

## Acne: New Concepts

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**E**merging concepts support a more serious view of acne vulgaris. Acne vulgaris is a chronic illness affecting individuals in the second (78.9% [398/504] of Korean teenagers aged 13–16 years)<sup>1</sup> to seventh decades of life.<sup>2</sup> The costs of acne are monetary, physical, and psychological. It is estimated that acne costs \$1 billion annually in the United States and individuals with acne experience extensive psychiatric morbidity (eg, anxiety, depression).<sup>1-7</sup> That being said, many manufacturers of prescription acne products are now addressing chronicity with long-term studies ( $\geq 52$  weeks), demonstrating that in the real world, acne does not permanently go away in 4, 8, or 12 weeks.

In the severe form, acne vulgaris is a systemic illness (eg, SAPHO [synovitis, acne, pustulosis, hyperostosis, and osteitis] syndrome).<sup>8</sup> It remains to be determined if severe acne vulgaris is its own autoinflammatory/autoimmune illness or part of the metabolic syndrome. As such, it should not surprise us that our severe chronic acne patients may develop thyroid disease or inflammatory bowel disease. Furthermore, dietary factors that promote insulin resistance also promote acne. In fact, perhaps we should be screening for thyroid disease and insulin resistance routinely in select patients. Here are the data in support of these statements.

### The Psychological Ramifications of Acne

As confirmed by studies published in the last 2 years across multiple countries, anxiety and depression are associated with having acne but are not limited by ethnicity, sex (teenaged boys have more acne but girls are more depressed with the disease),<sup>1,3,4</sup> or

age. Adults with acne also experience psychologic distress. Saitta et al<sup>5,6</sup> reviewed the presence of psychiatric comorbidities in acne patients in a 2-part series. In particular, they presented data on suicidal ideation and completion in acne patients.<sup>6</sup> (Part 2 is featured in this month's issue.<sup>6</sup>) It behooves us to remember that our patients with severe acne need screening for depression.

For teenagers in Japan and Korea, acne was associated with greater depression and poorer mental health inventory scores, especially in females. Prolonged illness, female sex, and severity were correlated with psychologic damage.<sup>1,3</sup> One retrospective study suggested that depression in acne is more prevalent for patients aged 36 to 64 years.<sup>2</sup> In a recent study, 57.5% (7/12) of adult males with acne vulgaris demonstrated depression, topping the incidence of depression in the psoriasis and vitiligo patients surveyed.<sup>7</sup>

### Acne is a Chronic Heritable Illness

Although it is estimated that 4 of 5 teenagers will get acne, 61.9% of acne patients in the United States are 18 years or older.<sup>6</sup> One cause of early-onset disease is genetically inherited acne. Many children with acne have parents with acne,<sup>10</sup> which may be linked to genetic polymorphisms in tumor necrosis factor  $\alpha$ .<sup>11</sup> The more family members with acne, the more likely a teenager is to develop acne<sup>12</sup>; however, the disease appears to be polygenic in nature.

Recently, a number of manufacturers have started to perform long-term studies of acne treatment. Topical agents with published safety and efficacy data for 52 weeks of usage include clindamycin phosphate 1.2%–tretinoin 0.025% gel,<sup>13</sup> adapalene gel 0.3%,<sup>14</sup> and dapsone gel 5%.<sup>15</sup> These studies highlight the realities of treating acne patients; acne may clear on therapy at 12 weeks, but if treatment is stopped, lesions soon recur due to disease chronicity. As such, long-term maintenance of topical agents is required for skin clarity to continue in most individuals.

### Factors Supporting Acne as an Autoimmune Versus Autoinflammatory Illness

The complexity of the nature of acne inflammation is beyond the scope of an editorial, but a brief

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overview is included. Despite the recent surge of late-night legal commercials, there have been scattered occasional reports of inflammatory bowel disease triggered by isotretinoin therapy since 1985.<sup>16</sup> Oral minocycline hypersensitivity can be associated with type 1 diabetes mellitus, thyroid disease, and generalized markers of autoimmunity.<sup>17</sup> Drug-induced lupus and hepatitis also are risks with prolonged minocycline usage.<sup>18,19</sup> The variety of agents used for systemic therapy for acne and the fact that multiple agents have been associated with autoimmunity in acne patients indicate that some forms of acne (eg, cystic), rather than oral medications, are associated with autoimmunity or autoinflammation. A recent study associated acne with an increased risk for thyroid disease in adult women,<sup>20</sup> and a recent study showed that 22% (20/90) of individuals with SAPHO syndrome have autoantibodies.<sup>8</sup> Identifying individuals with autoimmune susceptibility within the large pool of individuals with acne remains a challenge for the future.

### Factors Supporting Acne as a Form of Insulin Resistance

An article in this issue reviews the data on diet, obesity, and acne vulgaris.<sup>21</sup> Although the data are mixed, it is certainly clear that there is a subset of individuals with acne who have insulin resistance, and the high glycemic load diets eaten in the Western world likely exacerbate acne symptoms. Not every acne patient has insulin resistance, but individuals with a high body mass index may in fact benefit from low glycemic index diets and reduction in glycemic load to lose weight, to improve insulin sensitivity, and to reduce acne symptoms.<sup>22</sup> Although only females traditionally receive laboratory screening for endocrinopathy, overweight males certainly deserve review as potentially having insulin resistance. Larger-scale trials are needed to decide if universal screening for insulin resistance is necessary for acne patients or if limiting screening to heavier patients and those with signs of hyperandrogenism will be more cost effective.

### Conclusion

Acne vulgaris is not a minor illness of adolescence. It is a disease with extensive psychological morbidity and chronicity; disease can continue to affect adults through senescence. Recent data suggest that acne vulgaris may in fact signal other endocrinopathies and may relate to autoimmunity in both males and females, irrespective of the type of oral therapy. More attention needs to be placed on long-term therapy for acne and acne in the teenaged years as a potential identifier of individuals who can modify their lifestyle to prevent diabetes.

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