Topic 2 Translational aspects in pathobiology of AD: Targeting molecular Pathway

Scientific Panelist: Professor Thomas Bieber, MD

Community Panelist: Dr Catherine Besner Morin

Comments Regarding Key points for: Dermatology Trainees

- Dr. Besner Morin commented that the presentation touched on some less well-known aspects such as the fact that the innate immune system is triggered which results in an adaptive immune response etc., as well as that the cycle may be different with age, different ethnic backgrounds and the cytokine profile may be different. She noted that because AD is an autoimmune disease, it does not necessarily need an external factor to be triggered
- Dr. Besner-Morin also commented that if treatments are used early in the cytokine cascade, there is more potential for side effects as more is being blocked. Emerging therapies such as amlitelimab have the potential to stop the progression of the disease, keeping it at a mild level of severity or preventing its development in those genetically predisposed to AD.
- Dr. Asiniwasis commented that in indigenous patients she sees a lot of nummular and sometimes lichenoid morphologies (unpublished). Dr. Prajapati agreed, saying that he sees more nummular and lichenoid morphologies in Asian patients as well. Dr. Asai also agreed and Dr. Asiniwasis commented that this would be an interesting publication. She added that these patients still fit criteria for Hanifin and Rajka and UKWP for AD (typical pattern, etc.).
- Dr. Charles Lynde commented that this is noted in other richly pigmented patients.
- Dr. Prajapati commented that he is seeing more herpes simplex virus (HSV) in AD patients who are Asian than is reported in the literature, especially those on advanced systemic therapies.
- Dr. Purdy commented that she has noticed the same experience with her Mi'kmaq patients in Nova Scotia, in whom the nummular pattern is much more common.
- Dr. Jack agreed, adding that with nummular overlap, a study of staph prevalence would be relevant, to complement genetics and immunophenotype.
- Dr. Asai asked her colleagues if they thought it was the pigmentation itself that increased the risk, or whatever goes with/inherited with pigmentation.
- Dr. Jack replied that this was an interesting question, and she would predict that immunophenotype (types of cells) would relate to genetics more than pigment
- Dr. Asai agreed and said that the discussion made her wonder if anyone has looked at that in itself (eu/pheomelanin as immunomodulator or barrier effect).
- Dr. Joseph agreed, saying that it would be nice to have data contrasting HSV, staph (and even the microbiome) with different morphologies follicular, nummular, lichenification etc. but thought that it was likely largely tied to immunophenotype.

Comments Regarding Key points for: General Practitioners

- Dr. Besner-Morin commented that they take for granted that everyone understands the atopic march, but after asking some GP colleagues she thinks this may not be true.
- Dr. Lynde was surprised that the concept of atopic march was still in question.

Comments Regarding Key points for: Adults and Adolescents

- Dr. Besner-Morin commented that some environmental factors are within the control of the patient and therefore important to inform patients on these.

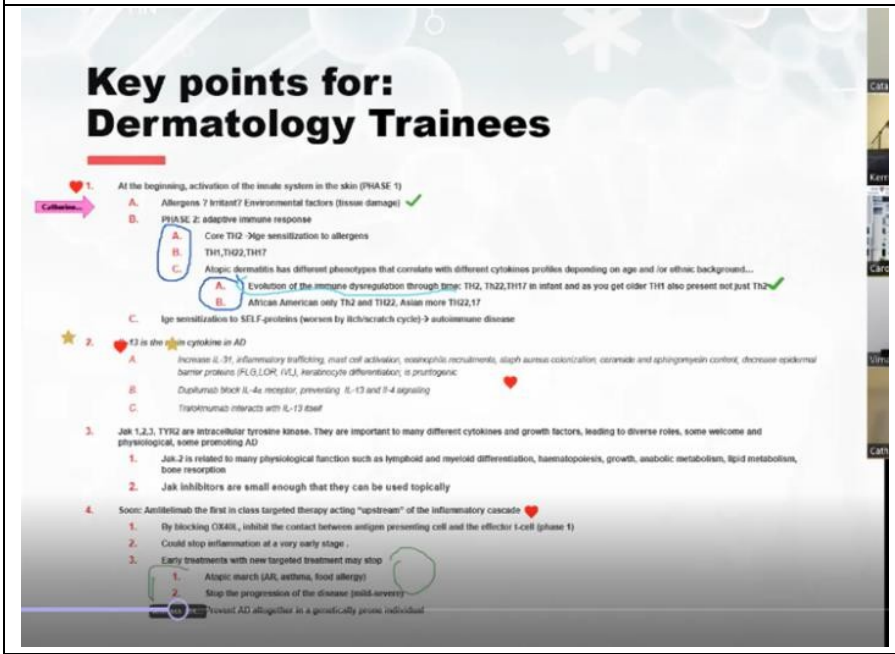
Comments Regarding What Added Information is Needed

- Dr. Besner-Morin commented, in addition to the bullets on the slide:
  - Dermatology trainees need to understand the upstream mechanisms
  - Regarding "eczema school", she noted that patients need a whole lecture to empower the patient and help them understand that AD will not go away with just emollients and understanding what treatment treats what aspect of AD pathophysiology can help.

Comments Regarding Three Points Most Relevant to my Practice/Points Relevant to my Practice Not Found and/or Irrelevant info

- Dr. Besner-Morin commented that more information is needed on whether certain treatments would work better in specific ethnic populations due to cytokine profiles.
- Participants agreed with Dr. Adam commenting that adult onset AD patients never fulfill Hanifin criteria

Key Takeaway: Vote Via Annotation

Slide	Results
	1. Phase 2 adaptive immune response-**7 votes** 2. IL-13 is the skin cytokine in AD-**4 votes** 3. Amlitelimab/early treatment may stop the atopic march-**2 votes**

Overall Comments

- Dr. Adam commented that he was unsure whether it was appropriate to include emerging treatments (e.g., amlitelimab**)** in the Phase 3 stage as drugs have failed in Phase 3 trials. He suggested not getting into detail about unlicensed therapies, but only addressing them conceptually. He added that the GPs/FPs he speaks to have no interest in learning about IL-13 etc. and suggested that discussing topics at this level will lose their interest, though it is definitely appropriate for dermatology trainees.

- Dr. Lynde agreed, saying that there is not a one size fits all approach for the three populations (Trainees, GPs and patients). He stated that dermatology trainees should have more pathophysiology information, but GPs/FPs are not interested and are only interested in what new drugs are available, as are patients. He also agreed that the presentation should not include drugs that may not make it to the market.
- Dr. Prajapati commented that what he thought was very interesting was that while it was established that IL-13 is the main cytokine, the role of IL-4 in AD is often up in the air and there are different views on its role.
- Dr. Asai commented that she always gets nervous picking a "boss cytokine" because this not yet definitively established and more information is needed. Drs. Purdy and Joseph agreed.
- Dr. Besner-Morin commented that she asked colleagues and came to the conclusion that GPs are not interested in cytokines, saying that this lecture is more for dermatology trainees than any other group. She added that the slide deck that she would build for GPs and patients would include 1) Immune dysregulation: what treatment where, 2) atopic march/dysregulation and 3) genetics. She added that the lecture is well done, but it is too dense and goes into immune dysregulation too soon.
- Dr. Asiniwasis agreed, saying that it as not a good idea to lump all into one, as the audiences are too different with different levels of understanding. Dr. Asai also agreed saying that this was especially true as the barrier is what patients can action themselves and it would be worthwhile to spend a lot of practical time there.
- Dr. Asiniwasis suggested adding a visual for resident on the cytokine pathway.
- Dr. Purdy commented that the nitty gritty doesn't matter directly to patients but she interprets the relevance in what she may consider when she sees patients and selects therapeutics. She added that this was a very basic science-directed talk but there were some clinical correlations with therapeutics
- Regarding what was missing, participants suggested that the core mutations should be included.
- Regarding whether this was relevant to their patients, Dr. Adam suggested that it was not as it was too detailed. Dr. Asai agreed that the details were not important to patients but the key point identified were: to explain to patients that they flared because they got a cold, used a fragranced soap or because their family is atopic. In this aspect she felty the presentation had relevance for patients. She added that the presentation was helpful for choosing therapeutics.
- Dr. Iannattone agreed, commenting that Gen Zs have a higher level of health literacy.
- Dr. Joseph agreed, stating that patients get a lot of competing information from their neighbors, naturopaths etc. and dermatologists need to compete with this information influx. She stated that greater patient understanding can help increase adherence as well as guide risk tolerance for advanced therapies.
- Dr. Lynde suggested that it provides patients with hope, saying that AD patients have suffered and telling patients that clinicians understand the pathophysiology of AD gives them hope and increases compliance.
- Dr. Purdy commented that she has recently taken over patch testing locally and the number of patients that have no clue as to why they are having it done and how it may relate to their clinical presentation is alarming.

- Dr. Besner Morin stated that she would not show patients the presentation because it is not "digested " enough for them but stated that pathophysiology is important for the patient, saying that it empowers them. She remarked that patients need another slide deck altogether and that the main point should be regarding skin barrier and inflammation. She added that having knowledge helps them protect them against misinformation.
- Dr. Asiniwasis commented that the question has become "How is it best translated from the granular basic stage to the patient level for understanding for what they deem important/their values?"
- Dr. Jack agreed with Dr. Purdy that information around the role of patch testing needs to be addressed.
- Dr. Asai commented that she once had a patient tell her "I think you just explained my whole life" when she gave them a summary of the pathophysiology. Dr. Jack had a similar experience with a patient .