



**Welcome to
this issue of
Pso Pscience from
PAPAA!**

**Over the past two-
decades there has
been a revolution in
our understanding of
psoriasis and psoriatic
arthritis, both in terms
of basic immunology,
disease mechanisms
and therapeutics.**

**This newsletter is
designed to provide a
summary of recently
published research.**

**Of course, it's never a
good time to have
psoriasis or psoriatic
arthritis,
but if you have to
have it, there has
never been a better
time!**

Dr David Ashton MD PhD

Stress and psoriasis flares

It is well recognised that stress tends to make psoriasis worse, but recent research provides compelling evidence that it may actually trigger relapses.

In this fascinating study, 25-immunodeficient mice, with human psoriatic skin grafts, were treated initially with topical steroids to completely heal the skin lesions. The mice were then exposed to sound stress or no-sound, for a period of 24-hours, and the recurrence of psoriasis tracked over the following 14-days.

Remarkably, sonic stress led to a relapse of psoriasis in all mice with human skin grafts within 14 days. This included increasing thickness of the epidermis, with inflammation and cellular proliferation – all key elements of psoriasis.

At the same time, the research team tested the efficacy of an anti-nausea drug, aprepitant, which is usually used in chemotherapy. Aprepitant prevented relapse of psoriasis in 80% of cases and normalised most inflammatory markers.



Comment:

The study underscores the complex link between the nervous system and the immune response in psoriasis. It also offers a potentially effective treatment for stress-induced psoriasis flares, though much more work is needed before aprepitant could be routinely used in this context.

Reference:

Presentation at the European Academy of Dermatology and Venereology (EADV) Congress, September 2024.

Childhood obesity and psoriasis

A remarkable study from Korea shows how childhood obesity can contribute to the development of common immune-mediated skin diseases (IMSDs), such as alopecia areata, atopic dermatitis, and psoriasis. These conditions have a significant detrimental effect on the quality of life for both the children and their families. Childhood obesity rates have surged in recent years, compounded by the impact of the Covid-19 pandemic and lockdown.



Numerous studies have examined the association between obesity and skin disease in children, but they have mostly been based around a particular point in time. Very few studies have followed children over an extended period to see how their body weight affects the development of these skin conditions.

This study is remarkable in that it used a national database to investigate the relationship between obesity or changes in body weight and the development of skin disease, in more than 2 million Korean children, followed between 2009 and 2020.

The results demonstrated that childhood obesity is associated with an increased risk for all skin diseases – alopecia, dermatitis, and psoriasis. However, the strongest association for weight and weight-change, was for atopic dermatitis. Children who gained weight (normal to overweight) had a higher risk of developing atopic dermatitis than children who maintained their normal weight, and children who lost weight (overweight to normal) had a lower risk of developing atopic dermatitis than children who maintained their overweight.

Comment:

This study unambiguously shows that obesity is a significant predictor of skin diseases – including psoriasis – in childhood, though the precise mechanisms involved remain unclear. Targeted interventions, primarily through physical activity and nutrition, are fundamental to preventing obesity in childhood and thus reducing the risk of IMSDs.

Reference: Seong Rae Kim, Seong-Joon Koh, Hyunsun Park. Childhood Obesity, Weight Change, and Pediatric Immune-Mediated Skin Diseases. *Journal of Investigative Dermatology*, 2024, 144:1975-1984.



Two in one

Numerous studies confirm that obesity is a risk factor for psoriasis, with rates of obesity and overweight being significantly higher in psoriatic patients. It is also well recognised that weight reduction may improve the severity of psoriasis in overweight individuals. This is because both obesity and psoriasis have a common origin, i.e. inflammation.

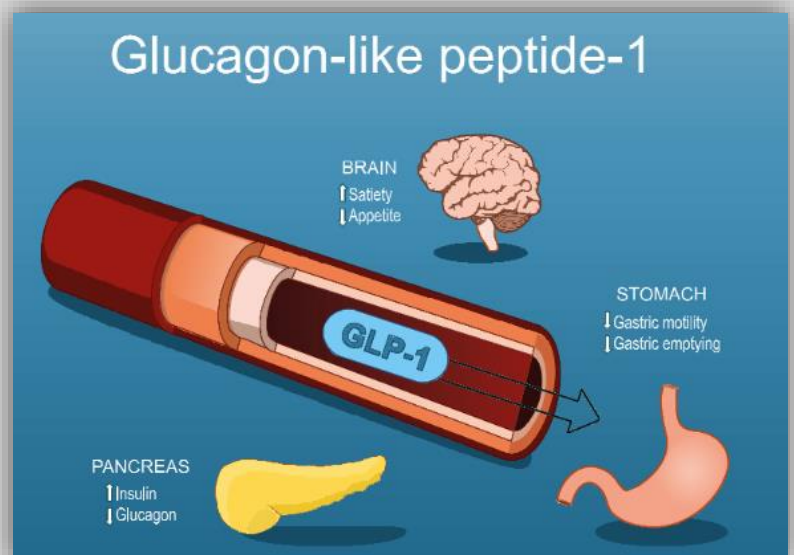


Over the last few years, the advent of a new generation of weight loss drugs, such as semaglutide (Ozempic) has ushered in a revolution in treatment for the overweight and obese. The latest addition to this rapidly expanding family of medications, is tirzepatide (Zepbound or Mounjaro). Given the observation that weight loss improves psoriasis, it might be expected that these drugs would have a similar effect, through a reduction in obesity-associated inflammation. A recent study showed exactly this. A 73-year-old male patient with diabetes and severe plaque psoriasis,

underwent treatment with semaglutide. Not only did he lose weight and improve his diabetes, but there was dramatic improvement in his psoriasis.

However, along with the growing list of weight-loss drugs, we continue to see new biologic treatments for psoriasis – the latest being ixekizumab (Taltz). So, the obvious next step in the treatment of overweight or obese psoriatic patients, would seem to be a combination of tirzepatide and ixekizumab. And this is precisely what is happening.

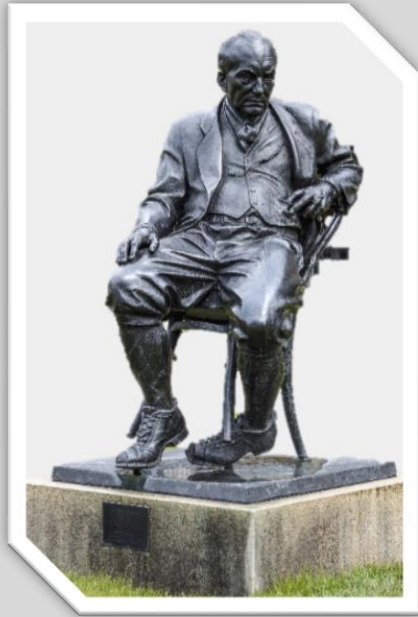
Eli Lilly & Co. is set to begin recruiting for trials to test a combination of tirzepatide (Zepbound) with ixekizumab (Taltz) and, according to reports, is also exploring combination studies with Zepbound in inflammatory bowel disease.



Comment

The combination of an effective weight-loss treatment, with a biologic in the management of overweight patients with psoriasis, would be a game-changer. Whilst drug trials invariably take longer than anticipated, it is reasonable to think that this new combination therapy could be available in the next two or three years.

Nabokov and psoriasis



Vladimir Nabokov (1899-1977) was one of the greatest writers of the twentieth century, best known for his novel *Lolita* which was published in France in 1954.

Many reports refer to the fact that Nabokov suffered with chronic psoriasis, but few have had much to say about its psychological impact on the writer. However, a research letter published some years ago in the *British Journal of Dermatology*, has suggested that the condition caused Nabokov considerable distress.

Researchers analysed Nabokov's letters to his wife written between 1923 until his death in 1977 and found that psoriasis was a recurring theme. He complains that his skin was extremely itchy, causing severe insomnia and a depressed mood – a common complaint among psoriasis sufferers. He writes:

"I don't sleep at night because of its furious itchy – and this greatly affects my mood". And: "Sometimes I simply thought I was losing my mind".

He also complains about stigmatization and worries about his personal hygiene. He says that he has *'...constant thoughts about my bloody underwear,and the scales pouring down on the carpet'*.

The researchers speculate that a particularly severe flare of psoriasis that occurred during Nabokov's time in France may have been linked to the stress of being unfaithful to his wife. Adultery is a theme addressed in Nabokov's work, notably in novels such as *Lolita* and *Invitation to a Beheading*. So severe though his psoriasis clearly was, it evidently did not get in the way of his infidelity.

Comment

This fascinating report paints a vivid picture of a man tormented by his psoriasis and struggling to deal with his anxiety and sense of shame. Of course, at the time when Nabokov was writing and long after his death, psycho-dermatology - the management of psychosocial impact of skin conditions - did not even exist as a discipline. Treatments for psoriasis have come a very long way since Nabokov's time, as has the availability of psychological support. Nevertheless, Nabokov's experiences remain a powerful testimony even today and serve to highlight how important it is for patients to feel in control of their condition and fully engaged with both the physical and psychological aspects of their treatment.

Reference:

Rousset L, Halioua B. The psychological impact of psoriasis on Vladimir Nabokov *British Journal of Dermatology*, 2019; 80, 925–926.

PAPAA is a UK patient-centred charity that supports and helps people affected by psoriasis and psoriatic arthritis. For full details about PAPAA and how to contact us go to: <https://www.papaa.org/contact-us/>