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THE IMPACT OF CHRONIC SOCIAL STRESS ON THE FUNCTIONAL STATE OF SKIN

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Introduction. The skin is the largest organ of the human body and represents a highly specialized multifunctional system that performs protective, metabolic, thermoregulatory, sensory, and immunological functions. As the primary anatomical barrier between the internal environment and external factors, the skin plays a crucial role in maintaining homeostasis and protecting the organism against mechanical injury, microbial invasion, chemical exposure, ultraviolet radiation, and excessive water loss. In addition to its barrier properties, the skin is considered an immunocompetent organ, as it contains a complex network of resident immune cells, including macrophages, mast cells, dendritic cells, lymphocytes, and other effector cells involved in both innate and adaptive immune responses [1].

Chronic social stress (CSS) is a systemic psychophysiological factor capable of disrupting neuroendocrine, immune, and metabolic regulation. Prolonged activation of stress-response systems, particularly the hypothalamic–pituitary–adrenal axis and the sympathetic nervous system, leads to sustained changes in glucocorticoid and catecholamine levels [2]. These changes may impair immune surveillance, alter inflammatory signaling, and disturb tissue repair mechanisms. The skin is especially sensitive to such stress-induced dysregulation because it is closely connected with the nervous, endocrine, and immune systems [3].

Under conditions of chronic stress, the functional state of the skin may become significantly compromised. Stress-related alterations include a reduction in epidermal lipid content, degradation or insufficient renewal of structural proteins, impaired

keratinocyte differentiation, and increased transepidermal water loss. Together, these changes weaken the epidermal barrier and create a vulnerable microenvironment. Such a condition may increase susceptibility to inflammation, infection, delayed wound healing, and exacerbation of dermatological diseases. Clinical and experimental observations indicate that chronic stress is strongly associated with the onset or aggravation of inflammatory skin disorders, including psoriasis, eczema or atopic dermatitis, rosacea, acne, and chronic pruritus. Elevated stress hormones may also stimulate sebaceous gland activity, promote neurogenic inflammation, and intensify itching and discomfort [4, 5].

Despite the recognized relationship between psychological stress and skin pathology, the specific structural and immunological mechanisms by which CSS affects intact skin remain insufficiently understood. In particular, it is important to determine whether chronic stress can pre-condition the skin into a pathological state even before any mechanical injury occurs. Therefore, the functional state of the skin under prolonged social stress remains a relevant and important area of experimental investigation.

This study aims to evaluate how CSS disrupts the fundamental barrier and immune functions of the skin.

Materials and methods. The study was conducted 50 on male Wistar rats. The experimental group (n=30) was subjected to a validated 21-day CSS model, which involved social isolation combined with continuous psycho-emotional pressure from aggressive conspecifics. Morphometric, histological, and immunohistochemical analyses were performed on skin samples taken from the interscapular region before any wound was inflicted. Evaluated parameters included epidermal thickness, vascularization, and the quantitative and functional dynamics of resident and systemic immunocompetent cells. The obtained data were analyzed statistically, and differences between the control and experimental groups were considered significant at the appropriate probability levels.

Results. Prolonged exposure to chronic social stress caused marked structural and immunological disturbances in the skin. These changes affected both the epidermal barrier and the dermal immune microenvironment, indicating a systemic stress-induced impairment of skin homeostasis.

A significant reduction in epidermal thickness was observed in stressed animals. The epidermis of rats exposed to CSS was considerably thinner, measuring 9.54 ± 0.43 μm, with statistical significance at $p \leq 0.01$ compared with the control group. This decrease in thickness was mainly associated with a reduction in the basal and spinous layers. In addition, the granular layer showed extreme thinning or complete focal absence in several areas. These findings suggest impaired keratinocyte proliferation, differentiation, and maturation.

Histological analysis also revealed local parakeratosis, which indicates abnormal keratinization and incomplete epidermal differentiation. The presence of parakeratosis reflects a disturbance in the normal renewal of the epidermis and supports the conclusion that chronic stress weakens the structural organization of the skin barrier. Furthermore, narrowing of the superficial dermal vascular plexus was detected, suggesting impaired local microcirculation. Taken together, epidermal thinning, abnormal keratinization, and vascular narrowing indicate substantial impairment of the barrier function of the skin.

The cellular immune component of the skin was also profoundly affected by chronic social stress. A significant decrease in the number of neutrophils was detected in the dermis of stressed animals, reaching 1.69 ± 0.12 cells/mm², with $p \leq 0.05$. The number of macrophages was also significantly reduced, amounting to 17.54 ± 1.45 cells/mm², with $p \leq 0.05$. Similarly, the total number of lymphocytes decreased to 22.59 ± 1.96 cells/mm², with $p \leq 0.05$. These findings indicate suppression of both innate and adaptive immune components in the skin.

Immunohistochemical analysis confirmed the development of immune dysregulation. The expression of $CD3^+$ T lymphocytes, $CD4^+$ helper T cells, $CD8^+$

cytotoxic T cells, and $CD20^+$ B cells was decreased in the experimental group. The reduction in these markers demonstrates that chronic social stress suppresses the cellular and humoral components of adaptive immunity within the skin. In addition, the CD4/CD8 immunoregulatory index was markedly altered, decreasing to 1.17 ± 0.60 in stressed animals compared with 2.81 ± 0.57 in the control group. This shift reflects an imbalance in T-cell regulation and may indicate impaired coordination of immune responses.

In contrast to the general suppression of systemic immune cell populations, chronic social stress induced a pronounced hypermobilization of resident mast cells. The number of mast cells increased approximately ten-fold, reaching 9.47 ± 0.23 cells/0.01 mm^2, with a high level of statistical significance at $p \leq 0.001$. These mast cells demonstrated increased basal activation, as shown by a high degranulation index of 36.37 ± 0.81, with $p \leq 0.01$. Mast cell degranulation is associated with the release of histamine, proteases, cytokines, and other biologically active mediators that may promote vascular changes, itching, inflammation, and neuroimmune interactions. An early infiltration of eosinophils was also observed in the dermis of stressed animals. A simultaneous increase in the number of activated mast cells and eosinophils occurs in parallel with a general depletion of macrophages, neutrophils and lymphocytes. Therefore, CSS produces a paradoxical immune state characterized by suppression of protective immune surveillance together with activation of resident pro-inflammatory mechanisms.

Discussion. The results of this study demonstrate that chronic social stress (CSS) significantly alters the functional state of the skin. The observed epidermal impairment—characterized by marked thinning, structural reduction of the basal and spinous layers, focal loss of the granular layer, and parakeratosis—indicates a major disruption in keratinocyte proliferation and differentiation. Because the epidermis serves as a critical barrier against dehydration and external pathogens, this structural degradation compromises resistance to environmental stressors, elevates

transepidermal water loss, and increases vulnerability to local inflammatory or infectious complications. Furthermore, the narrowing of the superficial dermal vascular plexus implies that chronic stress disrupts microcirculatory homeostasis, limiting the delivery of oxygen, nutrients, and immune cells required for effective tissue repair and regeneration [6].

Concurrently, CSS induced profound dysregulation within the skin-associated immune system. The depletion of protective cell populations—specifically neutrophils, macrophages, and lymphocytes—suppresses essential elements of antimicrobial defense, inflammatory coordination, and adaptive immunity. This systemic immunotolerance is accompanied by the hyperactivation of resident mast cells and eosinophilic infiltration, signaling the development of a neurogenic inflammatory state. Mast cells serve as key bridges along the neuroimmune axis and are highly responsive to stress signals. Their overactivation triggers an excessive release of mediators that can drive local inflammation, vascular permeability, and pruritus.

Ultimately, CSS creates a highly detrimental environment where the skin is immunologically weakened yet concurrently trapped in a persistent, low-grade inflammatory state. Such a state may explain why chronic stress is associated with worsening of inflammatory dermatoses, increased itching, impaired barrier function, and delayed tissue recovery [1, 4, 7].

Conclusion. CSS causes significant structural and immunological disturbances in the skin, leading to impairment of epidermal barrier integrity and dysregulation of local immune responses. Stress-induced epidermal thinning, abnormal keratinization, and vascular changes were accompanied by suppression of innate and adaptive immune components, while resident mast cells showed pronounced activation. These findings indicate that chronic stress disrupts skin homeostasis through combined barrier damage, immune suppression, and activation of pro-inflammatory neuroimmune mechanisms.

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