The Growing Pains of Changing Times for Acne and Rosacea Pathophysiology: Where Will It All End Up?

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It is interesting to observe the changes in dermatology that have occurred over the last 1 to 2 decades, especially as major advances in basic science research techniques have rapidly expanded our current understanding of the pathophysiology of many disease states—psoriasis, psoriatic arthritis, atopic dermatitis, alopecia areata, vitiligo, hidradenitis suppurativa, and lichen planus.[1] Although acne vulgaris (AV) and rosacea do not make front-page news quite as often as some of these other aforementioned disease states in the pathophysiology arena, advances still have been made in understanding the pathophysiology, albeit slower and often less popularized in dermatology publications and other forms of media.[2-4]

If one looks at our fundamental understanding of AV, most of the discussion over multiple decades has been driven by new treatments and in some cases new formulations and packaging differences with topical agents. Although we understood that adrenarche, a subsequent increase in androgen synthesis, and the ensuing sebocyte development with formation of sebum were prerequisites for the development of AV, the absence of therapeutic options to address these vital components of AV—especially US Food and Drug Administration (FDA)–approved therapies—resulted in limited discussion about this specific area.[5] Rather, the discussion was dominated by the notable role of *Propionibacterium acnes* (now called *Cutibacterium acnes*) in AV pathophysiology, as we had therapies such as benzoyl peroxide and antibiotics that improved AV in direct correlation with reductions in *P acnes*.[6] This was soon coupled with an advanced understanding of how to reduce follicular hyperkeratinization with the development of topical tretinoin, followed by 3 other topical retinoids over time—adapalene, tazarotene, and trifarotene. Over subsequent years, slowly emerging basic science developments and collective data reviews added to our understanding of AV and how different therapies appear to work, including the role of toll-like receptors, anti-inflammatory properties of tetracyclines, and inflammasomes.[7-9] Without a doubt, the availability of oral isotretinoin revolutionized AV therapy, especially in patients with severe refractory disease, with advanced formulations allowing for optimization of sustained remission without the need for high dietary fat intake.[10-12]

Progress in the pathophysiology of rosacea has been slower to develop, with the first true discussion of specific clinical presentations published after the new millennium.[13] This was followed by more advanced basic science and clinical research, which led to an improved ability to understand modes of action of various therapies and to correlate treatment selection with specific visible manifestations of rosacea, including incorporation of physical devices.[14-16] A newer perspective on evaluation and

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management of rosacea moved away from the "buckets" of rosacea subtypes to phenotypes observed at the time of clinical presentation.[17,18]

I could elaborate on research advancements with both diseases, but the bottom line is that information, developments, and current perspectives change over time. Keeping up is a challenge for all who study and practice dermatology. It is human nature to revert to what we already believe and do, which sometimes remains valid and other times is quite outdated and truly replaced by more optimal approaches. With AV and rosacea, progress is much slower in availability of newer agents. With AV, new agents have included topical dapsone, oral sarecycline, and topical clascoterone, with the latter being the first FDA-approved topical agent to mitigate the effects of androgens and sebum in both males and females. For rosacea, the 2 most recent FDA-approved therapies are minocycline foam and microencapsulated benzoyl peroxide. All of these therapies are proven to be effective for the modes of action and skin manifestations they specifically manage. Over the upcoming year, we are hoping to see the first triple-combination topical product come to market for AV, which will prompt our minds to consider if and how 3 established agents can work together to further augment treatment efficacy with favorable tolerability and safety.

Where will all of this end up? It is hard to say. We still have several other areas to tackle with both disease states, including establishing a well-substantiated understanding of the pathophysiologic role of the microbiome, sorting out the role of antibiotic use due to concerns about bacterial resistance, integration of FDA-approved physical devices in AV, and data on both diet and optimized skin care, to name a few.[19-21]

There is a lot on the plate to accomplish and digest. I have remained very involved in this subject matter for almost 3 decades and am still feeling the growing pains. Fortunately, the satisfaction of being part of a process so important to the lives of millions of patients makes this worth every moment. Stay tuned—more valuable information is to come.

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