

When Autoimmunity Outlives Its Trigger

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Abstract. Autoimmune disease may persist after an initiating infection or tissue injury because antigen spreading, persistent autoreactive populations, tissue damage and inflammatory feedback can become independently important. This is one of several pathways to autoimmunity, not a proof that every autoimmune disease began with a hidden pathogen.

Initiation is often uncertain

An infection can sometimes precede autoimmune disease, and microbial mimicry or tissue injury can plausibly contribute to loss of tolerance. Yet temporal proximity alone does not establish causation, and many autoimmune conditions have complex genetic and environmental susceptibility without a confirmed single microbial cause. The fact that patients worsen during infections can also reflect nonspecific immune activation rather than evidence that an occult organism is driving their illness.

How responses diversify

Once immune recognition of self becomes established, tissue injury may expose additional antigens. Recruited immune cells, cytokines and local antigen-presenting pathways can maintain inflammation. Epitope spreading is one possible process through which the target of an immune response broadens over time. Distinct autoimmune diseases vary in the relevance of this mechanism and in the degree to which antibodies, T cells and innate processes dominate.

The tissue also becomes a participant

Chronic immune injury changes fibroblasts, vessels and the extracellular matrix. Such local alterations can continue impairing organ function even if autoantibody levels improve or systemic inflammation diminishes. This provides a reason to distinguish immunological remission from reversal of structural damage. Persistent fibrosis after inflammation is controlled is not evidence that treatment failed to target the immune disease.

A causation problem

Consider three hypotheses: a current infection continuously drives inflammation; a previous infection initiated a self-sustaining autoimmune response; or infection is an unrelated coincident event. Each requires different evidence. One cannot assume the first merely because the second is biologically possible. Carefully evaluated serology, tissue pathology, microbiology and disease history help avoid category errors.

Limits and implications

This model should not be used to recommend prolonged antimicrobials for autoimmune diseases without documented infection, nor to discontinue disease-modifying treatment. The primary intellectual contribution is the separation of **trigger, perpetuator and damage**. Successful care may need to address the perpetuating immune process and manage residual injury even when the original initiating event can never be reconstructed.

A strong infection-triggered model needs specificity

A persuasive account should identify the microorganism, immune target, susceptible host group and expected timing. 'Infection causes autoimmunity' is too broad to be useful. Certain postinfectious autoimmune phenomena have recognizable links; others remain speculative or controversial. Genetic predisposition can help shape the response, and the absence of a clear infectious history does not invalidate a verified autoimmune diagnosis.

Durable immune activity may be independent of trigger

Once autoreactive populations or tissue-local immune loops become established, removal of an initial environmental factor may not be sufficient for remission. In some conditions, immune memory and ongoing target recognition continue. The result resembles the general problem of hysteresis: the path back is not identical to the path in. But unlike purely mathematical analogies, autoimmunity must be demonstrated with immune pathology and clinical course, not inferred from the mere persistence of symptoms.

Why therapeutics still matter

Disease-modifying therapy may reduce inflammatory damage and preserve organ function even when the initial cause remains unknown. Explaining persistence through self-sustaining immunity should reinforce, not undermine, rational treatment. In contrast, administering empiric antiparasitic, antibiotic or 'detoxification' regimens without evidence of an active organism risks distracting from effective care. The proper frontier question is which maintaining loop is present and accessible, not whether every autoimmune disorder conceals the same trigger.

Selected scientific reading

1. [Netea MG et al. Defining trained immunity and its role in health and disease. Nat Rev Immunol. 2020;20:375–388.](#)
2. [Serhan CN. Pro-resolving lipid mediators are leads for resolution physiology. Nature. 2014;510:92–101.](#)
3. [Tabas I. Macrophage death and defective inflammation resolution in atherosclerosis. Nat Rev Immunol. 2010;10:36–46.](#)

Editorial status: Conceptual scientific essay, not peer reviewed. Not original clinical data, a treatment protocol or medical advice. Selected readings are not a systematic review. Evidence and interpretation should be assessed independently.