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A Unified Spatial–Healing Threshold Model Explaining Minor Recurrent Aphthous Stomatitis

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ABSTRACT

Minor recurrent aphthous stomatitis (RAS) is a common, painful, and self-limiting disorder of the oral mucosa characterized by episodic ulceration, a strong predilection for non-keratinized sites, spontaneous healing, and migratory recurrence. Despite extensive investigation, prevailing trauma-based, immune-centric, and nutritional models fail to account simultaneously for the sharply localized onset of lesions, their intermittent nature, and their tendency to shift between sites. Here, we propose a Unified Spatial–Healing Threshold Model in which ulceration arises only when two necessary conditions converge at the same site and time: (i) the dynamic formation of localized epithelial–immune weak points driven by cumulative subclinical mechanical microstrain, and (ii) a transient reduction in epithelial reparative capacity due to systemic modifiers such as psychological stress or functional hematinic insufficiency. Ulceration represents a nonlinear threshold phenomenon. It occurs when the rate of epithelial damage exceeds contemporaneous repair capacity. Subsequent epithelial renewal restores local resistance, while redistribution of mechanical forces generates new vulnerable sites, explaining spontaneous healing and site-shifting recurrence. This unified framework integrates mechanobiological, immunological, and healing-based theories into a single coherent and testable model with clear clinical and research implications.

Introduction

Minor recurrent aphthous stomatitis is among the most prevalent disorders of the oral mucosa, presenting as shallow, painful ulcers that typically resolve within 7–14 days yet recur unpredictably over months or years. Although histopathologically benign, recurrent episodes significantly impair mastication, speech, and quality of life. Numerous associations—including genetic susceptibility, immune dysregulation, nutritional deficiencies, psychological stress, and local trauma—have been consistently reported.[1–6] However, no single explanatory framework adequately accounts for the defining clinical paradoxes of minor RAS: sharply localized lesion development despite diffuse exposure to potential insults, episodic onset with spontaneous resolution, and characteristic migration of lesions between sites.

The oral mucosa is continuously exposed to mechanical forces capable of producing microscopic epithelial disruption, yet clinically apparent ulceration remains rare, focal, and self-limited. This discrepancy suggests that minor RAS does not arise from a single dominant etiologic factor but from the convergence of spatially localized vulnerability and temporally reduced healing capacity. We therefore propose a unified hypothesis that explicitly integrates these spatial and temporal dimensions, reframing minor RAS as a dynamic, threshold-governed failure of mucosal homeostasis rather than a primary inflammatory or traumatic disease.[7]

Physiological Baseline: Mechanical Microstrain and Efficient Repair

Mechanical Microstrain as a Normal State

Normal oral activities—including mastication, speech, swallowing, parafunctional habits, and contact with dental restorations—generate continuous low-grade mechanical microstrain across the oral mucosa. Such forces frequently induce microscopic epithelial disruptions that are ordinarily clinically silent due to the exceptional regenerative capacity of oral epithelium. Mechanical microstrain should therefore be regarded as a physiological baseline rather than an inherently pathological insult.[8–11]

Robust Epithelial Repair

Under healthy conditions, oral epithelial homeostasis is maintained through rapid keratinocyte proliferation and migration, efficient differentiation, angiogenic support, and tightly regulated immune resolution. Minor epithelial injuries are rapidly repaired, preventing progression to overt ulceration. Pathogenic relevance therefore arises not from force magnitude or injury alone, but from conditions in which epithelial adaptive reserves are locally exhausted or reparative capacity is transiently impaired.

Spatial Axis: Dynamic Formation of Epithelial–Immune Weak Points

Oral Mucosal Heterogeneity and Site Specificity

Non-keratinized oral mucosa is thinner, more permeable, and more mechanically compliant than keratinized mucosa, rendering it particularly susceptible to repetitive loading. Keratinocytes in these regions exhibit heightened mechanosensitivity and rapidly upregulate stress-responsive mediators under load. Reduced keratinization, altered lipid composition, and looser intercellular junctions collectively lower the biomechanical and immunological thresholds for barrier disruption under repetitive stress, explaining the characteristic site specificity of minor RAS.[12]

Definition of Epithelial–Immune Weak Points

Epithelial–immune weak points are defined here as transient, spatially restricted zones in which cumulative subclinical mechanical microstrain has reduced epithelial adaptive reserve and primed local immune responsiveness without overt tissue injury. These weak points are clinically silent but represent areas of diminished resilience.

Cumulative Subclinical Microstrain and Mechanotransduction

While individual mechanical events remain below the injury threshold, repetitive site-specific microstrain may progressively erode epithelial adaptive capacity, creating localized zones of vulnerability. Through established mechanotransduction pathways involving integrins, cytoskeletal tension, and signaling cascades such as NF-κB and YAP/TAZ, repeated mechanical stress induces a primed epithelial state characterized by subtle barrier dysfunction, altered tight-junction organization, increased permeability, and low-level cytokine signaling. Importantly, weak-point formation is dynamic rather than fixed; these zones form, resolve, and migrate as mechanical forces are redistributed during routine oral function.

Temporal Axis: Impaired Healing Threshold

Concept of Healing Capacity

Healing capacity refers to the integrated ability of the oral mucosa to maintain barrier integrity through epithelial turnover, metabolic support, immune regulation, and timely resolution of inflammation. While weak-point formation is common, ulceration occurs only when this reparative capacity is temporarily reduced.

Systemic Modifiers of Repair

Functional or subclinical deficiencies in hematinic factors such as iron, folate, and vitamin B12 may impair epithelial proliferation and delay re-epithelialization even in the absence of overt deficiency. Psychological stress further reduces reparative efficiency through neuroendocrine–immune interactions that alter cytokine balance, cellular metabolism, and wound-healing dynamics. Acute illness, hormonal fluctuations, and systemic inflammatory states may exert similar permissive effects. Importantly, these systemic modifiers do not initiate ulceration; rather, they lower the biological threshold at which repair mechanisms can successfully counterbalance ongoing microinjury.[13_16]

Variability of the Healing Threshold

The healing threshold is probabilistic, site-specific, and temporally variable. At any given moment, the balance between epithelial damage and repair differs across mucosal sites depending on local vulnerability and systemic conditions.

Threshold Convergence and Ulcer Formation

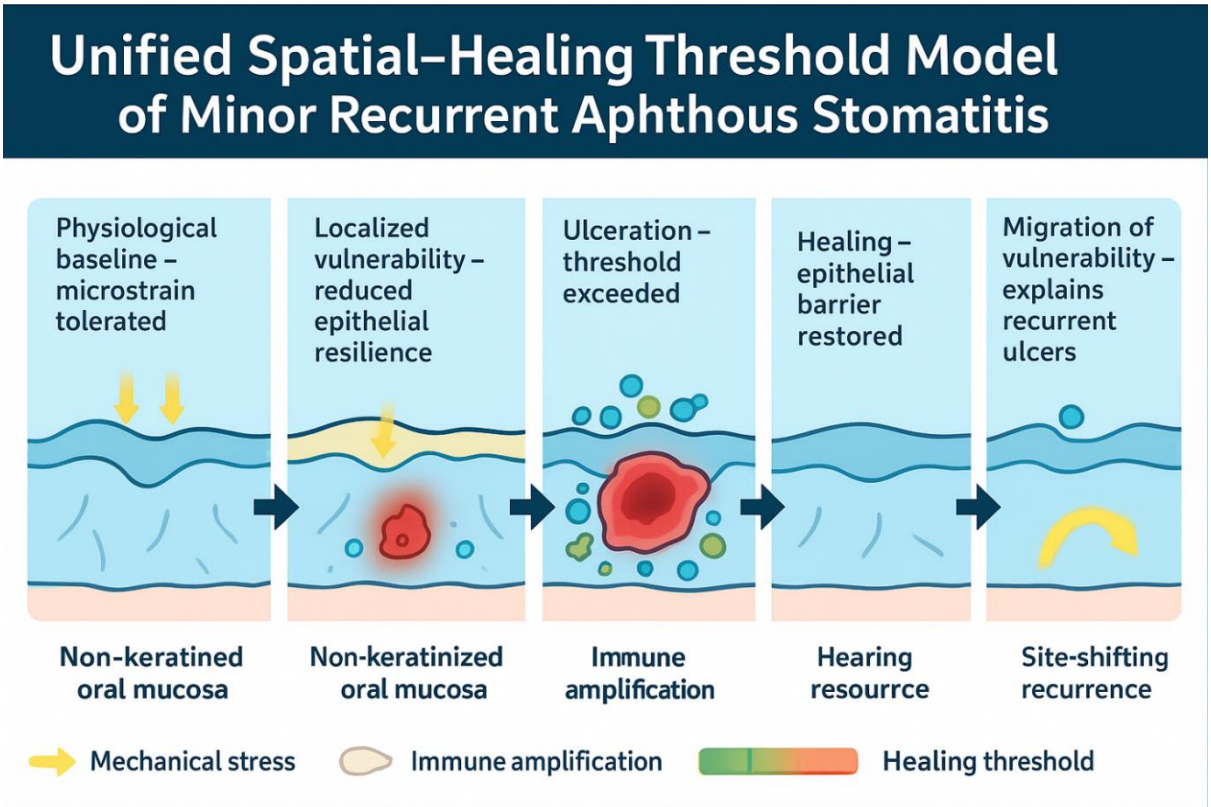
Ulceration represents a nonlinear threshold phenomenon that occurs only when two conditions coincide at the same site and time: (i) a spatially localized epithelial–immune weak point generated by cumulative mechanical microstrain, and (ii) a transient reduction in epithelial healing capacity. When the rate of epithelial damage at a vulnerable site exceeds the maximal achievable rate of repair under prevailing systemic conditions, localized epithelial breakdown ensues.[17]

The ensuing immune response is predominantly innate and spatially constrained, involving neutrophils, macrophages, and resident T cells. Tissue damage is amplified locally yet remains self-limited because adjacent mucosa has not crossed the same vulnerability–repair

threshold. Exposure of subepithelial nerve endings and sensitization of local nociceptors account for the disproportionate pain associated with small aphthous ulcers.[18]

Healing, Resolution, and Site Shifting

Once ulceration occurs, inflammatory and regenerative pathways are robustly activated, leading to rapid keratinocyte proliferation, migration, and re-epithelialization. Healing restores epithelial barrier integrity and is accompanied by temporary local resistance due to epithelial renewal and immune regulatory feedback. Importantly, healing also alters subsequent force distribution during routine oral function, biasing cumulative microstrain toward other non-keratinized regions. This redistribution explains the characteristic site-shifting recurrence observed in minor RAS.



Integration With Existing Theories

This unified model does not negate immune-mediated, trauma-based, or nutritional theories of RAS; rather, it integrates them within a hierarchical framework. Mechanical microstrain provides the initiating substrate, weak-point formation explains spatial specificity, systemic modifiers determine temporal permissiveness, and immune responses mediate focal tissue breakdown and repair. The explicit requirement for spatiotemporal threshold convergence distinguishes this model from prior association-based explanations.

Testable Predictions

The Unified Spatial–Healing Threshold Model generates several falsifiable predictions:

- Pre-ulcerative sites will demonstrate increased epithelial permeability, altered tight-junction organization, and markers of mechanical stress prior to visible ulceration.
- Periods preceding ulcer onset will be associated with reduced epithelial proliferative indices or delayed wound-closure capacity, even in the absence of overt hematinic deficiency.
- Interventions that reduce localized mechanical microstrain or enhance epithelial repair efficiency will decrease ulcer frequency and severity.
- Longitudinal mapping will demonstrate migratory lesion patterns consistent with redistribution of mechanical forces across non-keratinized mucosa.

Clinical and Research Implications

Reframing minor RAS as a disorder of convergent spatial vulnerability and impaired healing shifts therapeutic emphasis from nonspecific immunosuppression toward prevention and resilience enhancement. Strategies aimed at optimizing epithelial repair capacity, correcting functional nutritional deficiencies, mitigating psychological stress, and minimizing localized mechanical strain may provide more durable clinical benefit. From a research perspective, the model supports longitudinal, site-specific studies integrating biomechanics, epithelial biology, immune profiling, and microbiome analysis.

Limitations

This hypothesis is conceptual and does not yet quantify mechanical strain thresholds or reparative capacity parameters. The biological pathways proposed are broadly established in epithelial biology but require direct validation in the context of RAS. The model is primarily intended to explain minor RAS and may require modification to fully account for major or herpetiform variants.

Conclusion

Minor recurrent aphthous stomatitis is best understood as a dynamic threshold disorder arising from the intersection of site-specific epithelial–immune vulnerability and transient impairment of epithelial healing. By explicitly integrating spatial and temporal dimensions of disease expression, this Unified Spatial–Healing Threshold Model provides a coherent explanation for lesion localization, episodic occurrence, spontaneous healing, pain, and migratory recurrence, while offering a robust platform for future mechanistic and clinical investigation.

References

1. Scully C, Porter S. Oral mucosal disease: recurrent aphthous stomatitis. *Br J Oral Maxillofac Surg.* 2008;46(3):198–206.
2. Porter SR, Scully C, Pedersen A. Recurrent aphthous stomatitis. *Crit Rev Oral Biol Med.* 1998;9(3):306–321.

3. Akintoye SO, Greenberg MS. Recurrent aphthous stomatitis. *Dent Clin North Am.* 2014;58(2):281–297.

4. Preeti L, Magesh KT, Rajkumar K, Karthik R. Recurrent aphthous stomatitis. *J Oral Maxillofac Pathol.* 2011;15(3):252–256.

5. Feller L, Khammissa RAG, Chandran R, et al. Pathogenesis of recurrent aphthous stomatitis. *J Int Med Res.* 2017;45(6):1671–1681.

6. Field EA, Allan RB. Oral ulceration—aetiopathogenesis, clinical diagnosis and management. *Br J Oral Maxillofac Surg.* 2003;41(1):1–15.

7. Natah SS, Häyrinen-Immonen R, Hietanen J, et al. Immunopathogenesis of recurrent aphthous ulcers. *J Oral Pathol Med.* 2000;29(1):19–25.

8. Bosshardt DD, Lang NP. The junctional epithelium: from health to disease. *J Dent Res.* 2005;84(1):9–20.

9. Choi YS, Kim Y, Yoon HJ, et al. Tight junction proteins in oral epithelial barrier function. *Oral Dis.* 2019;25(4):1033–1044.

10. Prime SS, Pring M. Keratinocyte function and oral mucosal disease. *Oral Dis.* 2019;25(1):17–29.

11. McKay TB, Hutcheon AEK, Guo X, et al. Mechanotransduction in epithelial tissues. *Exp Eye Res.* 2020;197:108080.

12. Freysdottir J, Zhang S, Tilakaratne WM, Fortune F. The oral mucosa and immunity. *J Oral Pathol Med.* 2019;48(6):459–467.

13. Volkov I, Rudoy I, Freud T, et al. Effectiveness of vitamin B12 in treating recurrent aphthous stomatitis: a randomized, double-blind, placebo-controlled trial. *J Am Board Fam Med.* 2009;22(1):9–16.

14. Lalla RV, Choquette LE, Feinn RS, et al. Multivitamin therapy for recurrent aphthous stomatitis: a randomized, double-masked trial. *J Am Dent Assoc.* 2012;143(4):370–376.

15. Marucha PT, Kiecolt-Glaser JK, Favagehi M. Mucosal wound healing is impaired by examination stress. *Psychosom Med.* 1998;60(3):362–365.

16. Glaser R, Kiecolt-Glaser JK. Stress-induced immune dysfunction: implications for health. *Nat Rev Immunol.* 2005;5(3):243–251.

17. Chen GY, Nuñez G. Sterile inflammation: sensing and reacting to damage. *Nat Rev Immunol.* 2010;10(12):826–837.

18. Dutzan N, Konkel JE, Greenwell-Wild T, Moutsopoulos NM. Characterization of the human oral immune cell network. *Nat Immunol.* 2016;17(12):1395–1402.