor tralokinumab, which is the only approved drug of its kind) and small molecules (JAK inhibitors).
What are the differences between them? Biologics are stronger at inhibiting one pathway, while small molecules less intensely inhibit many different pathways.
Biologics present larger drug molecules: as such, they are administered via injections and they do not typically require monitoring. In these patients, immunogenicity is important. Above all, we should avoid

repeated treatments with discontinuations and inductions. Biologics have a strong safety profile, although these patients have increased frequency of conjunctivitis.
With dupilumab, facial redness occurs in 4% to 43% of patients, depending on the series. Tralokinumab may produce a reaction at the injection site or conjunctivitis. Dupilumab begins working faster than tralokinumab.
With regard to JAK inhibitors, there are four types of JAKs: 1,2, 3, and TYK2. We can be selective about the types of receptors, but if we increase the dosage of any JAK inhibitor, we can affect several receptors at once. When we use a non-selective drug, we have a smaller window for the therapy than we would have with a selective drug. However, non-selective drugs start working faster and are taken orally, but also require monitoring. They don't come with a risk of immunogenicity, making them eligible for on-and-off treatment. In a meta-analysis comparing all available treatments, the most effective treatment was upadacitinib followed by abrocitinib. However, there are few "head-to-head" studies. One study compared dupilumab to upadacitinib. It found that upadacitinib starts working faster than dupilumab, but at week 16, they had fairly similar results, although upadacitinib was still a bit more effective. In conclusion, when selecting a treatment, we should evaluate its efficacy, safety, and administration route.
We are learning more and more about the importance of microbiota in inflammatory diseases. Rates of allergies and autoimmune diseases have been increasing markedly since 1960 (asthma, rhinitis, and eczema). The hygiene hypothesis is gaining traction and the Western lifestyle also plays a role. The intestinal microbiome produces short-chain fatty acids that have an effect on immune tolerance and autoimmunity. The Western diet is lacking in fibre, causing the microbiome to have less prebiotics. To summarise, diet affects health and the immune system.
In the future, will dermatologists be able to treat the microbiome? A Spanish study showed that probiotics could decrease flare-ups of atopic dermatitis, but it's clear that such treatments are still in early stages of development. We still have a lot to learn about the role probiotics can play in treating atopic dermatitis.

Pruritus

Itching is caused by nerve inflammation, but that is the final phase. It starts with alteration of the skin barrier with triggering factors such as overgrowth of *Staphylococcus aureus* or exposure to haptens and irritants. This causes the release of inflammatory mediators, affecting blood vessels and nerves. Itching thus begins in peripheral receptors, but there are also effects in the central nervous system. There is neuro-immune communication between keratinocytes and inflammatory cells that causes itching, with numerous mediators involved in the itching. It is a vicious circle of atopic dermatitis induced by irritating factors, stress, or psychogenic factors that cause the patient to start scratching, which then alters the skin barrier and causes more inflammation.
Neuropathic itch is similar to chronic pain, releasing mediators. In fact, both are treated with similar drugs: aprepitant (NK1 receptor), naltrexone (mu opioid receptor), and calcium channel blockers such as gabapentin, pregabalin, etc.
With pruritus, IL-31 expression increases and the IL-31 receptor activates itching linked to TRP channels. These calcium channels can aggravate the itching.
IL-4 and IL-13 induce itching at low doses, more than histamine at higher doses. This is true in both mice and humans.
Other treatments to control pruritus include an ERK1/2 inhibitor that blocks IL-31.
To summarise, there is a vicious circle of itching and scratching in which damaged keratinocytes and inflammation play a role. Many immune cells and keratinocytes may directly activate the nerves via IL-31, IL-4, IL-13, calcium channels, ERK1/2, JAK, etc. As such, these are all targets for treatment.

Researchers also point to the role of cannabinoids in treating pruritus. Cannabinoids are a group of 60 bioactive compounds. The strongest agent is delta-9-THC, found in marijuana. The mechanism of action has been known since the late 20th century: the compound binds to the CBR (endocannabinoid) receptor. This receptor is expressed in both healthy and pathological skin. There are two types:

- The cannabinoid receptor type 1 (CB1 receptor) is located presynaptically to the GABA channel. It is found in small nerves of the skin. It is also found in CD68-positive macrophages and mastocytes.
- The cannabinoid receptor type 2 is found in tissues associated with the immune system (for this reason, it's also known as the "immune cannabinoid receptor"), including the skin.

There are other cannabinoid receptors, but also the TRPV1 receptor, a non-selective cation channel for calcium. TRPV1 activation induces vasodilation and the release of NO.
For this reason, cannabinoid derivatives are being used more and more to treat dermatological diseases and pruritus.
There are studies on the use of a topical cannabinoid receptor agonist for neuralgia, with good results. Also for prurigo nodularis. Itching was reduced by 86.4%.
In another study, relating to eczema, not only was itching reduced, but also skin dryness.
In another study using topical cannabidiol 1%, both EASI scores and itching were reduced.
In another study of patients with sensitive skin treated with CBD, symptoms were diminished for 67%, while eczema also improved for a similar percentage.
There have also been studies relating to uremic pruritus. A topical cannabinoid receptor agonist again reduced itching and skin dryness. However, it does not seem that uremic pruritus is related to the endocannabinoid receptor. In that case, the effect was only due to the hydrating effect of the cream.
To summarise, for patients with kidney failure and pruritus, upon review, cannabinoids are not indicated.
According to the 2012 European guidelines, the cannabinoid receptor can be an effective target for localised pruritus; however, since then, it has been shown that this effect may simply be due to the vehicle. In a comparative study, there was no significant difference between the CBD group and the placebo group. As such, in the 2019 guidelines, topical CBD is no longer listed as a treatment.
We must watch out because there are many cosmetic products containing cannabidiol, but currently, there is no evidence that CBD reduces itching.
In epidermolysis bullosa, it decreases pain and itching.
In conclusion, cannabinoids have important functions in the skin and may offer future dermatological therapies. However, we do not currently have solid scientific evidence to recommend topical cannabinoids. In a systemic form, they may reduce pain, and probably the associated itching.

Prurigo is a very difficult pathology to treat. It is a self-developing condition because the chronic itching, sensitisation processes, and repeated scratching lead to the appearance of pruritic lesions. It is a disease that requires treatment: currently, we have dupilumab, and soon nemolizumab.
In these patients, we should analyse the level of itching that they have using severity scales, evaluate the psychological burden, and offer them treatment for their pathology.
Treatment of itching in atopic dermatitis is no easy task. We have treatments such as cyclosporine, dupilumab, nemolizumab, antidepressants, JAK inhibitors, PDE inhibitors, opioids, and NK1 receptor antagonists. However, in some cases, patients have associated pain, which we can treat with analgesics, gabapentin, antidepressants, JAK inhibitors, PDE inhibitors, and opioids. We must not forget that there can be a placebo effect, especially with topical treatments.
Other treatments for uremic pruritus in patients undergoing haemodialysis include oral nalbuphine and difelikefalin. The drugs are tolerated well and they significantly reduce the severity of itching.
There are two drugs for pruritus in phase 2 trials: serlopitant and nalbuphine.
Finally, to support these patients, it has been shown that music therapy can help calm patients, particularly using music that the patients like. Listening to music for 20 minutes produced good results.

Breaking news

The monkeypox outbreak: where are we now?
Alba Catala

The virus primarily spreads through sexual transmission, causing genital and oral lesions as well as lesions in other body areas.
Additional symptoms may include fever, joint pain, and general malaise.
Dermatoscopy reveals distinct characteristics in the lesions, such as a whitish halo and a central crust on an erythematous base.
It is crucial to rule out other sexually transmitted infections and perform a differential diagnosis with similar diseases.
The virus can cause asymptomatic lesions, and in some cases, the disease resolves spontaneously, although scarring, pigmentary disorders, or alopecia may occur.
Complications may include mucositis, secondary bacterial infection, ocular involvement, cutaneous rash, and other manifestations like parotitis and meningoencephalitis.
Mortality is low, with only 140 reported deaths to date.
Diagnosis is made through PCR testing, and treatment is reserved for severe cases using Tecovirimat.
A third-generation vaccine has been authorized, although mass vaccination is not recommended.
Incidence is reduced with a single vaccine dose, but maximum effectiveness is achieved with a second dose.
The virus may become endemic outside of Africa due to human-to-human transmission and potential asymptomatic circulation in animals.
Security measures should be implemented to prevent future outbreak

New treatment options in metastatic melanoma
Martin Röcken

Anti-PD1 or PDL1 for "healthy" patients with persistent metastases. Not used as emergency therapy, but rather for slow response. Higher percentage of survivors compared to BRAF.
If surgery is not possible, three questions need to be addressed: patient's tumor burden, presence of BRAF mutation, and overall health status.
Pembrolizumab is used in advanced stages. Nivolumab with or without ipilimumab in advanced stages (2B). A study comparing combination therapy versus nivolumab alone showed higher survival rates with the combination.
Atezolizumab has also shown effectiveness.
In a study comparing relatlimab and nivolumab versus nivolumab alone in untreated advanced melanoma, the combination was more effective, but currently not available in Europe.
Neoadjuvant therapy following surgery has demonstrated increased survival. Immunotherapy is administered, such as nivolumab or nivolumab plus ipilimumab. Preoperative immunotherapy has proven to be effective, followed by postoperative treatment.
The focus in these patients is to control the melanoma, as tumor cells survive within a treatment-resistant microenvironment.

A new era in itch treatment
Bernhard Homey

Pain and itch are alarm symptoms. Pain signals the need to move away from something, while itch signals the need to address something.
There is a vicious cycle of scratching and perpetuated itch due to mechanical damage to the skin.
Tissue remodeling is a constant process. The pathophysiology of itch involves multiple mediators
New treatment strategies involve the JAK/STAT pathway mediated by cytokines, which encompasses a wide variety of cytokines.
When discussing type 2 inflammation, various cytokines are involved, such as IL31, TSLP, IL13, IL4, IL22, and IL5. The choice between a biologic or a small molecule depends on whether we aim to block a single inflammatory pathway or multiple pathways.
For example, dupilumab (anti-IL4) has revolutionized the treatment of atopic conditions and improves pruritus. When combined with topical corticosteroids, it achieves long-term improvement in pruritus.
Furthermore, dupilumab has demonstrated improvement in pruritus and nodular lesions of prurigo nodularis. Results at 12 and 24 weeks show a statistically significant difference compared to placebo, reaching up to 60% improvement (PRIME and PRIME2 studies).
Regarding the JAK/STAT pathway, baricitinib reduces pruritus from the early days of treatment. These drugs act more quickly than biologics (anti-IL4 or anti-IL13).
In a comparative study of upadacitinib versus dupilumab, the former is much faster in reducing pruritus and improving skin lesions.
In another study comparing abrocitinib versus dupilumab, abrocitinib was superior to dupilumab within a 2-week period, even as early as the fourth day. This superiority persisted until week 48. Dupilumab shows slower improvement, but does not reach the levels of abrocitinib.
Side effects of abrocitinib or upadacitinib include nausea, vomiting, and papulopustular lesions on the face. There is also an increased incidence of herpes.
Another drug for treating pruritus is nemolizumab, an anti-IL31 that has shown to decrease itch in pivotal studies. IL31 and its receptor are interesting targets for itch control because they not only affect the itch pathway but also modulate inflammation and tissue remodeling.
In conclusion, we have new pathways to treat pruritus that will enhance the quality of life for our patients.

Breaking news

Topical drugs in 2023
Jo Lambert

Psoriasis
• Roflumilast 0.3%: It is a PDE4 inhibitor. It has higher affinity than crisaborole, suggesting that it will provide better results. It has been approved by the FDA but not by the EMA. It is given once a day and provides rapid improvement. It is effective in skin folds without causing irritation. Currently in phase 3 studies; it works quickly on itching and is effective in hard-to-treat areas. The two phase 3 studies are called DERMIS1 and DERMIS2. There are also studies in children, indicating its potential use in this age group. It also appears to be useful in treating seborrheic dermatitis in the form of foam, with an 80% improvement.
• Tapinarof 1%: It is an aryl hydrocarbon receptor (AhR receptor) agonist. Currently in phase 3 studies. It reduces inflammation, oxidative stress, and normalizes the skin barrier. Results are long-lasting up to 52 weeks without tachyphylaxis. It is also useful in on-off therapies. Possible side effects include acneiform reactions and headaches.

Atopic Dermatitis

• Tapinarof is also being studied for this condition. It achieves a reduction in lesions to 0 or 1 in 46% of patients by week 8.
• Roflumilast 0.15% twice a day. It is not as effective as in psoriasis. Tested in patients over 6 years old, indicating its use in children with a 42% improvement in itching by week 8. It is a relatively safe outcome.
• Ruxolitinib, a topical JAK inhibitor, achieves better results with an improvement in over 50% of patients by week 8.
• Crisaborole has not been approved in Europe and has shown inferior results compared to the aforementioned treatments.

Vitiligo
• Ruxolitinib was approved by the EMA on April 19, 2023. The price is still unknown. In the USA, it is expensive (over $2,000 per tube of cream).
Results are shown from week 6 to 24. Always combined with phototherapy or sunlight for better results.
Long-term studies (over 100 weeks) show repigmentation in over 60% of cases. Side effects are well tolerated (different from systemic administration, although these effects are also mentioned in the technical specifications). It is used twice a day.

Actinic Keratosis
• Tirbanibulin 1%: It is a microtubule inhibitor. Studies were conducted on actinic keratoses on the face and scalp. It is applied once a day for 5 days, and the results are superior to placebo. There was a disappearance of actinic keratoses in 46% of patients, and there is inflammation in the area. There are no comparative studies with 5-FU or imiquimod.

Dystrophic Epidermolysis Bullosa: Collagen VII gene therapy improves wound healing and has just been approved by the FDA.

New systemic therapies and new approaches
Systemic drugs in 2023
Michel Gilliet

New therapies have emerged thanks to a better understanding of the molecular pathways of each disease.
There are many inflammatory pathways that we must be familiar with. The first step is to differentiate between innate immunity pathways such as IFN-alpha and beta or LI1, and adaptive immunity pathways such as Th1, Th2, Th17, Treg, or fTH.
And this directly links to specific diseases: psoriasis and Th17, atopic dermatitis and Th2, lichen, alopecia, or vitiligo with Th1, lupus with IFN, neutrophilic and pustular diseases with IL1, and blistering diseases with B cells.
New molecules:
• Bimekizumab is an anti-IL17 A/F. This is important because IL17F is more abundant than IL17A, which is blocked by the rest of the anti-IL17 agents. This is also reflected in clinical efficacy: 71% of patients achieve PASI 100.
• Deucravacitinib (Tyk2i) inhibits IL12, IL23, and the IFN signaling pathway. The results are promising because of its multi-specificity, especially in blocking the IFN pathway, which is important in unstable psoriasis.
• Blockade of the Th2 pathway: dupilumab (anti-IL4R), tralokinumab, and lebrikizumab (anti-IL13) and JAK inhibitors.
• Nemolizumab (anti-IL31R). Not approved in Europe but approved in Japan.
• Dupilumab may also be useful in nodular prurigo and bullous pemphigoid.

• Regarding the Th1 pathway, JAK inhibitors that inhibit JAK1 and JAK2 also inhibit the IFN pathway.
• JAK inhibitors for vitiligo: upadacitinib, baricitinib, retlecitinib, or povorcinib.
• Ritlecitinib, a JAK3 inhibitor, appears to be safer than the others for vitiligo. It inhibits IL4, IL7, IL9, IL15, and IL21.
• For alopecia areata, we also have JAK inhibitors: baricitinib, ritlecitinib, etc.
• Regarding the IFN pathway, it is useful for treating lupus. Anifrolumab has shown good preliminary results. Litifilimab also blocks it and has shown good results compared to placebo.
• In the neutrophilic pathway, blocking it helps treat pustular diseases. Spesolimab (anti-IL36R) is approved for pustular psoriasis and is given as a single dose of 900 mg over 90 minutes. Repeat after two weeks if there is no improvement. A clinical trial of this drug is underway for hidradenitis suppurativa.
In the future, we will create an individual disease profile for each patient to choose the most appropriate therapy.

New imaging techniques
Mariano Suppa

Until 2 years ago, imaging techniques consisted of confocal microscopy and optical coherence tomography (OCT). Confocal microscopy provides excellent resolution with limited penetration. However, OCT is less precise but has greater penetration.
Line field confocal optical coherence tomography (LC-OCT) combines the two aforementioned techniques with higher resolution and penetration. Additionally, there is a dermatoscopy camera for performing dermoscopic and image correlation.
With LC-OCT, it is very easy to diagnose basal cell carcinoma. It has a sensitivity of 90% with a specificity of 86%. It even helps differentiate the subtype, including cases of basosquamous carcinoma. It is also useful for monitoring after topical treatment.
LC-OCT also aids in classifying actinic keratoses.
In melanocytic lesions, there is a dermoscopic-histologic correlation with micrometric precision.
With this new technique, we can diagnose the most common skin cancers (basal cell carcinoma, squamous cell carcinoma, and melanoma), as well as inflammatory lesions, less frequent tumors, and other pathologies.
LC-OCT is even being associated with artificial intelligence. In the future, the machine will be able to indicate areas of risk, with a very rapid learning curve.
In summary, it will be a tool that we will use extensively for diagnosis, monitoring, and prognosis of patients.

Repurposing botulinum toxin
Oliver Kreyden

There are multiple indications for botulinum toxin in dermatology, not just wrinkles. In hyperhidrosis, it is important for it to diffuse well to act throughout the entire area. In palmar hyperhidrosis, anesthesia is the most challenging aspect. Emla cream is not very effective in this area, so cryotherapy is proposed to be used simultaneously during injection.
Microbotox is also proposed, with very low units diluted on the face, to improve rosacea and facial texture in patients. It also improves flushing and sweating.
A less known indication is blepharospasm nicticans, for which it is effective.
The same applies to migraines, where we must infiltrate the appropriate nerves in the frontal, temporal, and occipital areas. It mainly improves tension headaches.
In the future, new indications will arise.

Reports written by

Dr. Ruzica Jurakić Tonci

Dermatologist, Croatia

What is new in: “Acne”

Chairs: Vincenzo Bettoli (Ferrara, Italy)
Brigitte Dréno (Nantes, France)

Skin and gut microbiome modulation in acne
Brigitte Dreno

Skin microbiome is divided into resident microbiome and transient microbiome.
There is a crucial role of microbiome since it represents first segment of the barrier against environment. It also plays the big and important role since it contributes the differentiation and epithelization of the skin and has the effect of boosting the chemical barrier.
Microbiome nowadays is considered as a new human organ and is a central actor in acne pathogenesis. This is due to the fact that dysbiosis in acne is in link with loss of diversity of C.acne phylotypes. Today there is an important focus on C.acnes since they produce biofilm and extracellular vesicles (which causes increased proliferation of keratinocytes).
C.acnes is not the only actor in pathogenesis of acne since we have learned that S.epidermidids and C.acnes interact together. Balance between S.epidermidis and C.acnes is crucial and they are unmissable modulators of skin inflammatory response.
Loss of diversity is associated with selection of virulent C.acnes phylotypes IA1.
Sebum profile of follicle in acne modulates expression of virulent genes of C.acnes.
Gut and skin microbiomes interact in acne.
There are several ways of possible manipulation of microbiome by using vaccination, bacteriophages, probiotics (topical and oral), antimicrobial drugs.
Among probiotics some important bacteria species are streptococcus salivarius and Lacctococcus species
Conclusion: skin microbiome plays a central role in inflamation. Cacnes IA1 is predominant phylotype. SKin and gut microbiome have important interaction.

Female adult acne
Vincenzo Bettoli

Adult acne in women can be divided into 3 main clinical phenotypes: persistent acne (which start in adolescence and persist during the life), late onset (onset after 25 yrs of age), relapsing acne (this type starts in adolescence and is reoccuring during the life)
Adult acne is more frequent in female (82% versus 18% male)
Persistent type of adult acne is the most frequent form.
In some cases there might be a need of differentiation of acne and acne likeHS. Acne like-HS presents with irregular distribution, while acne has regular, typical V distribution on the chest.
Pathogenesis of adult acne is still not quite understood. Increase of sebum, increased follicular hyperkeratinization, P.acne inflammation and innate imunity play the role in pathogenesis.
Interestingly, isotretinoin acts reducing C.acnes genus levels, restoring normal levels.
A lot of focus has been put on hormonal status in adult acne. Still, hormones have controversial role.
PSOS is the most common endocrinopathy found in these patients.

Varietes of acne with PCO are more difficult to treat. PCO diagnosis and treatment of PCO is done by Rotterdam criteria. There are recomendations for female adult acne and androgen excess- in every patient measurement of serum androgen values should be done (serum levels of testosteron, free testosterone, DHEAS).
Adolescent and adult acne have different clinical presentation. There is a difference in clinical picture- adult acne usualy present as mild inflammatory-papular type of acne lesions. Face involvement- cheek, chin, mandibular is common while truncal involvement is rare. Usually comedones are not seen, just inflammatory papulopustular lesions. Scarring is very common, hormonal involement is very common. Regarding the other clinical symptoms, hisutism is very common, also alopecia and acanthosis nigricans.
There is a recommendation for screening for dyslipidemia, hypertension, and there is increased risk for greater insulin resistance and cardiovascular risk. In all the patients consideration of all triggering factors should bed one (hormones, smoking, diet). Hormonal work-up is necessary.
Treatment depends on mainly on the patients wish to get pregnant (or not), since oral retinoids are not allowed during pregnancy. We can use azelaic acid, topical retinoid, benzoyl peroxide oral isotretinoin, systemic antibiotic, aldosterone antagonist (spironolactone).

We should use the algoritm accoring to androgene levels (Marie-Ange Dagnelie et al. Int J of Dermatol 2022, 61:1205-1212)

Spectrum of severe forms of acne
Clio Dessinioti

In this lecture acne conglobata, acne fulminans and other forms of severe acne are discussed.
Acne conglobata is the most typical and the most severe form of disease.

A.fulminans is rare form, almost exclusively seen in adolescent boys, with sudden onset, caracterized by hemorragisc ulcerations and crusts. Etiology is unknown. Patients usually present with severe form and systemic symptoms. There is arthralgia involved, fever, leucocytosis, elevated ESR. In some rare cases patients can occur without systemic symptoms.
Evidence based treatment has been recommender (Greywal et al J am Acad dermatol 2017). It has been clear that prednisolon 0.5-1 mg/kg/day should be introduced and prolongued isotretinoin tretmant may be requiered. Another important issue is does the patient present with systemic symtpms and is it caused by isotretinoin (then, discontinuation of isotretinoin is required)
Treatment with anakinra, ustekinumab has been tried.

Congenital adrenal hyperplasia is AR disorder with etiopathogenic pathway of cortisol and aldosterone. In 95% of patients it occurs due to 21-hidroxylase deficiency. There is a lower production of cortisol and ACTH is overproduced with result of androgen hyperproduction. Treatment is done with glucocorticosteroids and isotretinoine with neccesary consulatation with endocrinologist.

Acne in PCOS is a clinical and biochemical hyperandrogenism.

PAPA-PAPASH-PASH-PASS
Represent syndromic acne-autoinflammatory syndromes (Gasparic et al. JEADV 2017)
There is a role of Proline-serine-threonine phospatase interacting protein 1
There can be arthritis, atrhtitis and acne.
Acne in PAPA is usually presenting in 53% of cases of nodulocystic type.
SAPHO sy presents with bone and joint involvement associated with severe acne, papulopustular psoriasis, sometimes chronic bowel diseases, synovitis , hyperostosis and osteitis . Tipical involvement is sternal region. In 55% of cases 1st symptoms are skin lesion and the mean age of

patients is 37yrs. 95% have both skin and bone involvement. There is a high frequency of symptomatic anterior chest pain.

Advances in topical treatments and dermocosmetics in acne
Jose Luis Lopez-Estebaranz

List of the topical drugs (J Drugs Dermatol 2021,20:648-651)

Minocycline foam 4%
1x daily
J am Acad Dermatol 2020;82:832-7
It can be used to treat moderate to severe acne

Microcapsulated BPO 3%+tretinoin 0.1%
It can have side-effects typically observed with retinoids
(Erlich M. J Colloid Interface Sci 2020
J Drugs Dermatol 2022 Oct 1;21(10))

Clascoteron 1% cream
Inhibitor of androgene receptor with antiinflamatory properties, efficacy and safety has been studied in patient older than 12 yrs of age
(J Drugs Dermatol 2023 Feb 1; 22(2) 174-181)

Trends in spironolactone prescription
Oral and topical spironolacton has been studied.
Topical spironolacton statistically has shown decrease in papules, comedons and pustules/ decrease of severity has been shown in the 5 study reviews.
Topical spironolaton 2% showed better efficacy over clindamycin, and can be used as 2-5% solution/gel.
Spironolacton has demonstrated long-lasting effects even several months after its discontinuation
(J Am Acad Dermatol 2022 sep;87(3):684-686)

N-acetyl-GED-0507-34-LEVO-gel (PPR-gamma modulator)
Phase II of testing, so far showed that is effective in moderate and severe acne
(Br J Dermatol 2022, 187, pp 507-514)

Fixed dose combination of clindamycine phosphate 1.2% , benzoyl peroxid 3.1% and adapalene 0.15% (IDP-126) gel
For moderate to severe acne
Phase II
(Am J Clin dermatol 2022)

Probiotics
Efricacy in sebum production and anti-aging

What is new in: “Aesthetic dermatology”

Chairs: Maurice A. Adatto (Geneva, Switzerland)
Moshe Lapidoth (Ramat-Gan, Israel)

Lasers and energy-based devices
Maurice A. Adatto

AFR with PICO or QS for tatto treatment

1 session every 3 months

QS microdrilling and multipass full beam (L:Marini)
Any microndrilling prior the tretment improvse the result

Iatrogenic cutanous siderosis
Iron goes paravenously during treatment for Iron deficiency
Used QS Nd:YAG laser #1064 nm or frequency
All pts achieved at least clearancy of 50% or more
Usually 10 sessions

Injections of lactic acid (REJUVI/SKINIAL) to remove tattoes
It is highly concentrated and causes necrosis- full necrosis of skin
Done by nonmedical/ promoted on social media

New generation of vascular lasers
Derma V 532
An important 532 nm is ability to treat both brown and red color.
Large spot size (up to 16 nm) provides more flexibility
Can be used for venous malformations, leg vens, hematomas after injectables
Resistant port wine stain, resistant thick spider angioma, poikiloderma, keratosis pilaris, acne scars can be treated

New hybrid lase-non-ablatibe and ablative fractional treatment has additive effect (Lux 1440&2940-1 (Alma Hybrid)
HyGrid
Over 60% coverage by the combination

Fillers and threads
Brunilda Bardhi

We can treat lips, lowe face, upper face, midface , nose, jawline and chin
AGing causes bone and fat resporption and loss of collagen – loss of skin texture and elasticity and quality
Changing paradigm from filling to volumetric
Iverted triange of youth
Age modification decrease facial expression.
SKin is more rigid due to less colagen
1st is to idetify patients needs, to assesment of the patient and design treatment plan.
Over 50 pt want to look less tired
Combination of minimally invasive treatments is needed- polycaprolactone based collagen stimulators (CaHa, polilactone)

Ca-hydroxyapatite is used for biostimulation. HA or Ca-Ha is used for eyebrow lifting after botulinum toxin.

For neck rejuvenation-hyperdiluted Ca-Ha as biostimulator more than volume,
Threads lifting procedures show good lifting effect. It is safe and effective procedure.
They are absorbable and biocompatible.
Main fixation point is important.
Biodegradation period is 6-24 months.

Botulinum toxin: what's new?
Oliver Kreyden

FDA approved since 1989
Increase of dose increases the liquid and the possibility of the side-effects
Xeomin has no evidence of neutralizing antibodies and can be stored at room temperature
Dysport with the highest diffusion rate (hyperhydrosis
Longer duration of efficacy is discused controversially
Lluziance- 1st ready-to use BTX on the market, under the licence of ipsen. Iti s on the base of Alluziance (125 speywood units), storage 2-8 degrees.
There is no need to calculate
Iti s approved in EU
Jeuveau – pra-botulinumtoxin A is manufactured in South Korea, =.5 mg HSA per 100 U. Very similar to the 1st Botox.
Daxxify- daxi-botulinumtoksin A, manufactured by Revance USA, 150kDA+patented stabilizing protein (priobably the longest lasting product in the family.
In preclinal development is gel.
Botulax
Let-botilinumtoxin A- manufactured in South Corea. Has many brand names. Iti s effective and safe as ona-
Botulinum toksin E-onset within hours and duration for 2-4 weeks (botox last minute!, last minute demand)
Bonti (Abbvie) is under testing.

Studies have to proof bioequivalence, safety and claimed duration.

Plast Reconstr Surg 2022- Tips and trick for
Upper face treatment is not a indication for beginners.

Approaches to restore skin laxity 2023
Moshe Lapidoth

Non-invasive procedures- demand is up to 174% more
Photogenic energies
Radiofrequency
Ultrasound

Body shaping- skin laxity, lipolisin and celulite
Need to reduce volume (fat, circumference, silhouette)
Not all the fat deposits are the same (fotol
Cryo afects succutaneous fat.
No single teqnology affects all.
For body shaping we use cryo lipolysis, ulktrasoudn, radiof, EMS-muscle toning
HIFU-results are less dramatic than surgery.

Fractional HIFU recently approved also for cellulite- delivers significant energy to mid-dermis. The best results are achieved by combination of
RF+EMS (EMFACE)- doesn't face FDA approval.

Interactive clinical cases: dermoscopy

Classical BCC
Susana Puig

At the begining of the lecture clasical criteria of BCC were described.
Classical dermoscopic criteria are arborizing vessels, ulceration, maple leaf criteria, blue gray ovoid globules and nestr, spoke-wheal areas.
Most criteria are most specific.
For pigmented BCC criteria have been described by Menzies, very specific criteria are maple leaf like area.
Ulcerations are typical.
Blue ovoid nests are histologically deep nests of tumor cells.
Negative maple leaf like ares is a nue clue for basal cell margin recognition (Br J Dermatol).
Arborizing vessels high in focus are typical, there are in focus since there are very superficial, more superficial than the nests.
Concentrical structures are new criteria. Sometimes , very rare, pigment network can be found (only 2% of cases).
In non-pigmented BCC arborizing vessels and shiny white streaks are seen more frequently.
After criteria description, interactive cases were shown and audience had to vote.

BCC mimickers
Roberta Giuffrida

Mimicker of BCC on the face have been shown in this lecture.
Sometimes seborrhoic keratosis can mimic pigmented BCC, but the dermoscopy is straightforward. In some cases seborrhoic keratoses can present in atypical way such as clonal seborrhoic keratosis.
Dermal nevus has curved vessles but sometimes can be difficult to differentiate. Dermal nevus usually has yellow background in contrast to pink background of BCC.
The most common cysts are epidermid cyst nad trichilemal cyst-not all the cyst come with a pore and can show arborizing vessels.
Skin adnexal tumor are variegated group of hamartomas- most of these are observed asr dermoscopy are BCC simulators, simulate more likely nodular type.
Present as translucid papules/ nodules, arborizing vessles are thinner, less branched, unfocus.
Cylindroma has orange salomon backround.
Sebaceus hyperplasia shows cumulus and bonbon tofee sign.
Trichoblastoma nad trichoblastic carcinoma have origin from follicle.
Proma is great dermoscopic imitator- there are 4 clinico-dermoscopic pattern- type 3 simulates BCC.
Vessels are usually thicker and blossom like apperance.
Inverted follicular keratosis has keratoacanthoma like pattern.
Pilomatrix carcinoma can be mimicker of nodular BCC.

Managing BCC in your office
Augustin Toll

Several therapeutic options in different individuals (classical presentation and syndromic BCC patients, such as Gorlin Golz, Sofu syndrome) have been presented and audience voted for the best therapeutic option. In some cases beside the surgical solution, genetic testing should be offered. Vismodegib and Mohs surgery , photodynamic therapy, imiqimod have been discussed.

Reccurent BCC
Zoe Apalla

Risk types are sclerotic, infiltrative.
Number of excision matters, and after first excision reccurence rate is 5%
Nonhealing ulceration, tissue destruction, enlargment of scar or development of nodule/papule.

3 classical scenarios:
1.Reccurent after BCC
2.Reccurent after topical treatment
3.Reccurent BCC after several tretment

Pink white structureless areas and short teleangietatic vessels can occur after treatment
- possibility of residual disease is 30%
- so close follow up is recommended.
In the presence of arborizing vessels and pigmented structure the possibiity is 100%.

Pigmented structures are highly suggestive of reccurence, bright vessels in focous but be carefull in radiodermatitis area and scars.

Interactive clinical cases: “Dermoscopy”

Chairs: Danica Tiodorovic (Nis, Serbia)
Raimonds Karls (Daugmale, Latvia)

In situ versus invasive SCC
Raimonds Karls

Actinic keratosis is multiple, ill defined, pigmented type isn't rare.
There are 3 targets in dermoscopy of SCC- keratin, vessels and follicles.
Vascular arhictecture is examined in non-contact mode.
The progression mode has been described, and clinical and dermosopic predictors in SCC in J Am Acad Dermatol 2022 Apr 86(4):791-794.
Rosettes are observed under polarized dermoscope.
Background erythema is typical.
There is a dermoscopic „signature“ pattern of pigmented and nonpigmented facial actinic keratosis.
Big follicles fullfilled with keratin indicates SCC.
Periferal red starburst fenomenon and targetoid follicules.

3 very strong indicatiors of SCC
1. Keratin
2. dotted or glomerular vessels
3. White structureless areas
4. Polymorphous vessels

5. Ulceration

Rule for hyperkeratotic lesion-remove hyperkeratosis in order to examine the lesion.

Interactive dermoscopy case-nodular SCC and keratoacanthoma

Felix Pham

Keratin can be white or orange/yellow if mixed with serum.
Arrangement of the vessels is important.
Polymorphic vessels can be seen.
The clinical and dermoscopic features of invasive SCC depend on their differentiation.
White circles are the most important dermoscopic sign for SCC.
There is
Papageorgiou C et al. J Am Acad Dermatol 2021 is paper dealing with differentiating irritated seborrhoic keratosis from SCC.

SCC in specific sites

Danica Tiodorović

Lips are specific localization.
Dermoscopic features are well known and are keratin mass, white structuress, white milky areas, keratin mass, white structureless area.
White colored structures it is a sign of well to moderate SCC. There is a new feature described and it is background of the lesion- white structure of the background is well dif ferentiated SCC, pink background is seen in moderate and red background in poorly differentiated SCC (paper on mucoscopy, IDS study).
Dotted vessels were found in well to moderate, linear irregular vessels in poor differentiated, and in the end, heavy vessel density shows poor histological differentiation. Therefore dermoscopy predicts histology of the tumor.
If you see white lines on lips, consider lichen planus also.

Eye lids can be additional localization.
SCC can occur on acral locations.
In nail SVV we find localized hyperkeratosis, onycholysis.
Localized hyperkeratosis is the first finding and the most common.
Preform free edge dermoscopy always.
Dermoscopy of onichomatricoma and onichopapiloma has been discussed- free nail edge pitting.

Erythroplasia Queyrat can be differentiated from psoriatic balanitis (glomerulal vessels versus dotted vessels), therefore dermoscopy can be use din genital lesions in order to exclude benign lesions.

New tecnologies and keratinocyte skin cancer

Elvira Moscarella

In some difficult face lesions, confocal microscopy can be of great help.
We have addition tecniques: RCM in vivo, Ex vivo RCM, OCT nad LC-OCT.
These tecniques re-discover dermatopathology.
They have diagnostic advantage in areas where clinico-dermoscopic evaluation is difficult,
RCM is the best use din facial lesion. In machine you can covert black and white into histological staining.
Line-field confocal optical coherence tomography- correlation between dermatoscopic criteria and LC-OPT.

The limit is the time- for 1 confocal microscopy of 1 lesion is 15 minutes! And another limit is learning curve since you need training in dermatohistopatology.
RCM shows keratinocyte atypia but you can not be sure about the depth of the lesion.

Interactive clinical cases: “Clues and pitfalls in your practice”

Acral Lesions
Aimillios Lallas

Dermoscopic images of acral lesion are shown and audience has to vote for correct answer.
Paralel furrow is not important if the lesion is big and asymetric- concept of BRAAFF checklist- published in Br J
Pattern peas in a pot is seen in congenital nevus.
Peas out of the pot (dots are in asymetric manner) is seen in melanoma.
Congenital nevus can look like melanoma.
Age is the single most important decision factor in acral lesions.
Acral dermal nenus has brown wavy lines-very typical.
Spitz nevus on plantar region can be fibrillar structure in unusual region.
Amelanotic lesion resistent to therapy should be biopsied.
Acral melanoma is not always lentiginous and it can be fast growing-often hypo or nonpigmented and ulcerated and with rich vascularity.

Genital Lesions
Mihael Skerlev

Penile pearly papules are common reason- are present in up to 40% patients
In female patient we have also equivalent lesions.
Hypertropic sebaceus glands can get inflammed.
Not all HPV is genital, it can occur oral.
37% patients with Crohn disas have perianal fibroms, so not all lesions are sexually transmitted.
Syphilis is stil great imitator. Sometimes the rash can be very subtle.
Extramamar Paget disease should be differentiated from condylomata lata.
Primary genital herpes causes ulcerations and should be differentiated from ulcus durum.
Ulcus durum can be seen anywhere!
Iritant contact dermatitis can happen due to drugs used to treat warts.
Scabies can be found in genital region.

Facial Lesions
Wilhelm Stolz

Dermoscopy of facial lesions is demanding.
Seborreic keratosis is seen better with non polarized mode.
BCC on face presents with typical criteria.
Red lesions on the face can be actinic keratoses, SCC and lupus.
Nodular melanoma can occur on face.
Flat pigmented lesions are difficult to differentiate and inverse approach is suggested.

Oral lesions
Mahtab Samimi

A burning tongue is a syndrome.
There are circumvallate and fungiform and filliform papillae .
Some patients have fissured tongue, it is normal condition (5% of population)
Geographic tongue -benign migratory condition.
Oral candidiasis- median rhomboid glossitis is treated with antimicotic treatment.
Oral lichen planus can be erosive and atrophic.
Angina bullosa hemorragiva is strange condition with spontaneous resolution without scarring.
Mucous membrane pemphigoid is rare presented with blisters- it presents with ulcers and pseudomemranes.
Lymphangiectasia is congenital vascular malformation.
Chronic cheilitis is another condition. Actinic cheilitis is found in lower lip.

Interactive clinical cases: “Clues and pitfalls in your practice”

Nails
Francesca Pampaloni

How t evaluate nail disorder-look at all nails, look at affecte nail-proximal nail fold, lateral nail fold, distal margin, hyponichium
There are nail changes in graft versus host disease, 30% of adult patients and 45% of children, may first present as acral erythema.
Acute kollonychia of fingernails due to Lye
Mycetoma is localized mainly on the extremities and the origin can be bacterial nad fungaland is prevalent in tropical and subtropical region of World.
Management of carpal tunnel syndrome can be conservative and surgical and can cause acro-osteolysis and amputation so early diagnosis and tretment is important.
Nails can show beau lines, onychomadesis, coilonichia and leuocnichia
Fungal melanonychia shows different colors, including black

Hives
Margarida Goncalo

Cases with urticarial lesions are discused.
We discussed CSU, autoinflamatory sy, urticaria vasculitis and hereditary angioedema.
Patients with slow response to omalizumab may respodn to increase of dose.
There are 2 types of autoimmunity, type II b have low IhE (auto IgG anti FceRI and IgG antiIgE) – these patients have more severe CSU, night lesions and less response to anti-H1
If you have auto-allergy, IgE anti-self, you have fast response to omalizumab

Schnitzler sy is associated with systemic symptoms and monoclonal gammapathy. Histology can show neutrophilic urticaria. Some of them progress to lymphoproliferative disease. This is autoinflammatory syndrome and respond to Anakinra.
Adult-onset Still's disease- typicaly high levels of ferritine.

If urticarial lesions persist more than 24hrs, you should do complement levels. Consumption of complement can be found in hypocomplementemic urticarial vasculitis or hypocomplemetemic urticarial vasculitis syndrome.

Isolated angioedema should be studied to differentiate between hereditary, acquired and drug induced angioedema.

Purpura
Angelo Valerio Marzano

In purpura patients we should do histopathology and direct immunofluorescence, along with complete blood count, urine analysis, CRP, along with screening of systemic involvement (pANCA, c-ANCA, antiphospholipid antibodies)
Small vessel vasculitis- IgA vasculitis
Cutaneous IgM/IgG vasculitis presents with polymorphic cutaneous picture- palpable purpura, livedo reticularis, blisters, necrosis, urticaria like and target like lesions- DIF is diagnostic (Marzano AV et al. J Am Acad Dermatol 2020; S0190-9622(20)30673-3)

Wegener disease can present with purpura.
Livenoid vasculopathy is severe form.
Pigmented purpuric dermatoses (capillaritis) Schamberg
Purpura associated with coagulopathies
Drug induced vasculitis

Exanthemas
Eva Chavarria-Mur

Exxagerated insect bite sydrome can present with multiple and infiltrated lesion.
For diagnosis of Sweet sy- dense neutrophilic infiltrate and systemic symptoms
Sweet sy presents with infiltrated lesions.
Wells sy- lesions are cellulitis rash- histology eosinophils anf flame figures
Hematologic-related malignancy induced eosinophilic dermatosis
Histocytiod Sweet syndrome is diagnosed by histologic examination (dermal infiltrate of immature neutrophil cells)
VEXAS sy- vacuoles, E1 enzyme, X linked, autoinflammatory, somatic) (J Am Acad dermatol 2023; 88(4):917-920.

Mycoplasma pneumoniae-induced rash and mucositis as a syndrome distinct from SJS and ertyhmea multiforme- the best treatment is supportive care.

Drug induced exanthema- DRESS presents with systemic symptoms, fever, eosinophilia, more than 1 organ is affected, atypical lymphocytosis. In 10% mortality due unrecognized myocarditis and CMV reactivation. Patch testing should be done after 6 months after resolution of the disease.

What is new in: “Pigmentary disorders”

Chairs: Mauro Picardo (Rome, Italy)
Reinhart Speeckaert (Ghent, Belgium)

The challenges of hyperpigmentation in individuals with dark skin
Rohit Kothari

Everyone has the same number of keratinocytes, but the variation of pigmentation occurs due to differencies in size, number and dispersion of melanocytes.
We know that postinflamatory hyperpigmentation occurs due to inflammation.
White skin- stage I/II melabosomes and has natural SPF 3.4

Melanosome size increase in size on fotoexposed skin. Africans have thicker SC and stronger barrier, and also more ceramides.
Hyperpigmentation occurs as a result of damage to upper layers of skin-basement membrane
There is a hypothesis that melanocytes go to the dermis through the gaps in the basal lamine.
Inflamation of the skin causes upregulation of prostaglandins(due to inflamamtory eractions and UV exposure, elevated dermal mealnine, trosinase activite due to keratinocyte growth factor . Dermal MC have role. Growth factor in fibroblasts have alos role in melanin production. Cytokine, chwmokines and ROS stimulate melanocytes
There is also impaited vascular and microvascular function.
There is thicker dermis with more macrophages
IL-6 has role in abnormal melanogenesis
Senescent fibroblast have importa role in abn pigmentation
Therapeutic approach should include: Rule out photosensiting/toxic medication; Topical agens, chemical peels, laser; Photoprotection is most important and triple formula (Hidrokinon, tretinoin and corticosteroid)

Photoprotection should be applied 8-11-2 pm or 8am-12pm
Tinted SPFs are better than micronized in protection.

Topical agents; retinoids, AHA, cortioc, tiadimol, niacinamid, plant derived products
Azelaic acid supress UVB induced expr and secretion of IL-1 and TNF alfa
Aloesin
Silpa-Archa et al 2017- most of the agens wotk on tyrosinase inhibition
Chemical peels-GA <70, SA<30, 40% mandelic acid, Jessner, 88%LA, phytic acid and TCA
Imediate application of corticosteroids

Laser: Qs Nd:Yag, Er-drop
Cloths-important strategy

Oral: niacinamide, tranexamid acid, oral melatonin 3 gm/day with topical melatonin
800 mg/d carotenoids
Gluthatione 50 mg
Procyanide

Authors clinial approach and recommendations:
Best result; HQ, retinoic acid, cortiocosteroids
Tretinoin,/tazaroten
o
Before procedure: 2 weeks photoprotection and retinoids 2 weeks before
Pre-procedure topical bleech cream
Epidermal cooling is important
Microneedling- minimal risk for hyperpigmentation.
Newer but still not established options are cisteamin and thiamidol.

What’s new in treatment of melasma
Mauro Picardo

Melasma is photoaging skin disorder occuring in genetic backround rather than simply a pigmentation disease. Hydroquinon is still referent drug. Cutaneous pigmentation occurs due to crosstalk between keratinocytes and fibroblast-derived soluble factors (dermal-epidermal cross-talk). In melasma there is also altered vasculature.
Melasma appears in areas rich in sebaceous glands. Female skin color depends on estrogens and progesterone levels.
Some common therapeutic options are: Tyrosinase inhibitors- hidrokinon, azelaic acid, arbutine, kojic acid; Chemical peels; Antioxidant treatments-oral lycopene-rich tomato

Modified klingman hidrokinon 4%, tretinoin 0.05%, fluocinolone acetonide 0.01% - treatment is used until needed. This triple combination is still the best treatment.
TXA- oral or topical – inhibits tyrosinase activity, reduces VEGF- angiogenesis, decreases melanocyte activity, prostaglandins, proinflamatory cytokines-it is administered 250 mg 3x per day/12 weeks but 250 mg 2x per day can be option
Niacinamide shows protective effect against UV-light induced DNA damage in epidermal melanocytes, decreases changes on collagen
Laser therapy can be used with-low-fluency 1064nm
Microneedling with combination with topicals is effective and safe since microneedling reduces solar elastosis and pendulum melanocytes
Possible future approaches; hUCMSC-Exos and intradermal injection with PRP
A combination of multitarget therapy results are the best approach

PRP and stem cells transplantation for vitiligo
Taige Cao

Repigmentation th: topical cortico/calcineurin inh and phototherapy
Cell based therapies are graphts, hair follicles
Regenerative therapy: PRP and stem cell therapy
PRP has anabolic and antiinflammatory effect and proliferation of KC and fibroblast, inhibits apoptosis of melanocytes
PRP can be used as combination with narow band UVB, laser therapy.
Multilineage-differatiating stress-enduring (MUSE) cells-form human dermis and adipose tissue using the embrionic antigen 3 marker
These are new promising approaches in treatment of vitiligo.

Will JAK inhibitors revolutionise the treatment for vitiligo?
Reinhart Speeckaert

Association of vitiligo is linked to response on pembrolizumab in melanoma patients.
There is decreased risk of MM and nonMM skin cancer in patienys with vitiligo (Br J Dermatol)
For vitiligo pts the balance is towards autoimunity
Melanocyte-specific T cells migrate towards the skin and produce IFN gamma which is key cytokine in vitiligo. Precurs of melanocytes are temporaly protected arround hair follicles- the origin of the repigmentation.
Most of the drugs act on stopping disease progression.
Ruxolitinib cream is in phase II trial and phase III (at week 52 75% improvement) (J am Acad Dermatol 2022;1398-1401) Women respond better than men.

Tofacitinib cream has been studied in 2 studies, not many data.
The outcomes in vitiligo are difficult to compare.

Oral tofacitinib-repegminatation can be seen on sun-exposed areas
Baricitinib- 2 pts with repigmentation in comb with nmUVB
Oral ritlecitinib (JAK3 inh) -phase 2b clinical trial

Other immunosupresant drugs: MTX with nbUVB -MTX is a JAK/STAT pathway inhibitor, therefore MTX acts as JAK inhibitors.
For the repigmentation we need UV light.
JAK inh and phototerapy- still we need to see side-effects.
Amelioration of unstable vitiligo with stabilisation of autoimmune throid disease

Side effect of JAK inh- venous thromboembolism should be always considered.

What is new in: “STIs”

Chairs: Carmen Maria Salavastru (Bucharest, Romania)
Valeska Padovese (Valletta, Malta)

Need for: HPV vaccination preadolescence and education on seks behavious.
Adolescents who have had sexual intercourse have the highest risk for STIs.
Higher risk is for those in detention facielities, with multiple partners, lower socioeconomic status, partnerships of limited duration.
If a preadolescent child has STIs, it should be considered if congenital tranmition has been excluded
Chlamidia trachomatis is the most common STI u adolescents. Rates for gonorrhoea are lower
Adolescents are not considered as prime risk group for syphilis.
HSV- type 1 can be found in genital region
Determinants of risk factors in adolescent population-cervix displays columnar epithelium („ectopy“) which increases the risk for chlamidia. Adolescents have thinner mucus making microoorganism easier to penetrate.
Possible future approach:
Adolescents do not have the basic information to make informed choices. We need to inform them better.
HPV vaccination showed rapid decline in genital warts.
Chlamidia vaccination is under development for adolescents before sexual debut.
Need of mass media for information dissemination.
Alternative -site STI/HIV testing and increasing adolescent care seeking should be promising strategies.

What's new in antibiotic resistance
Valeska Padovese

New super bug is multi-resistant neisseria gonorrhoae
Treatment of N.gonorrhoose is Ceftriaxone 1 g im as single dose, or Ciprofloxacin 500 mg orally as single dose
Alternative:
Cefixime 400 mg
Future: gentamicin, roxitromicin, zoliflodacin, gepotidacin

Macrolide resistance in syfilis

Trichomonas resistance to metronidazole is uncommon
Mycoplasma resisitence to macrolide is increasing
Macrolides were 1st line, with fluoroquionolones and tretracikline being alternative. Resistance is increasing (30-100%) worldide
Doxycikline 100 mgg 2x 7 dna followed by azitro 1 g orall as single than 500 mg orall for 2 days
Moxifloxacin 400 mg PO 1xdaily for 10 ays
Alternative:
Pristinamycin
Sitafloxacin

Shigella sonnei- an emerging XDR STI (G-neg enterobacteria)
Via fecal-oral route, bit sexual particulalry in GBMSM
Incubation 3 days
Fluoroquinolone 1st line, cephalosporines (2nd line), Beta -lactam for 7-10 days
Emergence of azitromyciin resistance, ciproflox resistanrt, ceftriaxone resisitant
Nanoparticles and vaccinate as future approach

Mycoplasma genitalium: to treat or not to treat?
Peter Greenhouse

M.genitalium is not very significantly causing pelvic inflammatory disease and the majority of patients are asymptomatic.
Probably just genetically asceptable patients will develop symptoms.
There is no evidence about the role of mycoplasma can cause any adverse event in pregnancy.
Should we test for it? The guidelines do not recommend to test for the m.genitalium.
Macrolide resistance is >50% in many countries
Fluorquinolone rezistence 5-6%

Start doxy 100 2x 10 days
Complicated moxifloxacin 400 mg odx14 days
The azitro 1 g 1 day and then 2 days 500 mg
2021 European guideline on the managemenet of M.genitalium Jensen JS et al. JEADV 2022
Sweeney EL et
Don't treat without resistance testing guidance

Is HIV-infection becoming a chronic disease?
Andrew de Burgh-Thomas

Nearly 50 drugs have been approved since 1985
Today we have 10 single tablet regims, +injectable
A person living with HIV under treatment will not transmitt the virus
By remaining compliant to medication you can forger about HIV being issue for your health
Issues of late diagnosis: more infections, inadequate restitution of immune function, AIDS, death, higher rate of cancers
In 2021 38.4 million of infections

ECOBIOLOGY AT THE SERVICE OF DERMATOLOGY

Learn more about NAOS, French ecobiology company founder of BIODERMA, on www.naos.com