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Drug allergies and hypersensitivity reactions are becoming more common as the population ages and multimorbidity increases

Q1 How has practicing in a wide range of healthcare systems, including the US, Europe, and Singapore, shaped the way you approach skin conditions, and are there any perspectives or practices from those experiences you think could add value here in the US?

All three are highly advanced healthcare systems, but they are organized very differently. For example, in Switzerland, the state decides pricing for medication, so we know how much a medication will cost. In Singapore, when I prescribed drugs, I saw the pricing on my computer, which was interesting and certainly helpful for discussions with the patients about alternatives and their affordability. In the US, that is a little bit more difficult, because the individual drug pricing is variable and not very transparent. However, with increasingly limited resources and strain on the healthcare system worldwide, access to treatments and medications is restricted because of constantly increasing healthcare costs. Switzerland has a mandatory health insurance, and everybody is insured, including a federal insurance for professional diseases and accidents. This is a very useful and important backup for patients with occupational allergies, where all the medical evaluations and changes in the workplace and profession are financially supported. Working across these very different systems and in different dermatology departments has reinforced for me that dermatology in the US needs to integrate allergic skin disease more fully, especially in the emerging area of drug allergies and hypersensitivities. Many of these are delayed-type reactions, and both allergists and dermatologists should be trained to diagnose and manage these complex, highly variable disorders.

In practice, dermatologists are often the first to recognize delayed-type reactions, which makes close collaboration between dermatology and allergy essential. Specialized training in skin diagnosis and testing is crucial in both fields. As treatments become more targeted, making the right diagnosis before starting therapy becomes even more important, so we can avoid expensive and ineffective treatment trials with biologics.

I'm a member of the American Contact Dermatitis Society (ACDS), and patch testing remains an important tool, but it only addresses contact dermatitis. Drug allergies, especially delayed-type reactions, are still underdiagnosed in dermatology and only partially addressed in allergy, leaving a real gap. To diagnose complex, often severe drug reactions properly, we need stronger diagnostic capabilities, including the ability to perform both immediate- and delayed-type testing in the same clinic. We also need continued progress in *in vitro* testing, particularly for drug allergies.

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and multimorbidity increases. Most patients who come to a clinic or hospital already have some kind of drug reaction documented in the electronic health record. For that reason, dermato-allergology should have a much stronger place in the training of future allergists and dermatologists.

Q2 Your research spans contact dermatitis, skin-barrier immunology, nerve receptors, and chronic itch. Can you give some examples where doctors are still missing signals that a skin problem is pointing to something bigger going on in the body?

One of the unique strengths of dermatology is that we can learn an enormous amount simply by looking at the skin and examining it carefully. From the beginning of my training, I learned that observation and touch can be extraordinarily valuable in a multidisciplinary setting, whether we are helping identify autoimmune disease, cancer, allergy, or another systemic process.

That clinical skill has become even more important in the era of targeted therapy. In the past, prednisone improved many inflammatory conditions. Today, we have far more targeted treatments, which is a major advance because they can reduce side effects. But precision therapy requires precision diagnosis. We need to determine which biologic is truly appropriate and what the best path forward is for each patient.

As the population ages, treatment regimens become more complex, and patients take more medications at the same time, I believe we will see more drug reactions and drug allergies, not fewer. Dermatology will therefore continue to play a crucial multidisciplinary role, especially when the skin is the first visible sign that something larger is happening in the body.

Q3 Where do doctors most often go wrong in diagnosing contact dermatitis, and what should clinicians across specialties watch out for when a reaction isn't behaving as expected?

A classic problem is the patient with dermatitis whose presentation could represent atopic dermatitis or allergic contact dermatitis. Histology cannot reliably distinguish the two, and clinically, they can look very similar. A patient may appear to have atopic dermatitis, receive a biologic, and improve only partially. Then the question becomes: Is the biologic failing, or is something else contributing? Very often, the answer is an undiagnosed contact allergy superimposed on underlying atopic dermatitis. That has to be identified through patch testing and addressed with careful counseling on allergen avoidance.

In many cases, management is a combination of identifying the allergen, helping the patient avoid it, and treating the atopic dermatitis itself. A large proportion of patients likely fall into this mixed category.

Another common error, especially outside dermatology, is to mistake eczema or an allergic reaction for an infection. There are often clinical clues that distinguish bacterial infection or cellulitis from eczema and allergic contact dermatitis, but recognizing them requires training in skin morphology and careful history-taking. The skin often reacts in similar ways, yet small differences in lesion appearance and patient history can lead us to the correct diagnosis. Itching indicates more of an allergic reaction, and pain points more towards infection. Combining all those skills is the art of an experienced clinician, and they will remain essential even as AI becomes more integrated into practice.

Q4 How has our understanding of itch and skin neurology evolved, and what treatment possibilities do you think are still being overlooked?

We have come a long way in our understanding of itch, and the interactions between skin, immune, and nervous systems are particularly important in itch disorders. There are now more studies, more treatment options, and more opportunities to reduce the burden of skin disease at a lower cost and with fewer side effects. One area that may deserve renewed emphasis is topical therapy for localized skin disorders, rather than defaulting too quickly to systemic treatment.

We are only beginning to understand how central the skin is to the two-way interaction between the immune system and the nervous system. As the body's largest organ, the skin can both reflect and influence what is happening elsewhere. Recent research also suggests that the skin has its own circadian rhythm. Cytokine expression in the skin differs between morning and evening, which may help explain why itching worsens at night in certain conditions. It also means that some cytokine studies could be misleading if we do not account for the time of day when biopsies are taken.

The skin is not only our largest barrier organ; it is also a highly sophisticated peripheral sensory and immune interface. We have identified an intricate sensory system in the skin, particularly in keratinocytes, including light, olfactory, taste, and pain/itch receptors, along with cytokines and neurotransmitters expressed in the skin. Skin cells can release cytokines and neuropeptides/transmitters; they not only shape local immune response, but also affect sensory signaling.

We still have much to learn about these peripheral interactions. Clinically, I would like to see more emphasis on localized, non-systemic treatments in dermatology. They have lost some ground, partly for financial reasons, but when only a limited area of skin is involved, we should ask whether it makes sense to treat the whole body rather than the affected area.

Q5 Do you think simple treatment approaches are an area that needs more attention or research? What aspects do you think clinicians and researchers should be looking at more closely?

Yes. If the issue is allergic contact dermatitis, the first step is to identify the allergen and avoid it. Today, we have helpful tools such as the ACDS (Milwaukee, Wisconsin, USA) and SkinSAFE (SkinSAFE Products Inc., Phoenix, Arizona, USA), which can guide patients toward safer products.

I tend to prefer simple formulations with as few additives as possible. Less is more. We do not always need expensive ingredients or complicated regimens.

That does not mean systemic therapy has no place. If 50% to 60% of the body surface is involved, we now have effective medications and should use them appropriately. But when the disease is limited to a smaller area, I believe we should place more emphasis on topical approaches that carry fewer systemic side effects and drug interactions.

Q6 As you look at the field today, which emerging allergens or exposure patterns do you believe clinicians should be paying much closer attention to, and why?

Patch-test panels should evolve continuously, and they do. I review my standard panel every year to decide which allergens remain important and which have become less relevant.

One substance I am seeing more often is propolis, a bee-derived product used as a "natural" disinfectant and increasingly found in natural cosmetics. The question is whether it is primarily an irritant or a true allergen. In my practice, I am seeing more genuine allergic reactions to it, so it is something clinicians should watch closely.

More broadly, it is important to follow the American Contact Dermatitis Society's Allergen of the Year and the exposure patterns it highlights.

Q7 Across your research, where do you think dermatology is closest to a meaningful breakthrough in diagnosis or treatment, and what would that change look like for patients and clinicians in practice?

I think dermatology is closest to a meaningful breakthrough in drug allergy evaluation. Our current research places strong emphasis on combining results from *in vivo* skin tests with future *in vitro* testing, especially for delayed-type drug reactions, so we can distinguish true drug eruptions from microbial exanthema or other immunologic disorders, including graft-versus-host disease. Moreover, all our efforts have to concentrate on identifying the specific drug responsible.

At the same time, new imaging methods and AI-assisted analysis are likely to change how dermatology is practiced. In underserved areas, telemedicine and supportive AI could significantly expand diagnostic support in allergology and dermatology, improve prevention, and strengthen early detection of skin cancer.

We also need more objective ways to evaluate what we see clinically. We want to know precisely how lesions change over time, how extensive the inflammation is, and what biological processes are driving it, and then correlate those findings with objective clinical data and molecular evaluation.

In one hair-growth study in Singapore, for example, we used the subjective Hamilton scale as one measure, but it did not reveal much. When we added objective measurements, such as hair papilla length, hair follicle length, and papilla size, clear biological pathways began to emerge.

Modern molecular medicine, including single-cell analysis, proteomics, lipidomics, transcriptomics, and metabolomics, will open new horizons in research, diagnosis, and treatment. But for those highly precise tools to be clinically meaningful, they must be paired with equally precise, objective clinical measurements and outcomes, including variations in circadian rhythm in skin expression patterns and organ-specific differences. Moreover, we should work in the future to develop meaningful organotypic skin culture models, to study toxicity, efficacy, particularly for cosmetics, but also for any product that can affect skin integrity. These models are human-specific and can reduce or avoid animal experiments for skin applications.