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PROFILE OF STEROID-INDUCED SKIN DISORDERS: FROM CUTANEOUS DAMAGE TO SYSTEMIC DISEASE - A COMPREHENSIVE REVIEW OF PATHOPHYSIOLOGY, NOVEL THERAPIES, AND CURATIVE STRATEGIES

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Abstract

Corticosteroids are widely prescribed dermatological medications, with an estimated 13.8 million prescriptions annually in the United States. Growing awareness of their insidious adverse effects has prompted official safety warnings from Health Canada in 2022 and the United Kingdom's Medicines and Healthcare products Regulatory Agency in 2021. This review provides a comprehensive analysis of the clinical spectrum of steroid-induced skin disease, ranging from local damage to systemic repercussions, and evaluates emerging data on steroid-sparing and potentially curative therapies. We examined large population-based studies, recent clinical trials, and mechanistic research published between 2020 and 2026. Key findings confirm that corticosteroid-associated cutaneous injury encompasses skin atrophy, topical steroid withdrawal syndrome (TSW), and systemic complications such as adrenal suppression, osteoporosis, and metabolic disturbances. Important mechanistic insights uncovered that NAD+ overproduction underlies the pathogenesis of TSW, while clinical trial evidence demonstrates that pimecrolimus can effectively reverse steroid-induced atrophy. Steroid-sparing therapeutic strategies have the potential to modify disease trajectories. The accumulated evidence mandates a fundamental shift in clinical practice: from sustained corticosteroid use toward early detection of steroid toxicity and timely implementation of steroid-sparing interventions. Targeted therapies designed to control excessive NAD+ production and repair atrophic skin now offer the promise of disease-modifying and curative treatments. The shift away from prolonged steroid use is now supported by robust mechanistic and clinical data, enabling a proactive approach. This strategy not only mitigates toxicity but also addresses the underlying pathophysiology, offering patients a path to lasting remission and improved outcomes.

1. Introduction

Corticosteroids are the mainstay of contemporary dermatological practice, with their potent anti-inflammatory, immunosuppressive, and vasoconstrictive actions transforming the treatment of a wide range of skin conditions such as atopic dermatitis, psoriasis and eczema. But the same properties that make these agents

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effective also cause a range of side effects, giving rise to the "corticosteroid paradox" (DiRuggiero & DiRuggiero, 2025)(Jain, Mohapatra, Mohanty, Jena, & Behera, 2020). These drugs are effective at controlling skin inflammation through modulation of nuclear factor-kappa B (NF-κB) and down-regulation of pro-inflammatory cytokines, but chronic or inappropriate use results in epidermal atrophy, fibroblast suppression, collagen breakdown, systemic absorption and endocrinologic side effects. The dilemma is further complicated by the lack of a completely "safe" mode of administration, potency, or duration of treatment (Hajar et al., 2015)(Parajuli, Paudel, Poudyal, & Pokhrel, 2018).

Topical hydrocortisone entered the market in the 1950s, and was the first steroid to really revolutionise dermatology, allowing unprecedented control over inflammatory skin conditions. In the 1960s and 1970s, more potent fluorinated steroids became available, giving dermatologists some new weapons, but also new side effects(Ravindran, Prabhu, & Nayak, 2021). It took Kligman and Frosch until 1979 to first notice what they termed "steroid addiction", a nasty withdrawal reaction with red, burning itchy skin immediately after steroid withdrawal. For the next 40 years this went mostly unnoticed, misdiagnosed as a simple flare of the underlying condition rather than the steroid-induced condition itself(Ravindran et al., 2021). It wasn't until the past 10 years, with the help of patients speaking up and sharing their experiences on social media, that topical steroid withdrawal (TSW) has been recognised as a real, proper syndrome requiring research (Brookes et al., 2023).

Every year, 13.8 million prescriptions for topical steroids are filled in the US, and that's just the prescriptions - we can also buy millions more over the counter in weaker formulations. Estimates of how widespread steroid-related skin issues are can be difficult to estimate as they might not be recognised, they could be confused with other skin conditions, or they may not be well documented(Paulmann & Mockenhaupt, 2015). But large population studies are beginning to give us a better picture of broader risks. For instance, a large Danish study of more than 700,000 users of topical steroids showed using strong steroids was associated with the development of osteoporosis, particularly once people reach a threshold cumulative dose (200 grams of mometasone furoate or equivalent). And another study from Taiwan, which examined almost 130,000 cases of osteoporosis, found the risk of fractures could be more than doubled (in women under age 50) depending on the strength of the steroid(Paulmann & Mockenhaupt, 2015). As for metabolism, pooling data from Denmark and the UK from more than 170,000 users found the risk of developing type 2 diabetes increases by around 27% when someone uses topical steroids, and increases with higher doses and duration of use (DiRuggiero & DiRuggiero, 2025; Sheikh et al., 2025).

The growing evidence of subcutaneous and systemic toxicity has led to regulatory statements in several countries. In 2021, the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) released a detailed public assessment report on topical steroid withdrawal reactions, recognising TSW as a known adverse event and recommending a need for clinician and patient awareness (MHRA, 2021)(Yasmeen J Bhat, Manzoor, & Qayoom, 2011). Meanwhile, in 2022, Health Canada released a safety brief on the risk of topical withdrawal reactions, noting that these may occur notwithstanding correct use of medium- or high-potency corticosteroids on sensitive sites like the face and genitalia (Health Canada, 2022). Most recently, in March 2025, the National Institutes of Health in the United States announced the development of diagnostic criteria for TSW, based on mechanistic studies that found high levels of the metabolite NAD+ play a significant role in the syndrome (NIH, 2025). These messages from the regulators signal a growing awareness that steroid-induced skin conditions are under-recognised public health problems(Choonhakarn, Limpawattana, & Chaowattanapanit, 2016).

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2. Pharmacology and Mechanisms of Steroid-Induced Damage

2.1 Percutaneous Absorption and Bioavailability

Transdermal corticosteroid pharmacodynamics is entirely dependent upon the capacity to penetrate the stratum corneum and gain access to viable epidermal and dermal target cells. Molecular weight is a crucial factor in the percutaneous absorption of drugs, with the well-known "500 Dalton rule" dictating that molecules with greater molecular weights (Da) have significantly lower skin penetration (Bos &Meinardi, 2000). The molecular weights of most topical corticosteroids range from 360 to 540 Daltons, which is close to the upper limit for efficient skin penetration. Clobetasol propionate (467 Da), betamethasone dipropionate (504 Da) and hydrocortisone (362 Da) lie at or close to this threshold, accounting for their variable but generally good absorption. Other factors, in addition to molecular weight, affect systemic absorption after topical administration(Rathi & Kumrah, 2011). Skin site has a profound impact, with facial and genital skin being 4-10 times more permeable than the forearm because of thinner stratum corneum and higher blood flow. Occlusion, whether deliberate (e.g. dressings) or unintentional (e.g. skin folds and intertriginous regions), increases absorption up to ten-fold by locking in water and increasing stratum corneum hydration. The vehicle also has a significant impact; ointments typically increase penetration compared with creams or lotions because they are more occlusive and have better penetration into the skin due to their lipid content. Similarly, the status of the skin barrier also plays a critical role; lesional skin, particularly in areas of inflammation, allows much greater absorption of corticosteroids than normal skin, accounting for the increased risk of systemic effects among patients with active dermatoses (DiRuggiero & DiRuggiero, 2025)(Prabhu, Patel, Kikkeri, & Athanikar, 2022). Age is also a critical factor in absorption; infants and the elderly show increased percutaneous penetration because of variations in skin thickness, hydration and blood flow.

2.2 Mechanisms of Cutaneous Damage

Skin atrophy is the major adverse effect of topical corticosteroids, as a result of their inhibitory effect on fibroblasts and extracellular matrix. Suppression of fibroblast growth and down-regulation of collagen type I and type III expression through negative regulation of transforming growth factor-beta activity and procollagen gene transcription are key effects of corticosteroids. This leads to gradual dermal thinning, loss of supportive connective tissue, and the clinical signs of skin atrophy, striae and thinning (Schoepe et al., 2006). Atrophy is dose- and potency-dependent and can be detected after only two to three weeks with continuous use of a superpotent corticosteroid(Marzano, Borghi, Stadnicki, Crosti, & Cugno, 2014). A second mechanism of injury is barrier disruption. The anti-proliferative and anti-differentiative effects of corticosteroids on keratinocytes lead to diminished synthesis of stratum corneum (skin surface) lipids, ceramides and filaggrin. This disrupts the mechanical strength and antimicrobial barrier, leaving the skin vulnerable to infection and dehydration. This impairment in barrier function establishes a vicious cycle of needing to apply corticosteroid to the damaged skin to suppress symptoms, thereby causing further damage. Impacts on vascular integrity are a major component of steroid-induced appearance(Makurina & Cherneda, 2024). Corticosteroids produce vasoconstriction by inhibiting vasodilatory prostaglandins and nitric oxide, leading to blanching. But long-term application results in endothelial damage, perivascular collagen fibrosis, and telangiectasia formation by destroying the supporting structures of the blood vessels. These widened superficial vessels are clearly visible, especially on the face and may remain visible for some time after ceasing corticosteroid use (Hengge et al., 2006).

2.3 Mechanisms of Systemic Toxicity

Topical corticosteroids can cause systemic toxicity when a sufficient amount of the drug enters the systemic circulation to suppress the hypothalamic-pituitary-adrenal (HPA) axis. Corticosteroids exert negative feedback on the

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hypothalamus and pituitary, resulting in decreased corticotropin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) release and subsequent suppression of cortisol release by the adrenal cortex(Barnes, Kaya, & Rollason, 2015). Prolonged HPA axis suppression can result in adrenal insufficiency, with symptoms of fatigue, hypotension and altered stress responses. Crucially, a review of 3,753 patients found no safe threshold for HPA axis suppression, with effects observed with all potencies, routes of administration and duration of use (Hajar et al., 2015). The metabolic effects of corticosteroids occur due to their binding to glucocorticoid receptors on hepatocytes, adipocytes and myocytes. In the liver, corticosteroids promote gluconeogenesis through the induction of phosphoenolpyruvate carboxykinase and glucose-6-phosphatase, which increase glucose production. And in fat and muscle, they promote insulin resistance via impaired glucose transporter type 4 translocation and insulin signaling, ultimately raising the risk of incident diabetes with an adjusted odds ratio of 1.27 in large-scale population studies (DiRuggiero & DiRuggiero, 2025).

In terms of bone metabolism, corticosteroids suppress osteoblast differentiation and function, and induce osteoclast activation and survival via increased receptor activator of nuclear factor-kappa B ligand expression(Pokhrel). This imbalance of bone formation and resorption results in bone degradation, with adjusted odds ratios for osteoporosis of 2.2 to 3.4 for different levels and types of corticosteroids, as determined through population studies (Sheikh et al., 2025). Figure 1 is showing Schematic representation of the vicious cycle wherein topical corticosteroid use leads to cutaneous atrophy and barrier disruption, prompting increased application frequency, which exacerbates damage and may precipitate topical steroid withdrawal syndrome upon cessation.

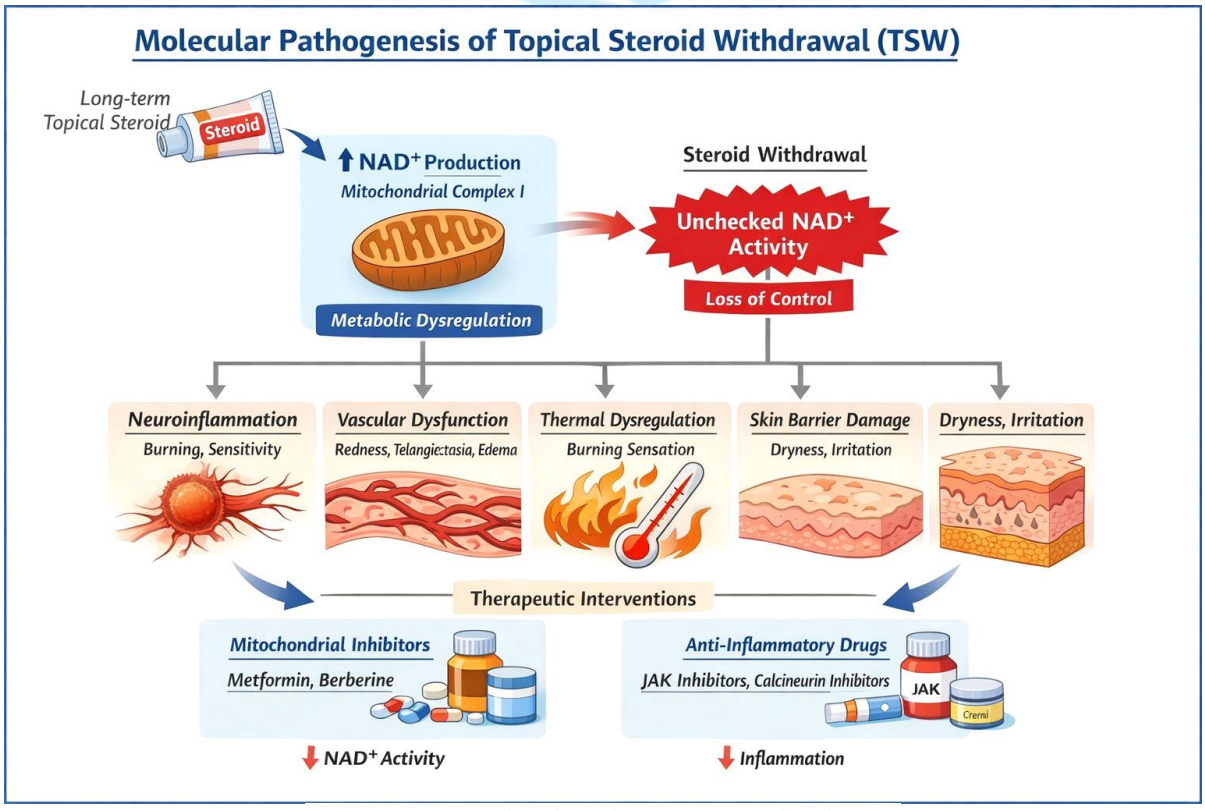

Figure 1: *Steroid-Induced Damage Feedback Loop*

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3. Clinical Spectrum of Cutaneous Adverse Effects

3.1 Atrophic Changes

The most common cutaneous side effect of topical corticosteroids is skin atrophy, caused by the corticosteroid-induced suppression of fibroblast proliferation and collagen synthesis. Atrophy presents with thinness, translucency and a crinkly, cigarette-paper-like appearance of skin, especially on the face, flexures and genitalia, where drug absorption is highest (Hengge et al., 2006). Striae distensae (stretch marks) are linear atrophic bands that occur when body areas are stretched while the skin is exposed to corticosteroid, most commonly on the thighs, abdomen and breasts(Noor et al., 2023). Telangiectasia, or widened superficial veins, manifest as fine red lines due to loss of perivascular supporting structures and damage to endothelial cells. When the damage is more severe, spontaneous bruising (purpura) and stellate pseudoscars result, characterised by white, star-shaped depressions after minor trauma. Severe atrophy can result in ulceration over bony areas. What's more, corticosteroids delay wound healing by inhibiting the inflammatory processes, fibroblast proliferation and angiogenesis, causing delayed re-epithelialization and a higher risk of infection (Schoepe et al., 2006)(Chua-Aguilera, Möller, & Yawalkar, 2017).

3.2 Inflammatory and Infectious Complications

Topical corticosteroids are commonly associated with paradoxical inflammatory reactions. Perioral dermatitis is characterised by papules, pustules and scaling around the mouth, nasolabial folds and periocular regions, and is often preceded by long-term use of medium- to high-potency corticosteroids on the face(Hengge, Ruzicka, Schwartz, & Cork, 2006). Steroid-induced acne and rosacea are characterised by inflammatory papules and pustules on an erythematous base, and may be accompanied by facial flushing and telangiectasia (Hengge et al., 2006). Most ominous is the masking of infections. Tinea incognito results from the misdiagnosis and treatment of a dermatophyte infection with corticosteroids, which mask the typical inflammatory response, but which permit the fungus to grow unchecked. Likewise, bacterial and viral infections can go undetected and the immunosuppressive actions of corticosteroids render the skin more vulnerable to secondary bacterial infections, such as Staphylococcus aureus superinfection(Bierzynska et al., 2017).

3.3 Pigmentary and Adnexal Changes

The effects of corticosteroids on skin colour can be a mixed blessing. At times, they can darken your skin, either in response to past inflammation or by directly stimulating the pigment-making cells to switch into overdrive(Petri, Genovese, Engle, & Hochberg, 1991). But other times they can make your skin less pigmented by suppressing these cells, particularly with stronger, fluorinated corticosteroids. And strangely, corticosteroids can cause hair to grow where you apply them, and if they enter your bloodstream, they can cause widespread hairiness in those who are susceptible. And to make matters more complicated, these medications make your skin more sensitive to the sun, so you're more prone to sun damage(Swarnalatha, Vinutha, Sonia, Babu, & SanthiLakshmi). This can accelerate thinning of the skin, and can cause wrinkles to appear earlier than usual (Sheikh et al., 2025). Table is showing summary of common cutaneous adverse effects associated with topical corticosteroid use, stratified by anatomical location and corticosteroid potency class.

Table 1: ***Classification of Cutaneous Adverse Effects by Anatomical Site and Steroid Potency***

Anatomical Site	Common Adverse Effects	Most Frequently Implicated Potency	Onset Timeline	Management Considerations
Face	Perioral dermatitis, rosacea, atrophy,	Medium-High (inappropriate	2-12 months	Immediate discontinuation,

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	telangiectasia	use)		topical calcineurin inhibitors
Flexural areas	Striae, atrophy, secondary infection	Medium-High	3-6 months	Potency reduction, barrier repair
Genital region	Atrophy, telangiectasia, striae	Any (enhanced absorption)	1-3 months	Lowest possible potency, limited duration
Trunk/Extremities	Atrophy, striae, purpura	High-Very High	6-24 months	Intermittent dosing, steroid-sparing agents
Intertriginous areas	Maceration, secondary infection, atrophy	Medium-High	2-6 months	Avoid high potency, non-occlusive vehicles

4. Systemic Complications from Topical Corticosteroid Use

4.1 Endocrine Complications

One of the biggest concerns about using topical corticosteroids is that they can in turn suppress your body's own hormone system, the hypothalamic-pituitary-adrenal (HPA) axis, and result in adrenal insufficiency. People think that creams and ointments are all skin deep, but the reality is that a substantial amount of the corticosteroid can be absorbed into your bloodstream. And this can cause your body to stop producing its own cortisol in all the wrong ways(Tinkle et al., 2017). A recent review of 74 studies with nearly 3,800 patients showed that this suppression can occur regardless of the strength of the steroid, form it comes in, or duration of use there really is no safe dose or duration. This turns on its head the old adage that low-potency cream or short-term use is completely safe. Adrenal insufficiency symptoms can be nasty fatigue, weakness, nausea, vomiting, low blood pressure, and in the worst instances, a potentially life-threatening adrenal crisis that can be triggered by stress, surgery or illness(Sen et al., 2021). Often people don't know until they're pushed to the limit, which could be when disaster strikes.

To determine who might be at risk of HPA axis suppression, doctors have identified some tell-tale signs. If more than 60 percent of the body's surface is treated with corticosteroids, there's a greater risk because the larger the surface area, the greater the absorption. A blood test for cortisol levels below 7 micrograms per deciliter is a good indicator of adrenal depression, but the gold standard is a test using a drug called cosyntropin. Children are particularly vulnerable in this situation because they have a higher surface area to body weight ratio, their livers are immature and they have thinner skin, which absorbs more of the drug(Rahayu & Emily, 2021). More seriously, we can get Cushing syndrome, which presents with a moon-shaped face, fat around the waist, muscle weakness and other metabolic disturbances. A case series looked at 43 cases of Cushing syndrome from topical steroids. Notably, this condition may develop rapidly - some patients developed symptoms after just nine days of using potent steroids, over a large area, with an airtight bandage(Brinkhaus, Lindner, Schuppan, & Hahn, 2000). Most people recover after they stop using the steroid, although it can take a long time for their hormone system to return to normal, so doctors watch cortisol levels during this time.

One of the cruelest side effects of steroid use in children is that they can suppress growth. When the HPA axis is constantly suppressed, it not only decreases the release of growth hormone but also the growth of cells at the growth plates that form bones. This can lead to them growing more slowly than normal when kids require topical steroids for a prolonged time to treat severe conditions such as eczema. The thing to watch out for here is that this may go unnoticed until the child is significantly shorter than their peers. The good news is that when the steroids are stopped or their dose is lowered, most children will catch up on their growth, but it may be too late and the effect may be severe (Wood Heickman et al., 2017).

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4.2 Metabolic Disturbances

When you apply topical steroids, they may not just affect your skin, they could mess with your entire metabolism by activating glucocorticoid receptors all over your body. In the liver, they kick up sugar production by turning on enzymes that make sugar, such as phosphoenolpyruvate carboxykinase and glucose-6-phosphatase(Sirikonda, Kolli, Rao, & Srujana, 2019). And in muscles and fat cells, they play havoc with insulin by fiddling with the transport of glucose into cells and the insulin signalling inside them. The end result? Your blood glucose levels increase and you're more likely to get diabetes. One study from Denmark examined more than 115,000 people who had just developed type 2 diabetes, and found that people who used topical steroids had a 27% increased risk of diabetes compared to those who didn't use steroids. And the more steroid they used, the greater the risk(Nikolova et al., 2013). Another study from the UK, involving almost 55,000 cases of diabetes, showed the same rise in risk. This means that the risk associated with potent topical steroids is the same as low doses of oral steroid use, and that ointments and creams are not necessarily safe for your metabolism.

Weight gain and fat redistribution are yet another side effect of corticosteroids. These medications promote the maturation of fat cells (particularly in the abdomen and chest) and increase insulin resistance, which promotes fat storage. So this can result in weight gain in the waist, a "moon face" and even the dreaded "buffalo hump" in the back of the neck, which are all lookalikes of what you see with oral steroids, but not always as bad(Patel & Marfatia, 2008). The bad news is these changes can last for months after you stop the drug, which can be emotionally wearing and make people less likely to follow their medication regimen.

4.3 Ophthalmic Complications

Corticosteroids can damage the eyes in a couple of different ways. A big one is cataracts, which occur when corticosteroids bind to receptors in the lens, causing proteins to stick together and give the lens a milky appearance(Kaka, Elshanawany, Abdelaziz, & Abd Almohsen, 2025). This is the classic posterior subcapsular cataracts, but sometimes other types occur as well. A large UK study examined more than 15,000 cases of cataracts and found those using topical corticosteroids were 43% more likely to get cataracts than those not using them. The more frequently and the longer you use these steroids, the higher the risk. The risk is lower than with oral steroids or steroids injected into the eye area, but high enough that doctors recommend eye checks if you're on steroids for a long time.

Steroid-induced glaucoma (and high eye pressure) can catch you by surprise when the corticosteroids interfere with the drainage system of your eye (the trabecular meshwork). The clog slows the drainage of fluid in your eye, increasing the pressure - sometimes just weeks after you start taking steroids(Akshaya & Bhattacharya, 2016). And this pressure can cause irreversible damage to the optic nerve, and vision loss. This is more likely with higher-strength steroids, taking them for a prolonged period, and putting the medications near the eyes, where they can easily be absorbed. The good news? Unlike normal open-angle glaucoma, steroid-induced glaucoma often gets better after you stop taking the drug - although some people may still require eye drops to lower the eye's pressure (Robert & Aydin, 2021).

4.4 Musculoskeletal Effects

The hardest side effect of topical corticosteroids to deal with is bone health, which causes osteoporosis and fractures. The steroids upset the balance between bone-forming and bone-destroying cells, causing bone degradation(Nadh & Nirupama, 2022). In other words, they skew the balance to favour bone degradation and weaken your bones, increasing the risk of fractures.

There is definitely a connection between using potent or very potent corticosteroids and the development of osteoporosis, particularly after you have used about 200 grams of mometasone furoate (or the equivalent) over time. One large study from Taiwan included almost 130,000

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people with osteoporosis, and another large Danish registry of over 700,000 adults who used topical steroids found that the risk of osteoporosis increases with stronger steroids. It looked like women under 50 were the worst affected. And for more serious fractures, such as those of the hip, spine and forearm, the risk was even higher - between 2.6 and 3.4 times for people who had used topical steroids for five years or longer(Yasmeen Jabeen Bhat & Bashir, 2022). And it's not just adults; there have been reports of children as young as 11 showing significant bone density declines after being on potent topical steroids for a long time. Table 2 is showing the major population-based studies reporting systemic effects of topical corticosteroids, showing study design, sample sizes and estimates of effect.

Table 2: ***Systemic Adverse Effects of Topical Corticosteroids: Evidence from Large Population Studies***

Systemic Effect	Study Population	Sample Size	Effect Estimate	Potency Relationship	Key Findings
Adrenal Insufficiency	Systematic review (2014)	3,753 patients	No risk-free threshold identified	All potencies	No administration route, regimen, or duration eliminated risk
New-Onset Type 2 Diabetes	Danish registry (2007-2012)	115,218 cases	aOR 1.27	Dose-response	Risk range overlaps with oral corticosteroids
New-Onset Type 2 Diabetes	UK database (2007-2015)	54,944 cases	aOR 1.27	Dose-response	Confirmed Danish findings
Osteoporosis	Danish registry (2003-2017)	723,251 users	Direct association	Potent/very potent only	Minimum 200g mometasone furoate equivalent
Osteoporosis	Taiwan database (2017-2020)	129,682 cases	aOR 2.2-3.4	All potencies	Higher risk in women <50 years
Major Osteoporotic Fracture	Taiwan database (2017-2020)	34,999 cases	aOR 2.6-3.4	All potencies	Five+ years exposure
Cataract	UK GPRD	15,479 cases	OR 1.43	Not specified	Lower risk than systemic/ocular routes

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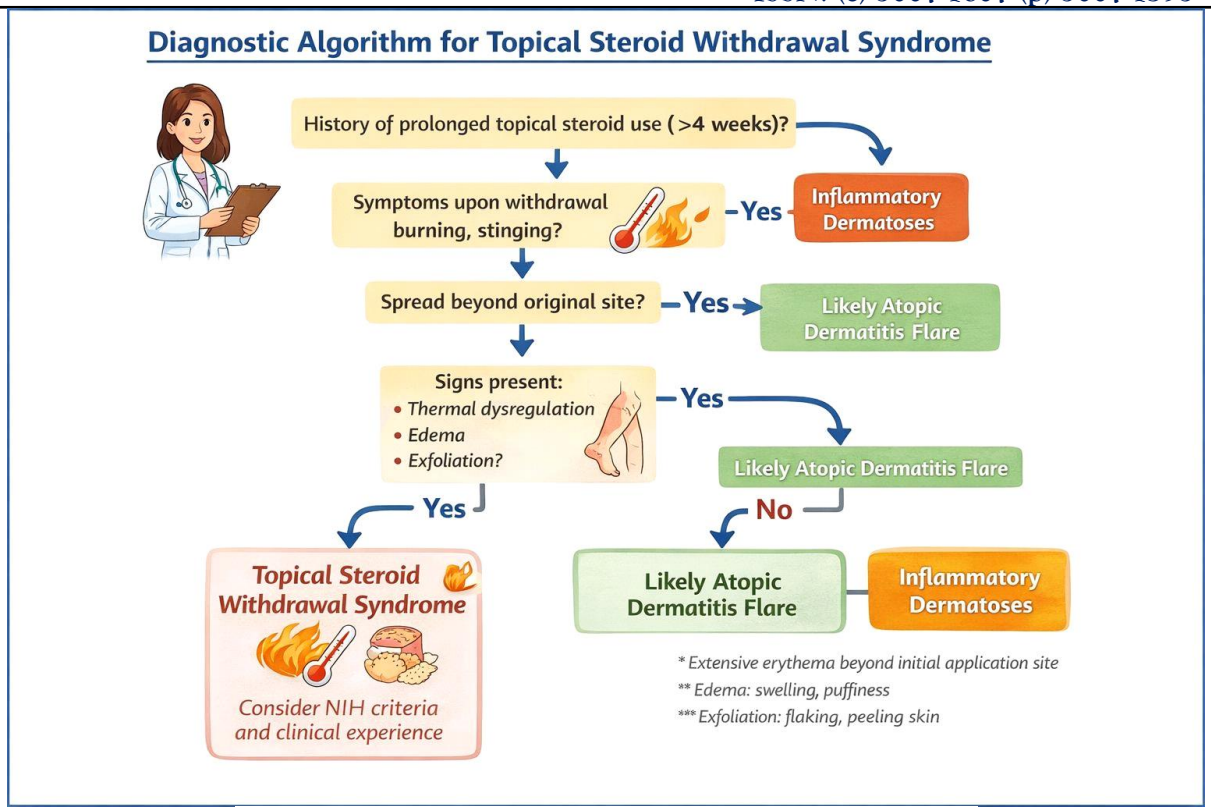

Figure 2: ***Systemic Absorption and Organ System Involvement***

5. Topical Steroid Withdrawal Syndrome: An Emerging Clinical Entity

5.1 Historical Context and Recognition

The first time we noticed topical steroid withdrawal syndrome was in 1979, when Kligman and Frosch first used the term "steroid addiction" to describe a mysterious and frustrating reaction in patients who were using potent fluorinated steroids on their face(Suryawanshi et al., 2009). They observed that, after using the steroids for a prolonged time, if you suddenly stop, you get a nasty rebound reaction: red, swollen, burning skin with pustules. And although applying the steroid again would help, this was only temporary, leading to more severe flares when these patients tried to stop steroids again. For almost 40 years after this discovery, it was largely overlooked, or dismissed as "resistant" skin conditions, rather than its own entity, caused by steroids themselves. But in the past 10 years, prompted by the voices of patients speaking up and sharing their experiences on social media and an ever-growing body of case reports, this condition has finally come into its own(Kleinhans et al., 2024). It's now recognised by regulatory bodies such as the UK's MHRA and Health Canada, and has even got specific diagnostic criteria from the National Institutes of Health (NIH) just this year, 2025.

5.2 Epidemiology and Risk Factors

It's been hard to work out exactly how common topical steroid withdrawal syndrome is, partly because it slipped under the radar for so long, and there was no specific way to track it(Panagariya, Kumar, Mathew, & Sharma, 2006). However, recent studies are beginning to give us a better understanding. It seems to mostly affect people who are using medium- to high-strength topical corticosteroids long-term, particularly on areas of the body where the skin is thinner, such as the face, genitals and skin folds. So the condition seems to affect two main groups: young adults with steroids on their faces to treat acne or mild irritation, and middle-aged people who need super-strong medication to treat more

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complicated chronic skin diseases such as eczema and psoriasis(Harcken, Scholl, Nabozny, Thomson, & Bianchi, 2019). As for risk factors, well, it's really bad news if someone is using really strong steroids (clobetasol and betamethasone) for more than a year, but we are seeing some cases with shorter-term applications on parts of the body where the skin absorbs medication more readily (Brookes et al., 2023).

5.3 Pathophysiology: The NAD+ Breakthrough

A groundbreaking study by the National Institutes of Health (NIH) and the National Institute of Allergy and Infectious Diseases in 2025 brought researchers a step closer to understanding the underlying mechanisms of topical steroid withdrawal syndrome. Their research revealed that individuals with this syndrome also had higher levels of nicotinamide adenine dinucleotide (NAD+) in affected skin, than both healthy controls and people with active atopic dermatitis(Soodan, Kaur, & Soodan, 2021). They confirmed this in mice, where the application and withdrawal of steroids resulted in raised NAD+ levels combined with the usual symptoms of redness and temperature changes. Further studies in skin cells found that corticosteroids increased NAD+ levels by stimulating mitochondrial complex I. This research not only reveals NAD+'s role in the syndrome but also its potential as a therapeutic target(Moreno, Milas, Carreño, De La Puente, & Calderon, 2024).

5.4 Clinical Presentation and Diagnostic Criteria

There's a fairly clear set of signs and symptoms that are unique to topical steroid withdrawal syndrome. It typically presents with a vivid red rash that extends past the site where the steroid was applied and a severe burning and stinging sensation, unlike the typical itchy feeling(Tsang et al., 2002). Other symptoms include swelling, peeling and temperature regulation issues, such as night sweats. In March 2025, the National Institutes of Health (NIH) released provisional guidelines for doctors to diagnose this condition, which include a history of long-term steroid use (typically more than a year), symptoms that start days to weeks after withdrawing from steroids, the characteristic redness and stinging, and excluding other possible reasons(Kavitha, 2021). It's crucial to differentiate it from an eczema flare because otherwise you can end up escalating things that make the condition worse.

5.5 The Vicious Cycle: Misdiagnosis and Steroid Escalation

Unfortunately the worst-case scenario is when topical steroid withdrawal syndrome is misdiagnosed as a flare-up of the original skin disease. They have red, burning skin, and rather than thinking withdrawal, doctors choose to prescribe them stronger steroids or to use the creams more frequently(Baumer, Hoppmann, Rundfeldt, & Kietzmann, 2007). This can temporarily relieve the symptoms, but it makes withdrawal all the worse when they do finally stop. And the body can become less responsive to the steroids (known as tachyphylaxis) and some people even get allergic reactions to the creams. All of a sudden, they're stuck in a vicious cycle of requiring stronger medications and developing a tolerance, which makes withdrawal symptoms worse, adds more side effects and prolongs the recovery time. Table 3 showing clinical features distinguishing topical steroid withdrawal syndrome from acute exacerbations of atopic dermatitis, based on NIH research and expert consensus.

Table 3: *Differentiating Topical Steroid Withdrawal from Atopic Dermatitis Flare*

Clinical Feature	Topical Steroid Withdrawal	Atopic Dermatitis Flare
Quality of Itch	Burning, stinging sensation	Classical pruritus

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Erythema Pattern	Confluent, bright red, extends beyond treatment area	Patchy, confined to typical sites
Distribution	May affect sites not previously treated	Limited to predisposed areas
Temperature Dysregulation	Common, nocturnal sweating	Uncommon
Edema	Frequent, particularly facial	Uncommon
Desquamation	Pronounced peeling and flaking	Mild scaling
Timing Relative to Steroid Cessation	Days to weeks after discontinuation	Variable, may improve with treatment
Biomarker Profile	Elevated NAD+ levels	Normal NAD+ levels
Response to Steroids	Transient improvement, then worsening	Improvement
Sleep Disturbance	Severe, often from burning	Moderate, from pruritus

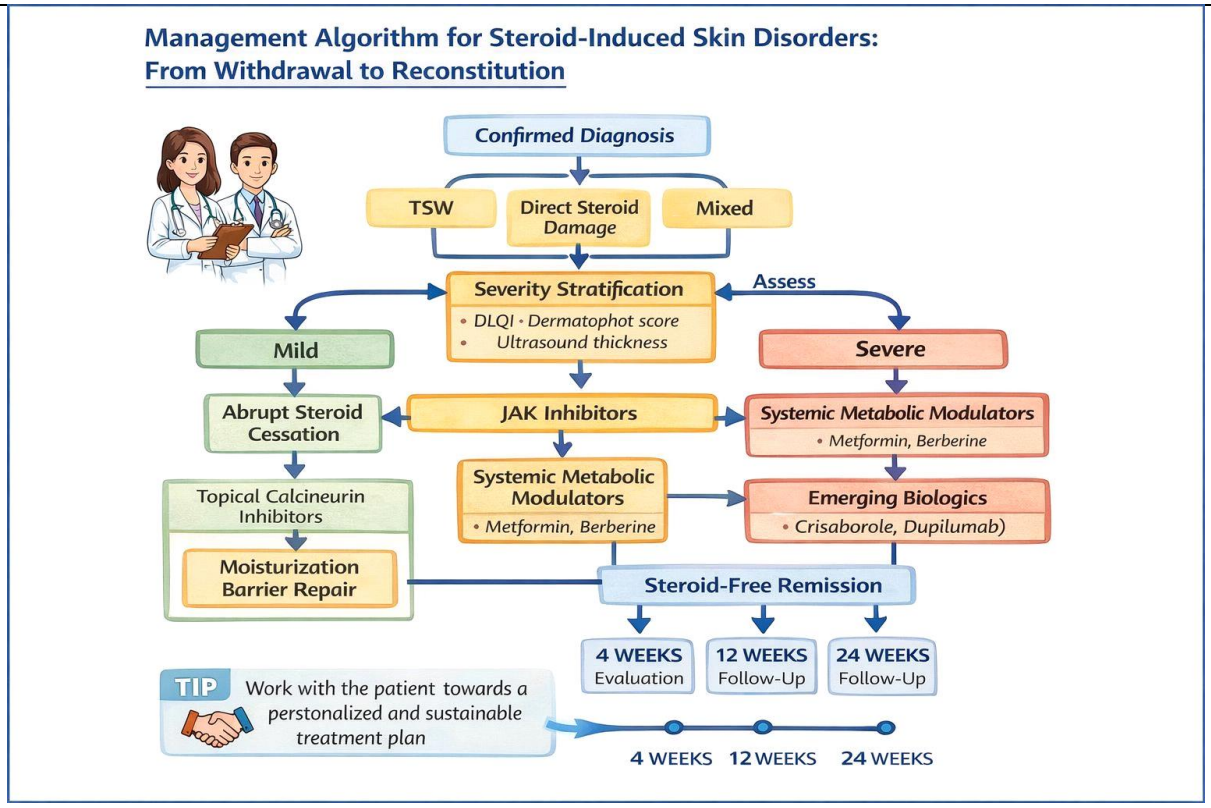

Figure 3: ***The Vicious Cycle of Topical Steroid Misuse and TSW Development.***

6. Emerging Therapeutic Strategies and Evidence for Cure

6.1 Steroid-Sparing Topical Agents

The major breakthrough in preventing steroid side effects is the use of topical calcineurin inhibitors, in particular pimecrolimus 1% cream(Koh & Tay, 2010). In a game-changing Phase 4 study published by Thaçi and colleagues in 2025, pimecrolimus not only reduces inflammation, but can actually fix steroid-induced skin thinning. After a year, people who had been using steroids for some time showed a

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30.5% reduction in their facial Dermatophot scores, which assess steroid-induced skin damage. And even better, ultrasounds revealed a 64.4% increase in facial skin thickness, indicating the skin was actually regrowing, not just de-inflating. It wasn't just faces that saw improvement: there was 38.6% improvement in the elbow. This finding challenges the conventional wisdom that steroid-induced skin thinning can't be reversed, and implies that calcineurin inhibitors make it easier for skin cells to recover, and begin to make collagen again(San & Shein, 2026). Other drugs in this class, like tacrolimus, are just as effective for keeping skin issues at bay once steroids are withdrawn, but studies favour pimecrolimus for reversing skin thinning, due to its superior absorption.

6.2 Novel Targeted Therapies

Knowing that an excess of NAD+ is involved in topical steroid withdrawal syndrome has created new options for treating it by blocking mitochondrial complex I. Medications such as metformin and berberine, which inhibit this complex, were used in a small NIH pilot study for this syndrome(Singh et al., 2021). The majority of participants reported improvement in their redness, burning, and temperature fluctuations, presumably due to normalisation of NAD+. Although we need larger, more formal studies, these findings are encouraging as they suggest that cheap and well-tolerated drugs already available could address the unmet need for effective treatment of a condition that until now has lacked specific treatment.

Efgartigimod is causing a commotion in the field of autoimmune blistering diseases as a new way to reduce steroid use(Hengge, 2017). Efgartigimod targets a receptor known as FcRn, which leads to a faster decay of the disease-causing IgG antibodies. It's currently being trialled in Phase 3 for bullous pemphigoid with the ultimate aim of putting the disease into complete remission without steroids. If successful, efgartigimod holds the promise of getting to the source of the problem (eliminating those nasty autoantibodies) and steering clear of steroids, a mainstay of therapy for these patients for decades(Berger, 2005).

6.3 Barrier Repair and Supportive Therapies

When it comes to treating steroid-related skin issues, it's not just the steroids that need to be discontinued - it's about restoring the skin's protective barrier. Ceramide-rich moisturisers, lipid-based creams and gentle cleansers and washes help repair the outer layer of skin that steroids can damage(Sparling & Butler, 2024). As a weakened barrier gives more opportunity for nasty germs like Staph and fungi to enter, preventing infections is important. But equally importantly, there are the psychological aspects - steroid withdrawal can have profound effects on sleep, mood, and quality of life(Cohen, 2007). People also find cognitive-behavioral therapy and being able to connect with others who are also going through withdrawal very helpful with the painful process of withdrawing from steroids (Brookes et al., 2023).

6.4 Device-Based Approaches

StrataCTX® gel is a new type of steroid-sparing treatment, currently undergoing a Phase 2 trial at Columbia University. Rather than using medication, this treatment is like a physical barrier, creating a film on the skin to reduce inflammation and itching(Schoepe, Schäcke, May, & Asadullah, 2006). It's currently being used to treat conditions such as cutaneous T-cell lymphoma and chemotherapy-induced skin reactions - primarily to avoid the use of steroids(Bienenfeld et al., 2019). If it continues to show promising results, StrataCTX® has the potential to revolutionise the treatment of long-term skin conditions without the side effects associated with long-term steroid use. Figure 4. showing Comparative illustration of the mechanisms by which emerging therapies address steroid-induced damage: (A) Pimecrolimus inhibits calcineurin, reducing inflammation while allowing collagen recovery; (B) Metformin/berberine block mitochondrial complex I, reducing NAD+-mediated inflammation; (C) Efgartigimod targets FcRn,

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reducing pathogenic IgG levels and enabling steroid reductios.

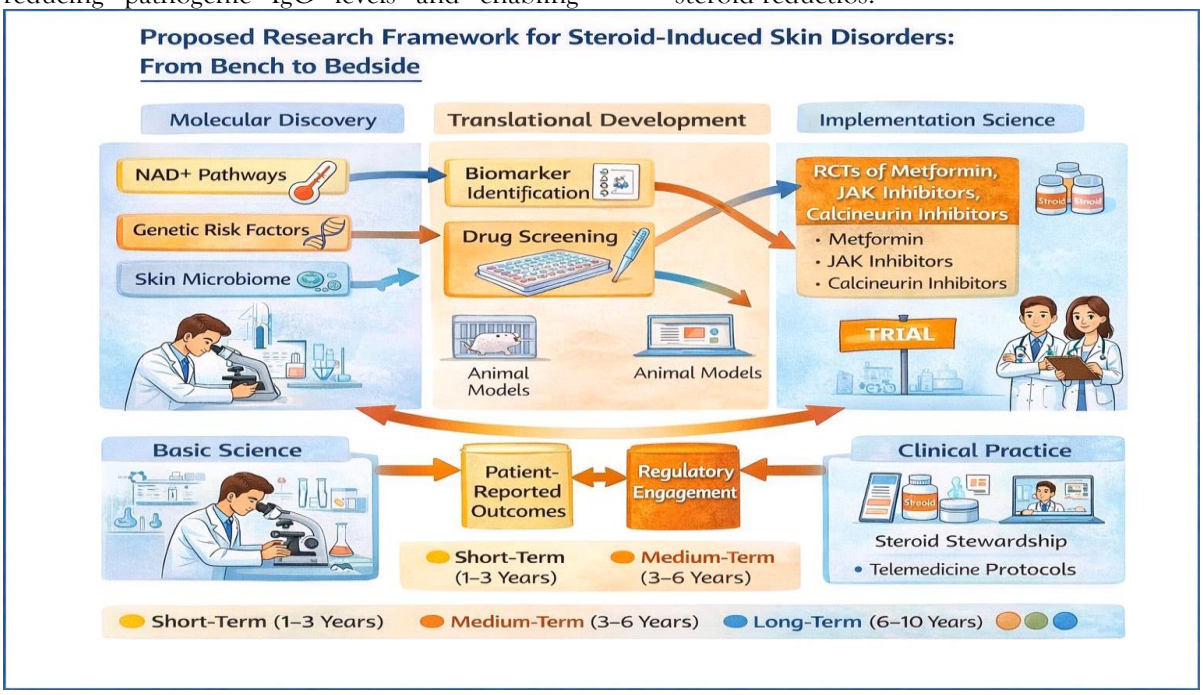

Figure 4: ***Mechanism of Action of Novel Therapies in Steroid-Induced Damage***

Table 4: *Emerging Therapies for Steroid-Induced Disorders: Evidence and Mechanisms.*

Therapy	Mechanism of Action	Indication	Evidence Level	Key Outcomes	Safety Profile	Development Stage
Pimecrolimus 1% cream	Calcineurin inhibition	Steroid-induced atrophy reversal	Phase 4 (N=41)	30.5-38.6% Dermatophot score improvement; 64.4% skin thickness increase	Favorable; no drug-related SAEs	Approved (new indication)
Metformin	Mitochondrial complex I inhibition	Topical steroid withdrawal	Pilot (N=16)	Subjective improvement in most patients	Well-established	Off-label use
Berberine	Mitochondrial complex I inhibition	Topical steroid withdrawal	Pilot (N=16)	Subjective improvement in most patients	Generally favorable	Off-label use
StrataCTX® gel	Physical barrier/steroid-sparing	CTCL, chemotherapy reactions	Phase 2 (N=70 recruiting)	Steroid-sparing effect (primary outcome)	Under investigation	Active clinical trial
Efgartigimod PH20 SC	FcRn blockade, IgG reduction	Bullous pemphigoid	Phase 3	Complete remission without	Under investigation	Active clinical trial

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				corticosteroids		
Topical JAK inhibitors	JAK-STAT pathway inhibition	Inflammatory dermatoses	Multiple phase 3	Disease control with steroid-sparing effect	Generally favorable	Approved for some indications

7. Clinical Management Algorithms

7.1 Prevention Strategies

The key to avoiding steroid-related skin issues is to prevent them in the first place, by prescribing steroids wisely(Mohamed Fathima, 2022). The first rule is: doctors should only use the lowest potency steroid that works, and for the shortest possible time. For sensitive areas such as the face, genital region or skin folds, only low to medium strength steroids should be used, and even these should be avoided if treatment is likely to take more than two to four weeks, when it should be time to re-evaluate(Bungau et al., 2025). For the really thick skin areas, like palms, soles, and scalp, stronger steroids can be used, again for a short time (two to four weeks) before taking a break. Also, no automatic refills, otherwise there is a risk of people being prescribed steroids for far too long with no-one watching out for them (Hengge et al., 2006).

Patient education and counselling is critical to avoid steroid complications. Prior to treatment, doctors must discuss the potential harms from using steroids for too long, thin skin, visible tiny blood vessels, steroid absorption into the bloodstream and withdrawal symptoms once treatment ceases. Doctors need to provide patients with written instructions about how to use the medication, how long to use it and when to return for follow-up(Hodgens & Sharman, 2023). They should also be instructed on how to recognise early signs of steroid damage, such as thinning skin, bruises and fine blood vessels. Oh, and make sure people who use over-the-counter hydrocortisone creams know that even these low-strength steroids can cause problems if they're used for too long and in sensitive places like their faces and genitals (Brookes et al., 2023).

It's important to keep a close watch on people using topical corticosteroids long-term, to spot any issues early(Alia & Kerr, 2021). For those who've been on these steroids continuously for more than a year, they should check in at least once a year. This visit should involve a full physical exam of the skin for signs such as "paper-thin" skin, fine red lines (spider veins) or stretch marks(Poudyal et al., 2025). They should also get a blood test early in the morning to check their cortisol levels, and ensure their body's response to stressful situations (the HPA axis) isn't affected. And they should get an eye check to keep an eye out for cataracts or glaucoma(Scott & Miller, 2010). If someone is using a strong steroid on more than 20% of their body, they should have a bone density test every two or three years - particularly if they are postmenopausal women or anyone else at risk of osteoporosis (DiRuggiero & DiRuggiero, 2025).

7.2 Management of Established Steroid-Induced Damage

Once steroid-induced, or steroid-related damage has occurred, the first step in managing it is to "wean" off steroids instead of abruptly ceasing use. Quitting cold turkey after long-term use can cause a bad rebound flare called topical steroid withdrawal syndrome. It's best to wean off over a period of two to three months(Meier et al., 2012). This can be done by stepping down the "ladder of strength" - from a super strong steroid to a strong steroid to a medium strength steroid and finally a mild hydrocortisone before coming off the steroid completely. Alternatively, you can keep using the same strength steroid but reduce the frequency of application from twice daily to once daily, then every other day, then a few times a week and then eventually stop(Caplan, Fett, Rosenbach, Werth, & Micheletti, 2017). The best approach depends on the patient's skin disease, their compliance and the extent of steroid damage (Hajar et al., 2015).

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It's a good idea to introduce steroid-sparing therapies early in steroid tapering to prevent a flare of the skin disease. Most people will use topical calcineurin inhibitors, particularly pimecrolimus 1% cream(O'BRIEN, GOLDENBERG, & RICE, 1983). The 2025 Phase 4 study by Thaçi and colleagues demonstrated that, if applied during steroid tapering, pimecrolimus not only prevents flare-ups but even reverses skin thinning - a remarkable 64.4% increase in facial skin thickness occurred in a 1-year period. If calcineurin inhibitors don't work due to side effects or other causes, some alternatives include using topical phosphodiesterse-4 inhibitors (crisaborole) or topical JAK inhibitors (ruxolitinib cream). But at present, only calcineurin inhibitors have good evidence for reversing skin atrophy.

There's no single key to treating withdrawal symptoms - it's a combination approach. For the severe redness and burning that typically occur with steroid withdrawal, treatments such as cold packs, barrier repair creams and oral antihistamines can help(Narang, Kumaran, Dogra, Saikia, & Kumar, 2013). For the more severe symptoms, such as those involving overheating and night sweats (well-known symptoms of topical steroid withdrawal), some patients have reported positive outcomes from using drugs such as metformin or berberine. These are drugs that work by blocking mitochondrial complex I, and, in preliminary research at the National Institutes of Health (NIH), most patients reported improvement(Nash, Nash, Leach, & Poetker, 2011). The good news for patients is that withdrawal symptoms typically reach their peak two to four weeks after the steroids are stopped, and can last for anywhere from three months to a year - but it does improve over time(Abdel-Wahab, Shah, & Suarez-Almazor, 2016).

7.3 Special Populations

When treating children with topical steroids, you've got to be super careful. They absorb these creams more readily, and their small body size with a larger surface area to weight ratio means it can have a stronger effect - and this can lead to growth retardation. So, the general rule is: use the lowest strength steroid that works, cover only the smallest possible area and do it for as short a time as possible(Gilmore, Liu, & Matsumoto, 2004). The use of strong or super strong steroids is usually avoided before age 12, unless it's for a very short, closely monitored course, like on palms, soles and scalp. And it's really important to counsel parents on how to apply the cream (using fingertip units and avoiding tight bandages or occlusive dressings). If kids need to be on steroids for a while, they should be checked for growth every six months and if they have growth delays, then it's time to see an endocrinologist (Wood Heickman et al., 2017).

Corticosteroids can cause skin to thin and thin skin is common as people age, so seniors are particularly vulnerable to this side effect(Mohta & Sathe, 2024). And they're more at risk of severe side effects, such as diabetes, osteoporosis and adrenal dysfunction because their organs are less efficient and they're taking several medications. If older adults need to use potent steroids for an extended period, it's worth measuring their bone density before they begin and throughout their treatment(Olbrich, Sadik, Ludwig, Thaci, & Boch, 2023). And because weak bones, coupled with poor balance, can cause older adults to fall, fall prevention strategies are a good idea (DiRuggiero & DiRuggiero, 2025).

Low-potency topical steroids are generally thought to be safe to use in pregnancy, as long as they are only used for a short time and on a small area. But stronger steroids, particularly potent and superpotent ones, should be avoided, especially during the first trimester of pregnancy to reduce the risk of potential side effects such as cleft lip or fetal growth restriction (based mainly on animal studies)(Walling & Sontheimer, 2009). During breastfeeding, it's best to apply these corticosteroids after feeding to minimise the baby's exposure and women should avoid applying the creams to their breasts. If you want to avoid using steroids during pregnancy and breastfeeding, importantly, evidence suggests that topical calcineurin inhibitors are safe to use as

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they don't have the same potential to affect metabolic processes (Butler et al., 2014).

7.4 Multidisciplinary Approach

Treating complex steroid-related troubles is not always possible with just one type of specialist; dermatologists and endocrinologists need to work closely together. If someone has HPA axis suppression, they need to see an endocrinologist for a full work-up so they can deal with their adrenocortical insufficiency, including making sure they get additional steroids in times of stress, such as illness or surgery(Ujiie et al., 2022). Patients with steroid-induced diabetes or bone fractures need to work hand in hand with endocrinology to manage their blood sugar levels and prevent or treat bone weakness. And they need to take care of their eyes, particularly if they are taking strong steroids near their eyes for a long time(Vedamurthy, Kumar, & Boda, 2024). They need an initial and annual eye exam and screening for eye pressure and cataracts. If they have any changes in vision, eye pain or halos around lights, they must see an eye specialist immediately. And the psychological burden of steroid withdrawal and steroid use can take its toll(Weston, 1984). Anxiety, depression and loneliness are common during this difficult period. Psychological support through cognitive-behavioural therapy, peer support and dermatology-specific psychological services can help patients stay committed to the treatment and improve their quality of life (Brookes et al., 2023). Figure 5 is showing the Stepwise algorithm for the assessment and management of patients presenting with suspecte`d steroid-induced skin disorders, including diagnostic evaluation, treatment selection based on severity, and monitoring parameters.

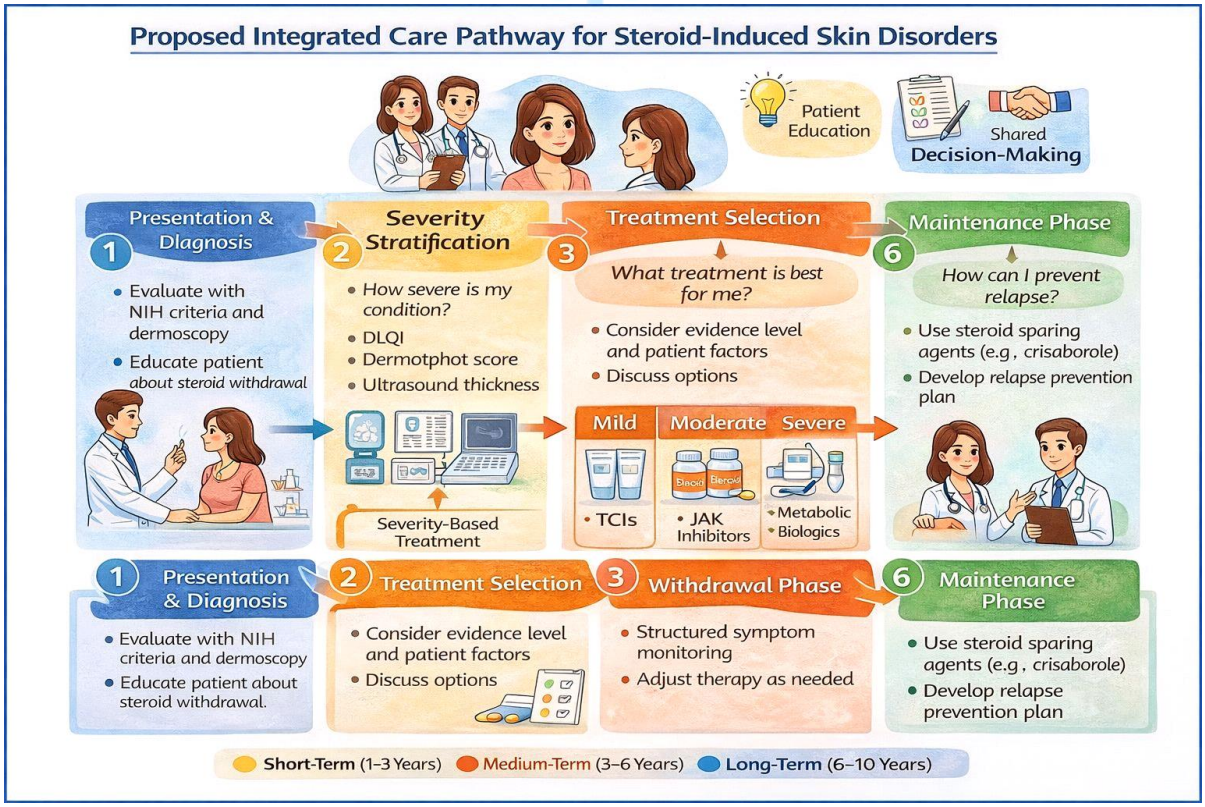

Figure 5: ***Clinical Management Algorithm for Steroid-Induced Skin Disorders***

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8. The Knowledge Gap: Toward Curative Strategies

8.1 Current Limitations in Evidence

While more people are beginning to recognise skin issues from steroids, there's still so much we're not sure about. A major problem is there are no good randomized controlled trials about topical steroid withdrawal syndrome(Segre, 2006). We mostly rely on case reports (looking at past cases) or surveys where patients report their own experiences - not the solid studies we would like to see. The National Institutes of Health (NIH) recently proposed some preliminary criteria to help diagnose cases, but so far, there hasn't been a validated method of diagnosing this condition so studies don't always agree(Paller & Mancini, 2020). Plus, we know nothing about how new steroid-sparing drugs compare with each other - such as pimecrolimus vs tacrolimus vs mitochondrial inhibitors - so doctors don't have the information they need to choose the best treatment (Brookes et al., 2023; Hajar et al., 2015).

8.2 Mechanistic Uncertainties

The discovery of NAD+ elevation as a cause of topical steroid withdrawal syndrome (TSWS) is a major breakthrough, but many mechanistic questions remain(Vaughan Jones, Hern, Nelson-Piercy, Seed, & Black, 1999). The variability of NAD+ elevation in affected patients indicates that not all patients share a common underlying process, and the threshold for NAD+ elevation to induce clinical symptoms is unknown. The role of genetic susceptibility has yet to be explored, with unknown reasons for why some chronic corticosteroid users suffer severe withdrawal(Sibaud, 2018). Also, the significance of skin microbiome changes, including Staphylococcus aureus overgrowth, in modifying withdrawal syndrome severity, and the potential for microbiome-targeting therapies in treatment, need to be explored (NIH, 2025)(Lee et al., 2020).

8.3 The Curative Potential: What the Evidence Suggests

Despite a few missing pieces in the puzzle, the newest research is beginning to bring hope for a cure. Consider pimecrolimus: it's no longer just about symptom relief. Researchers have shown it's able to actually regrow skin, with an impressive 64.4% growth in skin thickness after a year, so it's actually repairing damage caused by steroids, rather than just reducing inflammation. Or take metformin and berberine, which are tackling the underlying cause of the NAD+ in topical steroid withdrawal syndrome - it could be the game-changer from treating symptoms to actually changing the course of the disease entirely(Zulian et al., 2005). And for people with autoimmune blistering diseases, we have new drugs such as efgartigimod to help get off steroids entirely. Overall, these advances suggest a true cure - where the steroid damage goes away and patients can stop needing treatment - is on the horizon for many (Thaçi et al., 2025; NIH, 2025).

9. Future Research Directions

Biomarkers to identify high-risk patients for severe withdrawal syndrome are urgently needed to allow early intervention. Genome-wide association studies to detect risk loci will enable genetic risk identification and targeted prevention(Segaert et al., 2017). Prospective cohort studies are needed to understand long-term outcomes of steroid-sparing therapies, such as long-term maintenance of muscle mass and disease recurrence. Lastly, head-to-head studies of available steroid-sparing medications are needed to define treatment guidelines and improve outcomes.

Perhaps the most striking thing to come out of this review is just how big a gap there is between what we know and what we do, between the increasing body of evidence that steroid-induced skin damage can be reversed, and the current clinical practices, which are often to use steroids indefinitely(Stalder et al., 2014). Despite the wealth of research that has shown that the side effects of steroids (including steroid withdrawal syndrome, skin thinning, etc.) can be managed and even reversed with appropriate strategies,

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physicians continue to prescribe long-term use of topical steroids without attempting to wean patients off or use safer alternatives(Wolff & Stuetz, 2004). The disconnect between research and practice is not only a shame but it is delaying progress towards finding cures and unnecessary harm is being done.

This is really brought home by the data from the pimecrolimus trial. After one year of treatment with pimecrolimus 1% cream, Thaçi et al (2025) found that patients with long-term steroid-induced facial skin thinning had a whopping 64.4% increase in facial skin thickness, reversing the stereotypical steroid damage you see under the microscope(Husein-ElAhmed, Gieler, & Steinhoff, 2019). Yet despite these encouraging results, topical calcineurin inhibitors such as pimecrolimus are still being "pushed to the back of the bus" and only used after steroids have done damage, not as first-line drugs to avoid steroid damage in the first place. Similarly, the NIH's finding that an excess of NAD+ is driving topical steroid withdrawal syndrome has allowed for targeted therapy with mitochondrial complex I inhibitors such as metformin and berberine(Hodgins et al., 2018). Preliminary research indicates most patients improve with these medications (NIH, 2025). However, these new targeted treatments have yet to be widely adopted, with most patients remaining on extended steroid tapers, or being offered symptom-relieving treatments.

So here are a couple of reasons why we aren't seeing more of these new treatment options being used in clinics(de Gannes et al., 2007). First, many doctors haven't yet learned about the recent discoveries that steroid atrophy can be reversed and topical steroid withdrawal syndrome is not as mysterious as we once thought. Sometimes doctors are still taught steroid damage is irreversible and what's going on with withdrawal syndrome is not understood. Plus, there are no official guidelines that use these alternative treatments, so doctors don't have a guidebook to follow(Visvesvara, Moura, & Schuster, 2007). Let's face it - it's just easier to follow a steroid routine in clinic than to take on the more complicated process of weaning steroids and introducing alternatives, which demands more time to follow up and educate..

We need a paradigm shift in the way we use steroids, from the idea that patients need to be on them for the rest of their lives, to the idea that steroids can be used for a limited time to suppress flares while starting cures that alter the course of the disease. Rather than steroids being the key treatment, they should only be used as a bridge to control inflammation while steroid-sparing therapies are introduced, with a goal to withdraw steroids completely within a certain time period(Kageyama et al., 2023). This review helps bridge the gap by linking the latest research findings - such as the NAD+ pathway's role in steroid withdrawal syndrome, the fact that pimecrolimus can reverse skin damage, and new steroid-sparing therapies like mitochondrial inhibitors and FcRn blockers - to a practical approach for the clinic. By translating these developments into diagnostic criteria, treatment algorithms and monitoring strategies, we hope to accelerate the pace at which doctors get on board with cures, and to minimise the damage done by chronic steroid use(Li et al., 2020). We know a cure is possible; now the challenge is to make it practical.

10. Clinical Management Algorithms

10.1 Prevention Strategies

To avoid steroid-related skin issues, it's better to prevent them in the first place with wise prescribing. The mantra for doctors should be: use the lowest strength steroid needed and for as short a period as possible. For more sensitive sites such as the face, genitals and skin folds, only low to medium strength steroids should be used, and if it needs to continue for more than two to four weeks, take a break(Wollina, Hansel, Koch, & Abdel-Naser, 2006). For areas of thick skin such as the palms, soles and scalp, high potency steroids can be used, but only for a few weeks at a time before a break (Munro et al., 2003). Also, a strict no-no is giving automatic refills without a check-up - this can result in people taking steroids for too long without medical supervision (Hengge et al., 2006).

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Patient education and counselling is a key part of avoiding steroid-related issues. Doctors should have a frank discussion with their patients about the dangers of prolonged steroid use, such as thinning of the skin, the appearance of spider veins, steroid absorption into the bloodstream, and the possibility of withdrawal reactions when ceasing the medication. It's important to give patients written advice about how to use the cream, how long to use it for, and when to return to see their doctor. And make sure they know what signs to look out for, such as skin thinning, bruising easily and tiny blood vessels becoming visible(Yao, Englund, Hayden, & Tomecki, 2012). And remember, if people are using over-the-counter hydrocortisone creams, remind them that these low-dose steroids can cause problems if used too often, particularly if applied to sensitive parts of the body, such as the face and genitals (Brookes et al., 2023).

It's important to carefully monitor people who use topical corticosteroids over the long term. If someone has been using these steroids continuously for more than a year, they need to be checked annually, including a full skin exam to look for things such as thin skin, spider veins and stretch marks. They also need a blood test first thing in the morning to measure their cortisol level - so we know if their body's stress response system is getting damaged(Paul, Graeber, & Stuetz, 2000). And they should have an eye exam to check for cataracts or glaucoma. If someone is using strong steroids on more than 20% of their body, they should have their bone density checked every two to three years - particularly if they are a postmenopausal woman, or anyone else who might develop osteoporosis (DiRuggiero & DiRuggiero, 2025).

10.2 Management of Established Steroid-Induced Damage

Once steroid damage has occurred, the best way to treat it is to cut down on the steroids carefully - a sudden withdrawal will only make things worse with a severe rebound known as topical steroid withdrawal syndrome. The best way is to wean off the steroid over a few months. One method is to gradually reduce the strength of the steroid you're using: from very strong, to strong, to medium, and then switching to a low strength hydrocortisone, before finally stopping. Alternatively, you can keep the same strength, but apply it less frequently: from twice a day to once a day, then every other day, twice a week and so on until you stop(Bhardwaj, Chiu, & Pilkhwal Sah, 2022). The taper used will depend on the patient's specific skin problem, their adherence to the routine and the severity of steroid damage (Hajar et al., 2015).

It's a good idea to begin tapering and switching to steroid-sparing therapies early in the steroid withdrawal process to prevent the skin condition from returning. The most common treatment is topical calcineurin inhibitors, particularly pimecrolimus 1% cream. In a Phase 4 trial, Thaçi and co-workers (2025) demonstrated that by starting pimecrolimus along with steroid tapering, they not only prevented flares, but actually reversed skin atrophy (a 64.4% increase in facial skin thickness in one year). If calcineurin inhibitors aren't an option due to side effects or other reasons, alternative treatments include topical phosphodiesterase-4 inhibitors (such as crisaborole) or topical JAK inhibitors (such as ruxolitinib)(Abe et al., 2025). But at this point, only calcineurin inhibitors have good supporting evidence for their use to reverse skin thinning.

Treating withdrawal symptoms is a multifaceted approach. For people with intense redness and burning when they stop steroids, a few simple tricks can help, including cold compresses, creams that restore the skin barrier and oral antihistamines. For more persistent withdrawal symptoms, such as temperature fluctuations and night sweats (which are common when people have topical steroid withdrawal syndrome), some people have reported improvement with medications such as metformin or berberine. These drugs interfere with the mitochondrial complex I pathway, and preliminary research at the National Institutes of Health (NIH) found the majority of patients improved with this treatment(Tan, Chandran, & Choi, 2021). It's good to explain to patients that these steroid withdrawal symptoms tend to peak between two and four weeks after ceasing steroid use and can

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persist for three months to a year, but will generally improve gradually.

10.3 Special Populations

When prescribing topical steroids to kids, you have to be careful. They absorb the drugs more readily, and they have a greater surface area to weight ratio, so the drugs can have a greater effect. And they have a higher risk for stunting growth. So, it's important to use the lowest-strength steroid you can, apply it to the smallest area of skin possible, and for the shortest duration. Very strong or super strong steroids are generally avoided for children under 12, except for short treatments, and these should be closely monitored, for example on parts of the body that are hard to treat, such as the palms, soles and scalp. It's important for parents to know how to use the cream, things like applying the right dose (measured in "fingertip units") and avoiding covering the skin with occlusive dressings. And for children needing longer-term treatment, they should be checked for growth every six months and if they aren't growing, consult an endocrinologist (Wood Heickman et al., 2017).

Corticosteroid-induced skin atrophy is more common in the elderly due to thinning and decreased collagen content. They are also at greater risk of systemic side effects such as osteoporosis, diabetes and adrenal suppression because of age-related decreased organ function and polypharmacy. Baseline and ongoing bone mineral density screening should be undertaken in elderly patients on long-term potent corticosteroids. Fall prevention measures should be initiated due to the risk of fracture (osteoporosis) and balance issues (DiRuggiero & DiRuggiero, 2025).

Pregnancy and lactation is a special time to be extra careful due to the risks to the fetus. Topical steroids of low to medium strength are usually safe during pregnancy, but only if you only use them for a short time and on a small area. High to very high strength steroids (especially potent and super potent steroids) should be avoided, especially in the first trimester, because animal studies have shown they may increase the risk of malformations (such as cleft lips) or growth restriction in the uterus (womb). For women who are breastfeeding, it's best to apply steroids after breastfeeding to minimise any potential exposure to the baby and avoid applying steroids directly to the breasts. If you're not keen on steroids, topical calcineurin inhibitors are a better choice for pregnancy and breastfeeding as they don't have systemic effects (Butler et al., 2014).

10.4 Multidisciplinary Approach

It takes two to manage complex steroid issues: dermatologists and endocrinologists. If a patient has signs of HPA axis suppression, they need a work-up by an endocrinologist to treat any adrenal insufficiency, including ensuring that they receive additional steroid support during stressful events such as illness and surgery. For patients with steroid-induced diabetes or osteoporosis, a coordinated effort with the endocrinologist is needed to optimise their blood glucose levels and prevent bone degradation.

Regular vision screenings are essential for patients who're on long-term, high-potency steroids, particularly when applied around the eyes(Rick, De, & Shi, 2024). They should have a comprehensive eye examination before using the medicine and then an annual eye examination that includes eye pressure and slit lamp examination for cataracts. Patients should seek urgent medical attention from an eye specialist if they report vision changes, eye pain or halos around lights.

Emotionally, coping with topical steroid withdrawal and chronic steroid use can be hard. Patients often battle anxiety, depression and isolation during this difficult period(Parnes, Sun, & Freeman, 1999). Emotional support, such as cognitive-behavioral therapy, support groups, and psychological services for skin diseases, can really help them stay motivated to complete treatment and improve their quality of life (Brookes et al., 2023).

11. Conclusion

This review reveals that although topical steroids are very effective, they can cause a range of predictable adverse reactions, both localised and systemic, and there is no definitive threshold as to how much is safe.The induction of a new

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disease entity, topical steroid withdrawal syndrome, due to excess NAD+ production, and the 64 percent reversal of steroid-induced atrophy by pimecrolimus, overturns the conventional view that steroid damage is irreversible and that maintenance therapy is harmless.New steroid-sparing approaches, such as calcineurin inhibitors, mitochondrial complex I inhibitors, and FcRn blockade, target the disease process rather than the symptoms and have the potential to alter the disease course and cure the disease. The challenge is to translate this increasing knowledge into clinical practice. In conclusion, we argue that a shift from long-term steroid maintenance to early diagnosis and systematic steroid tapering, with early initiation of steroid-sparing treatments, is not only justified but essential to minimise iatrogenic complications and optimise patient outcomes.

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