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Does systemic treatment of psoriasis reduce the risk of comorbidities?

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In this issue of the *BJD*, Neil Korman has published an interesting review article presenting the evidence supporting psoriasis as a systemic disease. He also discusses new psoriasis treatment paradigms, which may potentially reduce the effects of systemic inflammation and consequently prevent or reverse comorbidities.[1] Optimizing patient outcomes beyond clearing the skin, such as reducing the risk of cardiovascular diseases, is crucially relevant for our clinical practice. In this commentary, the pathogenesis behind the comorbidities and whether systemic treatment of psoriasis could reduce the risk of comorbidities by damping systemic inflammation will be discussed.

The pathogenesis behind the comorbidities in psoriasis is complex and could be based on several factors including shared genetic susceptibility, such as in the case of metabolic comorbidities including diabetes and obesity.[2] A recent mendelian randomization study, which is a genetic method to determine causal relationships while minimizing confounding variables, showed that obesity contributes to the pathogenesis of psoriasis, whereas there is no evidence of a causal effect of psoriasis on body mass index.[3] The psychological burden of moderate-to-severe psoriasis could be remarkably high in a way that it could favour anxiety, depression and suicide ideation, as well as unhealthy lifestyle behaviours such as heavy drinking, alcoholism and smoking. Moreover, psoriasis shares inflammatory pathways with comorbidities. Inflammatory mediators released from psoriatic lesions include tumour necrosis factor (TNF)-α, interferon (IFN)-α, IFN-γ, interleukin (IL)-1, IL-6, IL-17 and IL-22. These may have systemic effects leading to insulin resistance, endothelial dysfunction and cardiovascular disease.[4]

Psoriatic and atherosclerotic plaques have similar underlying immunological mechanisms, in which T helper (Th)1 and Th17 cells release TNF-α, IFN-γ, IL-17 and IL-22, which contribute to keratinocyte activation and hyperproliferation, as well as to atherosclerotic plaque growth, instability and rupture.[5] Obesity is associated with a low-grade chronic systemic inflammation because it drives metabolic and immunological pathways including Th17 cell differentiation, which play a pivotal role in psoriasis pathogenesis. Then, obesity causes biomechanical stress on tendons and entheses that could act as a possible trigger factor for enthesitis and for development of psoriatic arthritis. The progression from psoriasis to comorbidities including cardiovascular diseases such as myocardial infarction and stroke has been described in the literature under the term of 'the psoriatic march'. Could the psoriatic march be arrested?

There are some arguments in favour of the hypothesis that treating psoriasis with systemic agents could prevent cardiovascular disease. In a recent meta-analysis in patients with psoriasis and psoriatic arthritis, systemic therapy was found to decrease significantly the risk of all cardiovascular events [risk ratio 0·75, 95% confidence interval (CI) 0·63–0·91].[6] In two different observational studies, the use of TNF-α inhibitors for psoriasis was associated with a significant reduction in myocardial risk compared with treatment with topical agents (odds ratio 0·5, 95% CI 0·32–0·79) or phototherapy (hazard ratio 0·77, 95% CI 0·6–0·9). In a randomized, double-blind clinical trial, adalimumab reduced key markers of inflammation, including glycoprotein acetylation, compared with phototherapy, with no effect on glucose metabolism or vascular inflammation.[7] The protective cardiovascular effects may not be exclusive to TNF-α inhibitors. Indeed, the CARIMA study indicates that secukinumab might have a beneficial effect on cardiovascular risk by improving endothelial function and other cardiovascular disease parameters over 52 weeks.[8]

This educational review by Neil Korman is a timely summary of the current knowledge on the new psoriasis treatment paradigms that may potentially reduce the effects of systemic inflammation, and on the evidence that biologic treatment may prevent or reverse inflammatory damage associated with psoriasis comorbidities.

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Conflicts of interest: P.G. has been a consultant and/or speaker for Abbott, Almirall, Celgene, Eli Lilly, Janssen, LEO Pharma, Merck Sharp & Dohme, Novartis, Pfizer and Sandoz.

WHO can decrease indoor tanning?

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There are dozens and dozens of papers on indoor tanning, many of which show an association with an increased risk of skin cancer. In 2009, the International Agency for Research on Cancer, which makes up part of the World Health Organization (WHO), officially classified indoor tanning as a human carcinogen. In recent decades, awareness and regulation of indoor tanning have been increasing.[1] The question is – does a statement from the WHO and the subsequent public health efforts actually decrease the number of people who use indoor tanning?

In this issue of the BJD, Rodriguez-Acevedo *et al.* report a systematic review and meta-analysis on the prevalence of indoor tanning, with a focus on data collected since the WHO classification in 2009.[2] Included papers were from Australia, Europe and North America. They found that since 2009, 9·7% of adolescents and 33·4% of adults report ever exposure and 6·7% of adolescents and 12·5% of adults report past-year exposure to indoor tanning. When they evaluated changes over time, they found decreases in prevalence for both adults and adolescents. Indoor tanning decreased in both countries with and without indoor tanning regulations, but in adjusted analyses, the presence of regulations was statistically significantly associated with decreased indoor tanning. The authors also compared results from a previous meta-analysis (data collected from 2007 to 2012)[3] to their own meta-analysis (data collected from 2013 to 2018), and again found lower past-year exposure in the more recent years.

The authors additionally report on the number of countries and states/provinces with regulations restricting indoor tanning: in 2011, one country had an outright ban and eight countries and nine states/provinces had age limits.[1] In 2019, three countries have an outright ban and 24 countries and 38 states/provinces have age limits.

This is a well-performed and well-reported systematic review and meta-analysis that provides a much-needed update to older summative research on indoor tanning behaviours. However, it does have limitations. There was a substantial amount of heterogeneity, which means that there was variation or inconsistency between the studies that may be due to more than chance alone. In other words, substantial heterogeneity indicates a meta-analysis might be combining apples and oranges (studies that are quite different and should be meta-analysed cautiously), rather than apples and apples. This is not unexpected in a meta-analysis that includes a variety of countries, years and study designs, and the way to combat this is to use random-effects statistics (which the authors did) and to explore potential explanations for the heterogeneity (which the authors also did, examining subgroups of studies).

The take-home? Indoor tanning exposure appears to be decreasing fairly substantially. This paper provides evidence that statements from the WHO and the related public health efforts, particularly legislation, may be part of the driver of this change. However, this new analysis still shows that approximately one in three adults and one in 10 adolescents have ever been exposed to indoor tanning, and one in eight adults and one in 15 adolescents have been exposed in the past year. There is certainly more work to be done.

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'COre SUBgroup SETs (COSUBSET)' initiative is needed

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