Psoriasis is one of the most confounding diseases in dermatology. It can have severe, crippling manifestations that significantly impact patients’ quality of life—and yet, there are many patients who exhibit only a milder form of the disease for their entire lives. Some patients have serious systemic manifestations, including psoriatic arthritis and cardiovascular disease, but it is not entirely clear why only a subset of patients develop these complications.

Alice Gottlieb, MD, PhD has been at the forefront of psoriasis research and her bench and clinical discoveries have been foundational in describing the interactions of the epidermis and T-cells, thus unveiling the importance of the immune system in active disease. This ushered in biologics for the treatment of psoriasis, which has been transformative. Yet, according to Dr. Gottlieb, there are still significant research and knowledge gaps that need to be addressed to further improve the well-being of many patients.

William Ju, MD: What are the biggest scientific hurdles to further clinical breakthroughs for psoriasis?

Alice Gottlieb, MD, PhD: Probably the first one is funding, especially at the NIH level and the dearth of scientists at the basic science level or even translational level willing to commit their career to psoriasis research, because the funding environment is so challenging.

There are knowledge gaps in the basic science and on the therapeutic side, ranging from the theoretical to the practical. For instance, what starts psoriasis? There are a number of genes that we know are turned on and off with treatment, but we do not know if there are psoriasis-specific genes. We have not defined what causes psoriasis genetically. For example, why does one identical twin develop psoriasis and the other one does not? We also do not have a clear picture of why some patients experience systemic complications and others do not. We have no way of predicting those complications or progression of the disease in general, and thus who may benefit from earlier intervention.

As an example of the theoretical and basic science aspects, there is a belief that the innate immune system is activated as an initiating step in psoriasis, which ultimately leads to Th-17 T-cells pathogenically making IL-17A and other inflammatory mediators downstream. If this is correct, knowledge of what happens in this pathway is still lacking. However, getting all the way upstream to the inciting mechanisms is an area of tremendous opportunity for new treatments and possible cures.

I’m discussing the basic science here, but there are also practical hurdles in advancing psoriasis care. At the moment, we do not have highly efficacious topical agents that can be used chronically, which is a large treatment gap and another opportunity in research.

Dr. Ju: You’ve spoken about knowledge gaps in understanding how psoriasis will affect patients along the spectrum of severity, as well as in who will manifest systemic complications. How does that impact the treatment and research realms?

Dr. Gottlieb: Those are actually pretty significant gaps, as well. There are some patients who have severe manifestations from the initial onset. There are others whose disease begins more subtly, but we can’t predict who will progress, and who live with a low-grade psoriasis their entire lives. Similarly, we don’t know who will develop psoriatic arthritis. We just do not have good risk profiles, and the same is true for many of the other serious systemic comorbidities, such as cardiovascular disease. What that ultimately means is that there is currently no mechanism to initiate potentially preventive treatments early in the course to stave off later complications. Being able to have effective early interventions would have implications not just for patients, but also for the healthcare system at large. Psoriasis can be very debilitating, and if we could save people from developing the more crippling aspects of this disease, we could have tremendous impact.

I would add that we will benefit from additional and better outcome measures to determine the efficacy, quality, and value of various treatments in both clinical trials and in clinical practice.

Dr. Ju: With all of the treatment gaps you identified, what is your sense of the landscape in the next decade for psoriasis?

Dr. Gottlieb: There is no doubt we have made strides in the understanding and treatment of psoriasis, but I would say 10 years from now, psoriasis may still be a chronic illness rather than a curable illness. I do think, however, that finding a cure is a reasonable eventual goal, especially as we learn more about the genetic underpinnings of psoriasis. In my view, whether we are able to find a cure will hinge on whether we are able to understand what happens at the very early stages of psoriasis, and that will likely require more research in the pediatric and young adult population.