

ONLINE FIRST

Psoriasis and the Obesity Epidemic

The Effect of Weight Loss

MAN'S DESIRE TO CONTROL CHRONIC DISEASE inevitably turns to how diet could effect the disease state; we would purport that this notion is likely related to the common wisdom "you are what you eat." Since even before the now widely appreciated association between obesity and psoriasis, the effect of weight loss on the management of psoriasis has been under consideration. Soon after World War II, Simons¹ reported observations of 13 subjects with psoriasis who were imprisoned in Japanese starvation camps in Java. He noted that weight loss and disease severity were inconsistent in these persons. The more recent associations of psoriasis and obesity—increased risk of onset of psoriasis, more of the body surface affected with disease, increased risk of psoriatic arthritis (PsA), and increased cardiovascular risk—establish that obesity has a very negative impact on psoriasis.^{2,3} Furthermore, these associations are strongly supported by the often dramatic response of psoriasis and PsA to treatment with agents that target tumor necrosis factor (TNF) and the fact that TNF has a strong association with obesity: levels of TNF increase and decrease, respectively, with weight gain and weight loss.⁴

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The effect of weight loss on psoriasis severity has been explored through single case reports and small series of patients undergoing bariatric surgery.⁵ Variable responses were the common outcome. Rigorous clinical trials assessing psoriasis severity and weight loss are long overdue. In this issue of *JAMA Dermatology*, Jensen et al⁶ must be acknowledged for reporting the first prospective, randomized, clinical trial examining the effect of weight loss on Psoriasis Area Severity Index (PASI) in overweight patients with psoriasis. After 16 weeks, overweight patients with psoriasis who were restricted to a low-energy diet (n=30) lost significantly more weight and had a decrease in PASI by 2 units more than those in the control group (n=30). Furthermore, there were significant improvements ($P=.02$) in the self-reported Dermatology Life Quality Index (DLQI), reduced levels of insulin, and reduced levels of plasma glucose in those receiving the low-energy diet.

Although the results of this study are encouraging, one must consider the limitations when interpreting the data. It was likely difficult to enroll patients into a study requiring the very restricted diet, suggesting the possibil-

ity of selection bias. A larger study population without entry bias and a longer duration is needed to validate their results. Unexpected was the fact that a decrease in PASI was not statistically significant ($P=.06$): a change of 3 PASI units was predicted to provide sufficient power to demonstrate an association of weight loss with decreased severity of psoriasis. This degree of significance ($P=.06$) indicates that the study was underpowered. From the results, we presume that the significant change in DLQI and PASI moved in parallel, and if so, it would further support the notion that weight loss decreased psoriasis severity. A graphic representation depicting the correlation of DLQI and PASI at each time point could provide further evidence in support of the authors' conclusion. Furthermore, having an unblinded primary investigator for the PASI scoring could have introduced observer bias, but again the DLQI results serve to negate some of this concern.

This study is the first to our knowledge to report on psoriasis severity and weight loss, and it also emphasizes the already noted associations between them and what we know of the pathophysiologic characteristics of obesity and psoriasis. Obesity is characterized by a state of low-level inflammation, which is characterized by elevated levels of the master regulator, TNF. This supports the notion that in psoriasis, the interaction of TNF-induced immune and metabolic responses by adipocytes, macrophages, and T cells in the dermis and epidermis drive genetic aberrations that lead to the clinical expression of psoriasis and PsA.⁷ It follows that subjects with obesity and elevated levels of TNF, along with the genetic elements that predispose them to develop psoriasis, are at increased risk of developing psoriasis and PsA.

The present editorial and the article by Jensen et al⁶ point the way to further research on the association between obesity and psoriasis, which many believe are inextricably linked. Out of this research will come answers to many persistent questions:

1. Will weight loss reduce the disease severity of psoriasis and its cardiovascular implications?
2. How quickly can this reduction be appreciated?
3. What are the most objective means to assess this reduction?
4. What measures can be used to most effectively reduce body mass index (BMI) to normal levels in the obese patient?
5. Will cost be an issue, as has occurred with the dramatic improvements we have seen emerge as a result of new and more effective treatment for psoriasis and PsA?

6. Will general health, quality of life, and cost of health care improve as dramatically as expected with a halt to the obesity epidemic in those with psoriatic disease?

7. Which is the better approach, to achieve normal BMI or to strive for below-normal BMI? Recently it was shown that an underweight cohort (BMI <21.0) in a large prospective trial was protected from developing psoriasis (relative risk, 0.81).³

8. Can education get us through this? If so, to whom should the education be directed, the patient or the health care professional?

9. Can we find the end of the rainbow, a program that causes psoriasis to go away or improve while the patient sheds weight at the same time?

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Published Online: May 29, 2013. doi:10.1001/jamadermatol.2013.4512

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Conflict of Interest Disclosures: None reported.

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