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Psoriasis, diabetes, and obesity: weighing the evidence

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Psoriasis is a common, chronic, inflammatory disease that is associated with an increased risk of cardiovascular, metabolic, and renal disease in a manner that varies with psoriasis severity and is often independent of traditional risk factors[1,2]. The clinical significance of these associations is emphasized by premature death, particularly in patients with more severe psoriasis were excess mortality is comparable to that seen in rheumatoid arthritis treated with disease modifying medications[3]. The association of psoriasis with diabetes and obesity has been extensively studied and has been the subject of numerous meta-analyses which clearly establish an association of psoriasis both with obesity and diabetes. Lønnberg and colleagues have added new insights into these associations by studying monozygotic and dizygotic twins with and without psoriasis. The main findings were that psoriasis is associated with diabetes independent of sex, age, smoking, and body mass index (BMI) (OR 1.53, 1.03–2.27) and that increases in BMI are associated with increasing odds of twins reporting a diagnosis of psoriasis. Similar findings were reported for patients receiving a hospital diagnosis of psoriasis. The unique twin design allowed the investigators to identify a genetic correlation between psoriasis and BMI of 0.12 (0.08–0.19). A similar magnitude of genetic correlation between psoriasis and type 2 diabetes 0.13 (−0.06–0.31) was observed but this finding was not statistically significant (the prevalence of diabetes in this sample was quite low yielding only 6 psoriasis patients with diabetes). The magnitude of the genetic correlation is modest and similar to what has been reported for age at menarche and type 2 diabetes (−0.13)[4]. Nevertheless, these findings are consistent with emerging genetic evidence linking psoriasis to diabetes. For example, genetic variation at IL12B, IL23R and IL23A has an influence not only on the risk for psoriasis, but also on disease severity and type 2 diabetes mellitus[5]. Other researchers have suggested a role for *CDKAL1* in conferring susceptibility for psoriasis as well as diabetes[6].

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Only a few studies have actually examined incidence (risk) of diabetes while adjusting for major confounding variables (such as body mass index and hypertension) and only a subset of these were able to evaluate effects of psoriasis severity on the association with psoriasis (using treatment patterns)[7,8]. These studies suggest that psoriasis is associated with an increased risk of diabetes independent of major risk factors in a manner the correlates with psoriasis severity. While the design used by Lønnberg does not address diabetes risk (i.e., incidence) or directly evaluate a psoriasis severity dose-response relationship with diabetes, its careful control for BMI, which most large population based studies are unable to capture, adds to the weight of evidence suggesting psoriasis is a risk factor for diabetes. Additional population-based studies have similarly noted an increased prevalence of insulin resistance in patients with psoriasis in a manner that varies positively with increasing body surface area affected by psoriasis and independent of major risk factors such as BMI, hypertension, and dyslipidemia[9]. While inflammation is often invoked as a mechanistic link to insulin resistance, simultaneous analysis of psoriasis and rheumatoid arthritis patients adjusting for major risk factors only demonstrated an increased risk for diabetes in patients with psoriatic disease[10]. The risk of diabetic complications in patients with psoriasis (compared to diabetic patients without psoriasis) is rather unexplored but emerging studies suggest that micro and macrovascular complications are more common in psoriasis patients with diabetes, that psoriasis is associated with worse HbA1c, and that increasing body surface area affected by psoriasis is associated with an increased risk for diabetic complications[11–13].

These epidemiological findings have clear implications for clinical practice. The dermatologist is on the front line in educating psoriasis patients about their disease, treatment options, and risks of comorbidities. The United States Preventative Services Task Force (updated 2015) recommends screening for abnormal blood glucose as part of cardiovascular risk assessment in adults aged 40 to 70 years who are overweight or obese. Moreover, the American Diabetes Association (2016) recommends testing (with fasting plasma glucose, or oral glucose tolerance test, or A1C) for asymptomatic adults of *any age* who are overweight or obese and who have one or more additional risk factors for diabetes. Given the association of psoriasis, particularly more severe disease, and increases in BMI, most of our patients would be recommended for diabetes screening based on standard recommendations. Importantly, level A evidence (i.e., derived from RCTs) indicates that lifestyle changes and pharmacologic interventions (i.e., metformin) can decrease the risk of diabetes in patients at high risk (i.e., impaired fasting glucose, impaired glucose tolerance, or both). Therefore, dermatologists have the opportunity to educate patients and initiate appropriate screenings (or refer the patient to primary care) which can result in better health outcomes through evidence-based interventions. Moreover, obesity and diabetes have important implications for the management of psoriasis. For example, psoriasis patients with diabetes or who are overweight are at increased risk for developing severe liver fibrosis when being treated with methotrexate. The effectiveness of psoriasis treatments, particularly non-weight based TNF inhibitors, are negatively affected by increased BMI. Weight loss can result in improved responsiveness to psoriasis and psoriatic arthritis treatments and improvements in psoriasis overall[14]. Despite these compelling reasons to identify diabetes in patients with psoriasis, a major practice gap remains in dermatologist screening and counseling of patients for cardiovascular risk factors[15]. The weight of evidence linking

psoriasis to cardiometabolic disease continues to increase, tipping the scale towards changing our clinical practice.

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