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A Report from the 25th World Congress of Dermatology (WCD)

Mona El-Kalioby, MBCh, MSc, MD, 2022 IPC Fellow

SUMMARIZING SESSIONS WITH A FOCUS ON PSORIASIS
INTRODUCTION
The World Congress of Dermatology (WCD) convenes every four years, and in 2023, Singapore had the honor of hosting this event from July 3–8. The Congress featured many captivating psoriasis sessions, including the International Psoriasis Council (IPC) Symposium: Psoriasis Management and Treatment – An International Perspective. The following report comprises 21 summaries, focusing on the most critical psoriasis sessions at WCD.

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>IPC Symposium – Psoriasis Management and Treatment – An International Perspective</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 A Patient-Inclusive Approach in the Treatment of Psoriasis: A Principal Without Borders</td>
</tr>
<tr>
<td>5 An International Perspective on Value-Based Healthcare</td>
</tr>
<tr>
<td>6 Genetic Differences Across the Globe</td>
</tr>
<tr>
<td>7 Pitfalls in Diagnosis and Phenotypic Differences Related to Skin of Color</td>
</tr>
<tr>
<td>9 Therapeutic Challenges Related to Skin of Color</td>
</tr>
<tr>
<td>11 Availability of Therapies Across the World: Data from the GPA</td>
</tr>
<tr>
<td>12 Every Patient in the World has the Right to Optimal Treatment</td>
</tr>
</tbody>
</table>

Other WCD Sessions (Psoriasis I, II, III, and IV)

| 13 Epidemiology and the Global Psoriasis Atlas. | Darren Ashcroft, BPharm, MSc, PhD, MRPharms, IPC Councilor |
| 14 New Developments in Biomarkers and Psoriasis | Qing Sheng Mi, MD, PhD |
| 15 Racial/Ethnic Disparities in the Prevalence of Psoriasis | Ricardo Romiti, MD, PhD, IPC Board Member |
| 16 Current and Emerging Treatments for Generalized Pustular Psoriasis | Siew Eng Choon, MBBS, FRCP, IPC Board Member |
| 17 The Importance of Early Detection and Management of Psoriatic Arthritis | Claudia de la Cruz, MD, IPC Board Member |
| 18 Challenges in Managing Psoriasis in Tropical Areas | Hazel Oon, MD, MRCP, M Med Int Med, GDFM, FAMS |
| 19 Cardiovascular Disease and Psoriasis: Can We Make a Difference With Our Treatments? | Andrew Blauvelt, MD, MBA, IPC Board Member |
| 20 Phototherapy for Psoriasis; Still a Viable Option? | Mark Berneburg |
| 21 Oral Therapies for Psoriasis; MTX, Apremilast or Deucravacitinib | April Armstrong, MD, MPH, IPC Councilor |
| 23 New Findings of Clinical Trials of Phototherapy for Psoriasis | Joel Gelfand, MD, MSCE, IPC Board Member |
| 24 TNF Antagonists With and Without Methotrexate; Indications, Risks, and Limitations | Lars Iversen, MD, DMSc, Former IPC Board Member |
| 25 IL-17 and IL-23 Antagonists | Kenneth Gordon, MD, IPC Councilor |
| 26 JAK Inhibitors | Melinda Gooderham, MSc, MD, FRCPC |
| 27 New Drugs in the Pipeline | Bruce Strober, MD, PhD, IPC Vice President/President-Elect |
A Patient-Inclusive Approach in the Treatment of Psoriasis: A Principal Without Borders
Claudia de la Cruz, MD, IPC Board Member
Clinica Dermacross, Santiago, Chile

The patient perspective is globally recognized as an independent dimension of healthcare quality, clinical effectiveness, and patient safety. Healthcare providers and dermatologists seek to understand the patient’s perspective of their experience. This allows us to obtain a better and greater understanding focused on the patient making their journey more affordable and with a better quality of life.

As dermatologists, we target calculating PASI, BSA, DLQI, comorbidities, etc., but from the patient’s perspective, the only goal is to eliminate the disease. They only need to be healthy. Psoriasis patients are impacted physically, socially, emotionally, and economically, carrying a stigma and significant impairment over their lifetime. They must make decisions (e.g., education, profession, and marriage) based on their disease. The disease harms patients’ relationships, productivity, and careers, in addition to increased risk for early mortality and increased prevalence of comorbidities (including depression and social isolation).

Six themes (and subthemes) for the patient’s perspective were identified related to psoriasis and psoriatic arthritis:

1. suffered uncontrollable and ongoing upheaval (dictating life choices and course, disrupting family and social roles, limited by debilitating symptoms, unstoppable and far-reaching fatigue);
2. weighed down by mental load (anxiety provoked by the volatility of symptoms, dreading deterioration, struggling with unrecognized distress, helpless and nihilistic);
3. harboring shame and judgment (marked as unhygienic and contagious, rejected and isolated, hiding away and resenting own appearance, pain, and embarrassment in intimacy);
4. demoralized by inadequacies and burden of therapy (disappointed by unmet expectations of treatment benefit, daily drudgery, deterred by unpalatable or inconvenient treatments, disempowered by lack of personalized care);
5. gaining control (making sense of the condition, accepting a new health status, regaining independence and normality, attuning to the body); and
6. making confident treatment decisions (trading off perceptible benefits against safety and convenience, relying on family input, and seeking empowering and reassuring relationships).

Patients with psoriasis and psoriatic arthritis contend with disruption in their functioning, roles, and life course and have unmet expectations about treatment. Enhanced therapeutic relationships, addressing treatment expectations, and supporting psychosocial needs may improve satisfaction and outcomes.¹

Inaccessibility to treatment adds to the burden of the disease. In one study, 14.3% of psoriatic arthritis patients had never seen a rheumatologist. Patients with psoriasis alone most frequently consulted a general practitioner, and 10.7% had never seen a dermatologist (although those with severe symptoms visited dermatologists more often). Negative impacts on HRQoL were reported by 38.1% of patients with psoriasis [mostly limitations on clothing (22.6%), sleep disorders (16%), and depression/anxiety (16%)] and by 73% of patients with PsA [mostly limitations on clothing (41.8%), sports/leisure (44.0%), or daily routine (45.1%), and sleeping disorders]. Sleeping disorders and depression are common and should not be overlooked. Therefore, it is essential to consider asking our patients about their feeling, sleeping, and signs or symptoms of anxiety.²
In conclusion, healthcare providers should try to put themselves in the patient’s perspective whenever they face their patients. The patient perspective is different, not only from patient to patient but also from country to country and from region to region. Also, facing the public system is different than facing the private system.

Healthcare providers and psoriasis-focused organizations have increasingly incorporated the patient perspective into their initiatives. Notable projects include the International Federation of Psoriasis Associations (IFPA), which is centered on the patient; PsoProtect Me, an international registry of patients to report the outcome of COVID-19 in individuals with psoriasis; and Clinica Dermacross, Santiago, Chile; a campaign in Chile directed to patients.

References
Treatments for psoriasis are quite expensive. The management of the overall care cycle for psoriasis patients is not adequate in many places of the world. Value-based healthcare had already bad connotations, but we are only at the beginning of applying it. It needs a validated patient-relevant outcome set, insights into the true cost range to achieve them, and accepting digital challenges. It is suggested to be considered for major skin disease groups like psoriasis. Value is equivalent to patient-related outcomes divided by the costs.

PsoPlus is a project set up in the academic hospital University in Flanders in Ghent, Belgium, to address value-based healthcare. It is a dedicated clinic for psoriasis patients. The project involved a structured checklist of health records used during the consultation and capturing data comprehensively and more completely. There was more emphasis on the education of the patients. There was also a communication channel between consultations with the patients. Results showed that this project put patients more rapidly on more efficacious medications, and patients had to return less frequently (better results).¹

References
Psoriasis prevalence is variable across the globe. The color of the skin and race highly modify the appearance of psoriasis. Genetic predisposition with more than 86 genetic loci has been identified in psoriasis. There is a diversity of biological processes that are involved in this predisposition: interferon/antiviral signaling, epidermal differentiation, autoinflammatory responses, IL-23/Th17 differentiation/IL-17 responses, antigen presentation, oxidative responses, TNF/NF-κB signaling, and T-cell development. There is also diversity in the MHC class I alleles across the globe. For example, IL-33 signaling seems to be more on the Chinese side. African Americans seem to have higher PASI scores compared to Caucasians. Most of the clinical trials are biologics on white men. There is little data on females and other races.

The genetic architecture of psoriasis is complex and incompletely understood. It needs larger and more diverse genetic studies. Each psoriasis patient carries a unique mixture of different risk alleles. The frequency of risk alleles differs between different ethnic groups. The types of risk alleles/genes differ between different ethnic groups. It is likely to contribute to molecular and clinical heterogeneity. It may contribute to variability in treatment response. Future studies will help address larger and expanded multiethnic GWAS studies to facilitate polygenic risk scores that factor in racial backgrounds.

References
Skin of color identifies individuals or racial groups with skin darker than Caucasians, such as Asians, Africans, Native Americans, and Pacific Islanders. Causes of skin color different distribution include genetics, environmental factors (e.g., sun exposure), and historical factors (e.g., mass migration, population mixing, and historical events such as colonization and the slave trade). Darker skin types can be found mostly between 20° North and South of the equator. It is estimated by the year 2040, the population of those with skin of color will increase.

While the basic characteristics of psoriasis remain the same across all skin types, there are certain pitfalls in diagnosis and differences in phenotypes of psoriasis in individuals with skin of color. These variations can sometimes pose challenges in accurately identifying and managing their condition. Here are some pitfalls and differences to consider:

- **Underdiagnosis:** Psoriasis may be underdiagnosed in individuals with darker skin tones due to the misconception that it primarily affects individuals with lighter skin. A 2014 review of 29 dermatologists in the Journal of Drugs in Dermatology found that African American patients have higher rates of underdiagnosed psoriasis than their white counterparts. They also found that people with underdiagnosed psoriasis were more likely to be males, less educated, and unmarried. Healthcare professionals may be less familiar with the diverse clinical presentations of psoriasis in skin of color, leading to missed or delayed diagnosis.

- **Atypical morphology:** Psoriasis has a different presentation, color, and scale shape in different skin types. The characteristic silvery scales may be less prominent or absent, and the lesion may be darker or more pigmented. This atypical morphology can make recognizing psoriasis difficult and differentiating it from other skin conditions. The red color or erythema typically seen in psoriasis with light skin often appears more purple or brown in darker skin types. Sometimes the scale accompanying psoriasis is so thick that it is difficult to appreciate the underlying color of the plaque itself.

- **Rupioid psoriasis and ostraceous psoriasis** in skin of color may present a diagnostic challenge for healthcare providers. Rupioid psoriasis is a rare type of plaque psoriasis. It causes skin plaques with a distinctive cone shape. Ostraceous psoriasis is one type of psoriasis with a typical lesion form of a circular hyperkeratotic lesion resembling an oyster shell.

- **Diagnostic confusion:** the clinical features of psoriasis in individuals with skin of color can mimic other dermatological conditions such as lichen planus, discoid lupus erythematosus, seborrheic dermatitis, acanthosis, eczema, cutaneous T cell lymphoma or even fungal infections. These conditions’ overlapping symptoms and similar visual appearances can lead to misdiagnosis or delayed diagnosis.

- **Diagnostic challenges:** because of the difficulty diagnosing psoriasis on darker skin. People of color are four times more likely to require a skin biopsy or dermoscopy to diagnose the disease and wait three times longer for a definitive diagnosis compared to white people.

- **Koebner phenomenon:** in individuals with skin of color, post-inflammatory hyperpigmentation is a common response to injury, and psoriatic lesions may be mistaken for post-inflammatory hyperpigmentation. This can result in a misdiagnosis or an appropriate treatment.
• Variation in distribution: Psoriasis lesions may have a prediction for specific anatomical sites depending on the individual’s skin color. In individuals with skin of color, psoriasis lesions may be more common in areas such as the face, flexural areas (e.g., under the breasts, groin, armpit), and scalp. Healthcare providers should be aware of these distribution patterns to even accurate diagnoses. Scalp psoriasis may be more common in Asian and black patients than in white patients and can be more severe in black women.

• Cultural factors: cultural practices and preferences, such as skin-lightening creams, may alter the appearance of psoriasis lesions or affect the patient’s willingness to seek medical attention. These factors can contribute to delayed diagnosis or reluctance to disclose symptoms during a medical consultation.

• Post-inflammatory hyperpigmentation: after the resolution of psoriasis lesions, individuals with skin of color may experience post-inflammatory hyperpigmentation (PIH). PIH can complicate the evaluation of the disease activity and response to treatment.

• Phenotypic racial differences in presentation: Plaque Psoriasis is the most common type of psoriasis among all races. Pustular psoriasis is more likely to be seen in Asian and Hispanic populations. Asian populations are also more likely to present with erythrodermic psoriasis and less likely to have inverse psoriasis. One study found that Asian and Hispanic populations are more likely to present with greater disease severities than Caucasian patients. East Asian patients often had smaller, less widespread plaques than Caucasian patients. Asian and black patients are also more likely to present with scalp psoriasis.

To overcome these pitfalls and address the differences in phenotypes, dermatologists and healthcare professionals should receive education and training regarding the diverse presentations of psoriasis in individuals with skin of color. Increased awareness, improved diagnostic criteria, and personalized treatment approaches can help ensure accurate diagnosis and effective management of psoriasis in all patients, regardless of skin color.

References
Therapeutic Challenges Related to Skin of Color
Mahira El Sayed, MSc, MD, IPC Board Member
Ain Shams University, Cairo, Egypt

Race is different from ethnicity. Race combines geographic, cultural, bioancestral, and sociopolitical inferences. In contrast, ethnicity refers to people who may share a common nation, tribe, religion, or cultural background. Currently, race is accepted as a social construct, with the understanding that there is fluidity in racial classification among different countries, cultures, and time periods.

Skin of color is defined as “Black, Asian/Pacific Islander, American Indian/Native Alaskan, Indigenous Australian, Hispanics/Latinx, Middle Eastern/Arab/North African, and individuals who identify as nonwhite.”

In skin of color, psoriasis is different regarding genetic basis, clinical presentation, and treatment availability and effectiveness. Continued research efforts are necessary to determine the precise genetic and environmental contributions to psoriasis pathogenesis in various racial and ethnic groups. By 2021, people with skin of color will make up 40% of the US population. Current research suggests that, despite a somewhat lower frequency in nonwhite ethnic groups, psoriasis presents thicker, scalier, and more extensive plaques in individuals with skin of color. In addition to greater disease severity, psoriasis has an increased impact on the quality of life in nonwhite individuals compared with white individuals. These significant differences highlight the importance of prompt diagnosis and culturally sensitive and evidence-based management of this condition in diverse ethnic groups.

Erythema is not characteristic of psoriasis of skin of color. The involved area may have a dark brown or violaceous hue. Erythema can be mistaken for post-inflammatory hyperpigmentation when it may be a marker of active inflammation. Noting that the severity of psoriasis is commonly assessed using the PASI score, where erythema is one of the indices. The severity of psoriasis tends to be increased in women of African descent. Small plaque psoriasis is a less severe phenotype unique to Asian populations. A study on 2534 patients in a tertiary care center in Egypt reported a high frequency of erythrodermic and pustular psoriasis in the studied Egyptian cohort. In addition, there was a higher frequency of pruritus and a lower frequency of positive family history in the studied population than in other ethnic groups.

There is an unmet need for clinical guidelines on managing patients with plaque psoriasis in Africa and the Middle East. Choice of treatment in high-income countries relies on the severity of the disease, impact on quality of life, and presence of comorbidities. In low-income countries, treatment choice is primarily based on economic availability. Methotrexate is the most prescribed drug for moderate to severe psoriasis; however, in the presence of viral hepatitis, the use of Methotrexate is contraindicated. Further, it is hard to ensure treatment compliance for methotrexate after the hospital discharge and follow-up for people from rural, remote areas. Phototherapy is another appropriate treatment. Phototherapy is widely used, but there is a risk of post-inflammatory hyperpigmentation if phototherapy is associated with burns. There is also an effect of phototherapy on pre-existing post-inflammatory hyperpigmentation. Phototherapy remains a safe and effective treatment option for patients with skin of color. Regarding biologics, skin of color is underrepresented in psoriasis clinical trials. The stepwise approach is still followed for psoriasis in low-income countries.
There are unmet needs, including educating dermatologists, national guidelines, access to biologics, and more biosimilars are needed. In conclusion, psoriasis in skin of color is different in genetics, clinical presentations, and treatment. The potential genetically mediated difference in clinical presentations, complications, and consequences of psoriasis between the various ethnic groups warrant further investigations. There is an urgent need in developing countries, especially in Africa and the Middle East, to implement a national strategy involving both physicians’ and patients’ awareness of the importance of early diagnosis and treatment of the disease.

References
An unmet need for psoriasis epidemiology exists. The Global Psoriasis Atlas (GPA) is a joint project of the International League of Dermatological Societies (ILDS), the International Federation of Psoriasis Associations (IFPA), and the International Psoriasis Council (IPC). The mission of the GPA is to provide a common benchmark for the complete burden of psoriasis in all countries and regions worldwide. GPA is based on the diabetes atlas. The vision of the Global Psoriasis Atlas is to become the leading epidemiological resource globally on psoriasis.¹

To map epidemiology, accurate diagnosis is essential. Missing opportunities to diagnose psoriasis exist in UK primary healthcare. Diagnosis can depend on definitive and supportive criteria. Illustrations rather than clinical images are more helpful for healthcare providers to diagnose psoriasis. Psoriasis training tools can improve diagnostic ability, especially for non-dermatologists.

GPA studies in Greenland found patients having psoriasis there. That is opposite to what is known, and this is probably can be explained that the diagnosis of psoriasis has been missed before. Regarding access to therapy, GPA showed limited accessibility to treatment in some regions. For example, Chile has less access to systemic therapy and biologics than Brazil.

In conclusion, the GPA addresses key questions about psoriasis epidemiology. Global teamwork and task sharing are essential to achieve the objectives of this project.

References
Every Patient in the World has the Right to Optimal Treatment
Hoseah Waweru, MD
International Federation of Psoriasis Associations (IFPA), Nairobi County, Kenya

All patients with psoriasis worldwide deserve optimal care. There has been great progress in developing vast treatment options such as topicals, biologics, and biosimilars. Yet, we face many challenges, e.g., inequalities and limited access in some regions, high cost of medications, limited insurance coverage in middle- and low-income countries, and uneven distribution of dermatologists.

Optimal treatment and holistic care are important. This involves expanding measurement beyond clinical endpoints, incorporating patient-reported outcomes in study design, and evaluating overall improvement using quality of life, mental health tools, and DLQI.

It is important to follow a patient-centered approach. This involves joint treatment decision-making, involving the patient in treatment decisions, determining the most appropriate plan together, and considering the quality of life and other aspects of the patient’s life.

It’s important to evaluate the safety and effectiveness of the medications and the availability of treatment worldwide. It’s important to screen for comorbidities, including associated depression and anxiety. Measurement of well-being is an important outcome in clinical trials.

In conclusion, the path to optimal care includes addressing access barriers, being patient center, and using better outcome measurements.
Epidemiology and the Global Psoriasis Atlas.
Darren Ashcroft, BPharm, MSc, PhD, MRPharms, IPC Councilor
University of Manchester, Manchester, United Kingdom

The scope of the research program for the Global Psoriasis Atlas’ (GPA) response to the World Health Organization’s call to fight global knowledge gaps for this series of non-communicable diseases. The GPA identified 60 million people with psoriasis globally, with higher rates of psoriasis in Western countries.

Findings from a systematic review highlighted marked variations in the reported prevalence and incidence of psoriasis, both within and between countries. Much variation within countries is likely due to methodological differences in study design. Lack of standardization has limited the ability to compare disease prevalence rates between studies in a meaningful way.¹

The systematic review also showed an important knowledge gap. Most of the studies contributing data on disease prevalence were conducted in Western Europe and the US, with far fewer studies identified from Asia, Africa, Eastern Europe, and South America. Very few studies focused on the incidence of psoriasis and trends in the incidence over time. Very few studies have simultaneously compared trends in incidents, prevalence, and mortality longitudinally in patients with psoriasis to determine whether the prevalence of psoriasis is increasing over time. If so, whether increasing trends in incidents drive this or whether patients are now living much longer with psoriasis due to a reduction in early mortality.¹

The GPA studied the epidemiology of psoriasis in Chile, Taiwan, and Malaysia. A key finding in the epidemiology in Malaysia is that the prevalence of psoriasis was highest in the Indian ethnic groups.² Efforts were made to map the opportunities for earlier diagnosis of psoriasis and primary care setting in the United Kingdom using clinical diagnostic criteria for psoriasis.³

References
Psoriasis involves gene-environment interactions. Human genetic variation can be due to single nucleotide polymorphism (SNP), copy number variation (CNV) insertion and deletion, protein-truncating variant, and structural variation. Genetic research is evolving. Genome-wide linkage analysis identified susceptibility genes at PSORS1. Refined mapping of PSORS9 identified IL-15 to be a susceptibility gene.1 Genetic studies revealed the complex genetic variation and ethnic heterogenetics of psoriasis and the importance of various pathways of skin barrier, antigen presentation, NF-κB, and Th1/Th17 in the pathogenesis of psoriasis. The genetic basis of psoriasis differs according to the clinical subtypes of psoriasis. In plaque psoriasis, the HLA-C*06:02 genotype is a predictive biomarker of biologic treatment response in psoriasis. The major genetic risk factor for the early onset of psoriasis is HLA-C*06:02, and most susceptibility genes contribute to plaque psoriasis. Mutations in the IL36RN gene are associated with pustular psoriasis forms of psoriasis, particularly generalized pustular psoriasis (GPP). HLA-B*08:01:01-HLA-C*-07:01:01 were associated with joint fusion, deformities, asymmetrical sacroiliitis, and dactylitis. Non-HLA loci associated with psoriatic arthritis, including IL-23R and TNFAIP3. There is an urgent need to identify early diagnostic tests or biomarkers with high sensitivity and specificity for psoriatic arthritis. Current research is trying to address whether circulating noncoding RNAs/miRNAs serve as biomarkers for psoriatic arthritis and if single-cell mass cytometry profiling of the peripheral blood immunome uncovers potential biomarkers for psoriatic arthritis.

References
Racial/Ethnic Disparities in the Prevalence of Psoriasis
Ricardo Romiti, MD, PhD, IPC Board Member
University of São Paulo Brazil, São Paulo, Brazil

There are generally no significant ethno-racial differences in the anatomical locations of psoriasis lesions. Asians and Hispanics/Latinos have higher odds of having pustular psoriasis than Caucasians. Asians also have a higher frequency of erythrodermic psoriasis but a lower frequency of inverse psoriasis than Caucasians.\(^1\)

Even though those of African descent have less psoriasis than whites, they tend to have more severe skin involvement with greater psychological impact and impaired quality of life and present a significantly lower likelihood of receiving biologic medications. A similar response to biologic therapy across racial and ethnic groups was observed among patients with psoriasis enrolled in the CorEvitas Psoriasis registry.

In adults, the prevalence of psoriasis varies between 0.17% in East Asia to 2.5% in Western Europe [GPA]. Only 19% of countries have epidemiological data on psoriasis [GPA]. In the United States, the rate is highest in white individuals, followed by African Americans and Hispanic individuals/others. In Africa, a wide variation in the prevalence of psoriasis between different countries has been reported, the highest rate being seen in eastern and western sub-Saharan Africa. The Amazon study involved Yanomami Indians in villages in the Amazon rainforest on the border between Venezuela and Brazil. During the dermatological evaluation of the studied population, no cases of psoriasis were found. The lower prevalence value probably reflects the role of specific genetic factors, lack of environmental triggers, and sun exposure.

References
Current and Emerging Treatments for Generalized Pustular Psoriasis
Siew Eng Choon, MBBS, FRCP, IPC Board Member
Hospital Sultanah Aminah Johor Bahru, Johor, Malaysia

Generalized pustular psoriasis (GPP) is a rare, potentially life-threatening auto-inflammatory disease characterized by recurrent flares of widespread painful erythema studied with sterile pustules that make pus lakes. 66.5% of GPP patients have associated Psoriasis Vulgaris. Flares are a hallmark of GPP. Common triggers include steroid use/withdrawal, infections, pregnancy, and stress. GPP has high clinical burden: cutaneous [pain, itching, scaling, redness, burning, dryness, pustules], systemic [fever, malaise, fatigue, edema, joint pain, uveitis] laboratory [leukocytosis, neutrophilia, elevated CRP, hypocalcemia, hypoproteinemia, liver function abnormalities], complications [sepsis, liver failure, renal failure, cardiac failure]. Mortality rate is highest in patients on systemic corticosteroid monotherapy. IL-36 is the key driver of disease pathology in GPP. IL36RN mutations exist in 20% to 80% of pustular psoriasis patients. IL-36 is upregulated in GPP regardless of IL36RN mutation status. There is no robust evidence to guide treatment decisions for GPP; current treatment guidelines are based on limited evidence. In published guidelines, first-line treatment for adult GPP includes acitretin, cyclosporin, methotrexate, and infliximab.

Interleukin 36 can be targeted in GPP by IL36R antagonists, including spesolimab, Imsidolimab, and HB0034. Phase 1 trial of spesolimab showed rapid pustular and skin clearance in patients with GPP flare. In Effisayil 1 study, spesolimab was given a 900 mg single IV dose in GPP flare. Another rescue shot could be given after a week and after that if needed. Spesolimab is approved for treatment for GPP flares in the US, Europe, Japan, Taiwan, China, and Canada. Spesolimab is the first GPP-specific treatment with robust evidence of its efficacy in rapidly aborting GPP flares. Effisayil 2 study involves the prevention of GPP flares using subcutaneous doses of Spesolimab. GALLOP is an open-label phase 2 trial of imsidolimab in GPP. Finally, further research and clinical trials using disease-specific assessment tools are needed to identify treatment options that rapidly abort GPP flares, prevent further flares, and save long-term use.

References
The Importance of Early Detection and Management of Psoriatic Arthritis
Claudia de la Cruz, MD, IPC Board Member
Clinica Dermacross, Santiago, Chile

It is estimated that 15% of patients with psoriasis have undiagnosed psoriatic arthritis. Diagnosis and treatment are suboptimal, complicating the diagnosis of the condition’s similarities to other arthritic diseases and potential heterogeneity. 52% of patients with psoriasis have joint pain without diagnosing psoriatic arthritis, and the average diagnostic delay for psoriatic arthritis is five years.1 Early detection and treatment are critical for improving long-term patient outcomes, as psoriatic arthritis can progress rapidly and causes irreversible joint damage. Specifically, diagnostic and treatment delays of more than six months contribute to preferred joint erosions and functional outcomes. Dermatologists are uniquely positioned to identify psoriatic arthritis. Screening tools such as CASPAR and PEST questionnaires can be useful for differential diagnosis. Psoriatic arthritis and gout are different diseases with distinct causes and treatments, despite having similar symptoms. SIJ inflammation occurs in 26% to 50% of patients with psoriatic arthritis but is virtually absent in rheumatoid arthritis and osteoarthritis. Enthesitis and dactylitis occurred in 35% and approximately 50% of patients with psoriatic arthritis, respectively. Best practice indicators for psoriatic arthritis involve shortening the time to diagnosis, improved multidisciplinary collaboration, optimized disease management, and improved disease monitoring.

References
Challenges in Managing Psoriasis in Tropical Areas
Hazel Oon, MD, MRCP, M Med Int Med, GDFM, FAMS
National Skin Centre, Singapore

It remains challenging when managing psoriasis in tropical areas. Dr. Hazel Oon highlights some differences regarding psoriasis in tropical areas in this talk. In tropical areas, psoriatic arthritis is significantly associated with a family history of psoriatic arthritis and the maximum BSA involved. Indian patients were more likely to have psoriatic arthritis than other races. The e-catalyst study showed that the prevalence of metabolic syndrome by the modified NCEP-ATP III guidelines in patients with psoriasis was as high as 45.1%.

References
Psoriasis confers an independent risk for myocardial infarction and CVD in psoriasis. Traditional CVD risk factors are associated with psoriasis, especially severe psoriasis. Chronic inflammatory diseases (e.g., rheumatoid arthritis and severe psoriasis) are associated with increased CVD. FDG-PET/CT scanning showed subclinical inflammation in psoriatic patients’ skin, muscles, joints, liver, and arteries. There is a high relative risk of cardiovascular disease (CVD) even in young psoriasis patients.¹

In inflammatory diseases, the skin is the source of systemic inflammation. Extensive psoriasis is characterized by an estimated 20 billion T cells infiltrating the skin. CVD risk increases with increasing body surface area involvement with psoriasis. Greater psoriasis severity correlates with increased aortic inflammation.

Regarding psoriasis therapies, there is a decreased incidence of myocardial infarction in psoriasis patients treated with TNF blockers or methotrexate. There is a decreased risk of MACE with TNF blockers (compared to methotrexate and phototherapy) and with ustekinumab. The therapeutic improvement in psoriasis correlates with less aortic inflammation. There is a decreased systemic inflammation in multiple tissues after treatment with ustekinumab. Studies showed that low-dose aspirin and atorvastatin reduce vascular endothelial inflammation in psoriasis. A randomized, placebo-controlled trial with adalimumab, ustekinumab, and secukinumab utilizing FDG-PET/CT scanning showed that aortic inflammation didn’t progress over one year.²

References

Phototherapy for Psoriasis; Still a Viable Option?
Mark Berneburg
University Hospital Regensburg, Regensburg, Germany

Phototherapy is still a viable option for psoriasis with good efficacy and safety. Phototherapy can be combined with topical therapy, systemic therapy (classical immunomodulator), and with biologics. It is well-known that acitretin can be combined with UVB or PUVA (RE-PUVA). Combining phototherapy with cyclosporine is unfavorable because of the increased risk of squamous cell carcinoma. Studies showed a combination of nb-UVB with etanercept adalimumab and Ustekinumab.
Oral Therapies for Psoriasis; MTX, Apremilast or Deucravacitinib
April Armstrong, MD, MPH, IPC Councilor
Keck School of Medicine, USC, California, United States

Methotrexate
Indications:
In the United States, methotrexate is prescribed for psoriasis patients who lack health insurance, in patients with peripheral psoriatic arthritis with a lack coverage for biologics [methotrexate is ineffective for axial disease] and is combined with a biologic or phototherapy.

Dosing:
- The oral dosing of methotrexate in psoriasis is a median dose of 15 mg/week, ranging from 7.5 mg to 25 mg per week.
- The dose can be given as a single or three doses over 24 hours.
- It takes time to see improvement, at least six weeks.
- The route of administration can be SQ, IM, and IV.

Baseline and ongoing monitoring:
- Baseline testing: TB testing, hepatitis B, and hepatitis C. Then monitor the CBC and liver function every three to six months, assuming no abnormal laboratory results. Additional monitoring recommended for patients with impaired kidney functions includes blood urea nitrogen and creatinine levels and check CBC five to seven days after a test dose. Methotrexate is contraindicated in creatinine clearance less than 50 mL/minute.
- Erroneous daily dosing of methotrexate can lead to methotrexate toxicity which presents with bone marrow suppression, mouth ulcers, rectal bleeding, and myalgia.

Methotrexate and vaccines
- For non-live vaccines, consider delaying methotrexate two weeks after vaccination to increase the host immune response.
- For live vaccines, most live vaccines are not contraindicated if the dose does not exceed 0.4 mg/kg/week (based on expert opinion). If the dose exceeds 0.4 mg/kg/week, consider holding 0.4 mg/kg/week for two to four weeks before vaccination. Defer the next dose until two to four weeks after vaccination.

Cyclosporine
Cyclosporin can be used in “crisis” patients (like erythrodermic psoriasis, severe pustular psoriasis, or severe plaque psoriasis) or as a bridge to other long-term therapies such as biologic, and possibly in pregnant women with severe flares.

Dosing:
- For severe psoriasis, it starts at 4 - 5 mg/kg/day and is divided into twice-daily doses.
- It has good efficacy, 70% clear or almost clear in 8 to 16 weeks at 5 mg/kg/day.
- Cyclosporine should be tapered and not stopped abruptly.
Cyclosporine and vaccines:
- Inactivated killed vaccines: should be continued without interruption or dose modification.
- Live vaccines are generally contraindicated. If the benefit of receiving a live vaccine outweighs the risk, delay the cyclosporin dose until two to four weeks after administering live vaccines.

Acitretin
The dosing is 10 to 50 mg/day, given as a single dose. Lower doses (25 mg/day) are often used to minimize adverse effects. When acitretin is added to phototherapy, the light should be reduced by 30-50%. It is contraindicated in women in their childbearing period with severely impaired liver or kidney function and chronic abnormally elevated blood lipid values.

Apremilast
Apremilast was approved by the United States Food and Drug Administration (FDA) in 2014. Apremilast is an oral PDE 4 inhibitor. It is indicated for moderate to severe plaque psoriasis. It is FDA-approved for plaque psoriasis regardless of disease severity and approved for psoriatic arthritis. Renal adjustment is necessary for those with severe renal impairment (creatinine clearance less than 30 ml per minute).

Deucravacitinib
- Deucravacitinib is a Tyk2 inhibitor. Tyk2 is a key mediator of psoriasis pathophysiology through modulation of the IL-23/IL-17 axis. It also mediates the signaling of IL-12 and type 1 interferon.
- Deucravacitinib is FDA approved at 6 mg once daily oral medication for moderate to severe plaque psoriasis in adults. A study of Deucravacitinib shows a clear, almost clear response at week 16 and through week 24. Deucravacitinib was also superior to apremilast.
New Findings of Clinical Trials of Phototherapy for Psoriasis
Joel Gelfand, MD, MSCE, IPC Board Member
University of Pennsylvania, Pennsylvania, United States

Phototherapy is recognized as an effective and safe therapy for psoriasis. Patients frequently prefer it because it is

1. a “natural” treatment;
2. cost-effective;
3. has high efficacy;
4. associated with a lower risk of infections; and
5. can be performed as a home or office treatment.

Regarding efficacy, studies showed that phototherapy may achieve a better patient-reported outcome than adalimumab. Regarding vascular inflammation, phototherapy can decrease the level of CRP and IL-17 and improve HDL-P (accordingly, improving lipid metabolism). UVB can decrease and regulate cytokines like IL-36G and interferon and restore keratinization. Phototherapy can also clear psoriasis even in the hardest-to-treat patients, for example, diabetic patients or hypertensive patients who fail apremilast and methotrexate.

Regarding safety, a study showed that phototherapy has fewer adverse effects than secukinumab.¹

The LITE Study is a large pragmatic randomized study to compare the effectiveness, safety (tolerability), and duration of treatment response at 12 weeks of home versus office-based narrowband ultraviolet B phototherapy for treating plaque or guttate psoriasis. Results showed that office-based phototherapy is superior to home treatment.

Yet phototherapy has several barriers, e.g., inconvenience and insurance coverage. Additional research to investigate the effect of phototherapy on cardiovascular risk is needed.

References
TNF Antagonists With and Without Methotrexate; Indications, Risks, and Limitations

Lars Iversen, MD, DMSc, Former IPC Board Member
Aarhus University Hospital, Aarhus, Denmark

In clinical trials, a combination of adalimumab with methotrexate (MTX) showed that significantly more patients achieved PASI 75 at week five. Gastrointestinal complaints were more common when adding methotrexate with adalimumab; however, both groups had the same infections. The benefit of concomitant use of methotrexate with TNF inhibitors include less antibody formation, better efficacy, and longer drug survival. The risk of the combination includes increased immune suppression, infection, and increased risk of cancer.

Combination treatment of TNF inhibitors and MTX can be considered in individual patients. For dermatologists, no data support the systematic use of TNF inhibitors in combination with MTX (different from rheumatology). If methotrexate is added, it should be started before or at the initiation of treatment with the TNF inhibitors.

References

IL-17 and IL-23 Antagonists
Kenneth Gordon, MD, IPC Councilor
Medical College of Wisconsin, Wisconsin, United States

To create optimal systemic therapy, we need to
1. find the optimal target and deactivate strongly;
2. design a molecule that has a persistent effect;
3. impact on special areas and comorbid conditions, e.g., nail and psoriatic arthritis; and
4. limit the cross-reactivity to provide the smallest impact on the generalized immune system [safety].

P19 Versus IL-17 Inhibition:
IL-23 [P19] inhibition partially attenuates IL-17 production, but “basal” levels are maintained. Other cytokines can synergize with low-concentration IL-17. IL-17 antibodies fully block IL-17 signaling. Thus, IL-17 direct antagonism will likely completely shut down feed-forward keratinocyte response. IL-23 (P19) specifically switches nonpathogenic/regulatory Th17 cells to pathogenic IL-17 producers (in mice).

Both IL-17 blockers and IL-23 blockers usually can maintain PASI 90 responses through two years with persistent efficacy. Regarding special areas, bimekizumab is more effective in nail psoriasis than secukinumab. Whether these classes of biologics will be able to inhibit the development of psoriatic arthritis is still a topic of research.
Several clinical trials studied the efficacy and safety of tofacitinib (an oral Janus kinase inhibitor) in treating psoriasis. Tofacitinib failed to gain regulatory approval in the United States for psoriasis, and clinical development of JAK1-3 inhibitors for psoriasis has largely been abandoned.

Generally, inhibiting the JAK-STAT pathway blocks IL-23, IL-22, and IFN. This is an effective method for treating psoriasis. Targeted TYK2 inhibitors have good efficacy, and allosteric inhibitors have favorable safety profiles in managing psoriasis. Further development of JAK inhibitors and allostatic TYK2 inhibitors can be promising.
New Drugs in the Pipeline
Bruce Strober, MD, PhD, IPC Vice President/President-Elect
Central Connecticut Dermatology, Connecticut, United States

Dr. Bruce Strober showed some updates about psoriasis treatment. A new study showed the efficacy and safety of apremilast in pediatric patients with moderate to severe psoriasis. A randomized, double-blind, placebo-controlled trial showed the efficacy of apremilast for patients with moderate to severe genital psoriasis.

Next comes the “oral” biologics. Studies introduced:
1. Phase 1c proof-of-concept study of DC-806, an oral IL-17A inhibitor, for adult patients with mild to moderate psoriasis; and
2. An oral therapeutic peptide that selectively targets IL-23 receptor.