

Root Causes of Autoimmune & Immune Dysregulation Disease

A Comprehensive Framework

Integrating Biological, Environmental & Psycho-Emotional Root Causes

Framing Principles

Before examining root causes, three foundational principles shape how this framework is organized:

Inflammation is not a root cause.

Inflammation is the immune system's output when it detects an unresolved threat — it is the alarm, not the fire. The clinical question is always: what is keeping the alarm activated? Chronic inflammation, once established, becomes self-sustaining and is treated as a root cause in this framework for that reason — but the origin is always upstream.

Autoimmune disease is not a root cause.

An autoimmune diagnosis describes what happened, not why. It is a downstream outcome — a label for the pattern of immune failure rather than its origin. The question behind every autoimmune diagnosis is: what broke immune tolerance, and why can the body not restore it?

Pathogens occupy a dual position.

Terrain weakness allows chronic pathogen establishment, but once established, viruses, bacteria, parasites, and fungi actively engineer immune suppression to ensure their own survival. They become self-sustaining root causes — not merely passengers in a weakened system. A healthy terrain may clear the same exposure that becomes chronic in a compromised one.

Root causes compound and interact.

Rarely is a single category sufficient to produce disease. It is typically an accumulation — genetic susceptibility combined with toxin burden, emotional trauma, and pathogen load — that crosses the threshold into immune dysregulation. Some traditions describe this as a person's overall vital force or resilience; science maps it as allostatic load. Both point to the same reality: the body has a threshold, and crossing it requires multiple simultaneous pressures.

TIER 1 — Root Causes

The following categories directly dysregulate immune terrain. They are the originating pressures that, alone or in combination, break the body's capacity to maintain immune balance.

1. Genetics

Including methylation disorders (MTHFR and related variants). Genetic variants affect detoxification pathways, neurotransmitter production, DNA repair, and immune regulation at the most fundamental level. Risk is polygenic — it accumulates across many variants rather than residing in a single gene. Cannot be acquired, only managed.

Methylation is of particular importance: impaired methylation reduces the body's ability to clear toxins, regulate inflammation, and maintain immune homeostasis. Primary mitochondrial genetic disorders also belong here — individuals born with impaired cellular energy production face immune vulnerability from the outset.

Some frameworks describe genetic predisposition as the hand one is dealt at the soul level — the constitutional terrain into which a life unfolds.

2. Epigenetics

Ancestral and maternal programming that alters gene expression without changing DNA sequence. Includes inherited trauma responses, in-utero toxic exposures, and generational patterns of illness or stress. Your immune baseline is partly set by what your mother and grandmother experienced — their nutritional status, toxic burden, emotional landscape, and infections during pregnancy.

Epigenetics is distinct from genetics because it is potentially reversible. What was imprinted through ancestral experience can, in principle, be reprogrammed through environment, nutrition, therapy, and practice. This distinction carries both clinical and philosophical significance — it suggests that inherited patterns are not fixed destiny.

Many healing traditions speak of ancestral burdens carried in the lineage. Epigenetics gives this idea a molecular language.

3. Heavy Metals

Mercury, lead, arsenic, cadmium, aluminum. These accumulate in tissue and organs over decades with no natural elimination pathway adequate to the burden of modern exposure. They directly impair enzyme function, mitochondrial integrity, immune cell activity, and neurological function.

Mercury is of particular concern — profoundly mitotoxic and immunotoxic, it is found in dental amalgam, certain fish, vaccines (historically thimerosal), and industrial pollution. Lead accumulates in bone. Aluminum, the most abundant metal in the Earth's crust, is increasingly

present in food, water, antiperspirants, and vaccine adjuvants, where it functions as a deliberate immune stimulant.

Removal requires active intervention — the body cannot clear these through ordinary detoxification. Genetic variants (particularly in MTHFR and metallothionein pathways) determine how much an individual accumulates from the same level of exposure.

4. Chemicals / Xenobiotics

Synthetic foreign molecules for which the body has no evolutionary clearance toolkit: pesticides (glyphosate being the most pervasive), PFAS ("forever chemicals"), BPA and phthalates (endocrine disruptors in plastics), fossil fuel byproducts, pharmaceutical residues in water supply, flame retardants, and industrial solvents.

Mechanisms include direct endocrine disruption, gut microbiome disruption, mitochondrial interference, and immune dysregulation. Microplastics — now documented in human blood, brain tissue, placenta, and breast milk — represent a subcategory with no known clearance pathway. The immune system encounters them as foreign but cannot resolve the encounter.

Glyphosate deserves particular attention: it chelates minerals (impairing nutritional status), disrupts gut bacteria, impairs cytochrome P450 liver enzymes (critical for detoxification), and has been found in a high percentage of conventional food samples tested.

5. Microtoxins

Persistent biological debris — not living pathogens, but their toxic byproducts or structural fragments. The defining characteristic is that the immune system is triggered but has nothing to resolve: an alarm with no off switch.

Key examples:

- Spike protein (viral debris): whether from infection or exposure, spike protein can persist in lymph nodes and tissues, bind ACE2 receptors, trigger innate immune alarm signals, and drive autoantibody formation through molecular mimicry — without the active virus being present.
- Bacterial LPS / endotoxins: lipopolysaccharide from gram-negative bacteria is one of the most potent innate immune triggers known. Gut permeability allows LPS into systemic circulation, driving chronic low-grade inflammatory activation.
- Mycotoxins: chemical outputs of fungi (aflatoxin, ochratoxin, trichothecenes) that persist in the body and food supply. Simultaneously immunosuppressive and pro-inflammatory, directly disruptive to mitochondrial function.

If pathogens are the invaders, microtoxins are the wreckage left behind — and wreckage, unlike invaders, cannot be fought.

6. Nutritional Deficiencies / Diet

The immune system requires specific raw materials to function. Chronic deficiency impairs immune competence at the cellular level. Diet is the behavioral input; deficiency is the biological consequence.

Processed food, industrial seed oils (high in omega-6 linoleic acid), and ultra-refined carbohydrates drive chronic low-grade inflammatory signaling independent of specific nutrient deficiencies. The modern Western diet is, in mechanistic terms, a slow inflammatory stimulus.

Critical nutrients for immune regulation include vitamin D, omega-3 fatty acids, zinc, selenium, iodine, magnesium, vitamin A, and vitamin C. Deficiency in any of these directly impairs specific arms of the immune response.

7. Vitamin & Mineral Imbalances

Distinct from pure deficiency: imbalance includes excess and poor cofactor ratios. The body operates on mineral relationships — calcium requires magnesium for proper metabolism; iron requires copper; zinc and copper compete for absorption. Supplementing one without the other can create functional deficiency in its cofactor.

Vitamin D is the most researched immune regulator — it directly governs T-cell differentiation, promotes tolerance, and modulates both innate and adaptive immunity. Low vitamin D is strongly and consistently associated with increased autoimmune risk across diverse populations.

Iron dysregulation deserves mention: both deficiency and excess impair immune function. Excess iron feeds pathogenic bacteria and drives oxidative stress. Ferritin elevation is increasingly recognized as a marker of chronic immune activation rather than iron sufficiency.

8. Gut Dysbiosis & Intestinal Permeability

The gut houses approximately 70% of immune tissue. The microbiome is not a passive passenger — it actively trains the immune system, regulates inflammatory tone, and maintains the integrity of the intestinal barrier. Dysbiosis (disruption of microbial balance) impairs all of these functions simultaneously.

Intestinal permeability ("leaky gut") allows bacterial LPS, undigested food proteins, and microbial fragments into systemic circulation, triggering sustained immune activation and driving food sensitivities, systemic inflammation, and autoantibody formation.

Gut dysbiosis can be established at birth through maternal microbiome status, C-section delivery (bypasses vaginal seeding), formula feeding (bypasses colostrum and breast milk immune factors), and early antibiotic exposure. This means the foundational immune terrain can be compromised before a child encounters any other environmental challenge.

Once established, dysbiosis becomes self-sustaining: dysbiotic bacteria produce metabolites that suppress beneficial species, maintain permeability, and perpetuate inflammation.

9. Viruses

Intracellular pathogens that hijack host cell machinery. Some establish latency — integrating into the genome or persisting in immune cells (EBV, CMV, herpes family, enteroviruses). Latent viruses reactivate under conditions of stress or immune suppression, creating cycles of chronic immune activation.

Viruses are well-documented drivers of molecular mimicry: viral proteins that share sequence homology with human tissue can, after the acute infection resolves, leave behind autoantibodies that cross-react with self. EBV has been linked to multiple sclerosis, lupus, rheumatoid arthritis, and Hashimoto's thyroiditis.

A first viral hit — in a person with no prior terrain compromise — can be sufficient to initiate immune dysregulation that persists for decades. The virus need not be ongoing; the immune reprogramming it triggered may be.

Note: Chronic viral infection produces sustained cytokine release that crosses the blood-brain barrier, activates neuroinflammation, and dysregulates the limbic system — creating a biological state of chronic threat that is indistinguishable from the neurological pattern of unresolved trauma. These two pathways compound each other powerfully when both are present.

10. Bacteria

Extracellular pathogens with potent immune-activating properties. LPS from gram-negative bacteria is among the most powerful innate immune triggers known. Chronic bacterial infections form biofilms — structured communities highly resistant to both immune clearance and antibiotic treatment — allowing indefinite persistence in tissues.

Molecular mimicry is well-documented: group A streptococcus triggers rheumatic fever through cross-reactivity with cardiac tissue. *H. pylori* is linked to autoimmune gastric conditions. *Borrelia* (Lyme) has been associated with diverse autoimmune presentations.

A key clinical question with chronic bacterial infection is always terrain: why is the immune system failing to clear what a healthy system would resolve? The answer typically involves one or more upstream Tier 1 factors — nutritional deficiency, toxin burden, genetic immune variants, or emotional suppression of immune function. Treating the bacteria without addressing terrain typically produces incomplete or temporary resolution.

Note: Chronic bacterial burden drives the same neuroinflammatory pathway as viruses — sustained cytokine elevation, microglial activation, and limbic dysregulation that entrench the fight-or-flight state.

11. Parasites

Eukaryotic organisms ranging from single-celled protozoa to macroscopic worms. Rather than triggering a straightforward immune response, parasites often hijack it — driving a Th2-dominant immune shift that actively suppresses the Th1 response needed to fight bacteria and viruses. Chronic parasitic burden creates broad immune vulnerability across all pathogen categories.

Parasites actively secrete immunosuppressive compounds, manipulate Th1/Th2/Th17 balance, and engineer host tolerance of their presence — making them, like all chronic pathogens, active architects of the immune dysfunction that sustains them.

Massively underdiagnosed in developed countries, where the assumption that parasites are a developing-world problem delays recognition. *Blastocystis hominis*, *Toxoplasma gondii*, *Giardia*,

and intestinal helminths are more prevalent in modern populations than commonly acknowledged.

Toxoplasma deserves specific mention: it crosses the blood-brain barrier and has been documented to alter host behavior, personality, and risk tolerance — serving its own survival at the cost of the host's neurological integrity.

The psycho-emotional parallel is striking: the inability to expel what drains and feeds from you at the relational level may mirror — and may reinforce — the biological inability to clear what parasitizes at the physical level.

12. Fungi / Yeast / Mold

Fungi are eukaryotic organisms — sharing cellular machinery with human cells — which makes them uniquely difficult to treat without collateral damage, and uniquely capable of establishing chronic residence. Three distinct but interacting threats operate under this category:

Yeast Overgrowth (Candida)

Candida is normally present in small amounts. Under conditions of dysbiosis, antibiotic disruption, high-sugar diet, or immune suppression, it morphs from benign yeast to invasive hyphal form — physically penetrating the gut lining and directly contributing to intestinal permeability.

Candida produces gliotoxin, which specifically impairs neutrophil and macrophage function — the immune system's first responders — and forms biofilm that hides it from immune detection. It actively maintains the intestinal permeability it helped create, establishing a self-perpetuating cycle.

Environmental Mold

Aspergillus, Stachybotrys, Penicillium, and others colonize sinuses, lungs, and gut simultaneously. Colonization can persist for years following exposure to water-damaged buildings — which affect a substantial proportion of structures in regions with significant rainfall. Mold creates local immunosuppressive environments that enable deeper colonization and systemic impact.

Mycotoxins

The chemical output of fungi. Aflatoxin, ochratoxin, and trichothecenes are simultaneously immunosuppressive and pro-inflammatory — an unusual combination that destabilizes immune calibration. They persist in the body and in the food supply long after the mold source is removed, and directly disrupt mitochondrial function.

13. Radiation

An underappreciated category with distinct subtypes:

- Ionizing radiation (X-ray, CT scan, nuclear, radon gas): directly damages DNA, destroys immune cells, and causes long-term immune suppression. Cumulative medical imaging exposure is a largely untracked burden in modern populations.

- Non-ionizing radiation (EMF, wireless frequencies, 5G): the mechanistic evidence for mitochondrial disruption, oxidative stress, and immune dysregulation is accumulating, though population-level causal evidence remains under active investigation. The precautionary case for minimizing exposure is reasonable given the pace of proliferation.
- UV radiation: well-established immune modulator — immunosuppressive in excess, beneficial in appropriate doses through vitamin D synthesis and other photobiological mechanisms.

14. Chronic Inflammation (Self-Sustaining)

Mechanistically downstream in origin, but clinically self-sustaining once established. Chronic inflammation rewires immune programming, damages tissue, generates new autoantigens from that damaged tissue, and thereby creates its own ongoing triggers. It is an alarm that has learned to sound itself.

NF- κ B (nuclear factor kappa B) is the master switch for inflammatory gene expression. Once chronically activated, it maintains a state of immune alertness that requires active intervention to downregulate. Pro-inflammatory cytokines (IL-1 β , IL-6, TNF- α) at chronically elevated levels directly damage mitochondria, impair hormonal signaling, and dysregulate neurotransmitter systems.

Chronic inflammation is included as a Tier 1 root cause because it actively perpetuates all other categories — it impairs pathogen clearance, worsens gut permeability, depletes nutritional reserves, and drives the limbic dysregulation that sustains psychological stress. It is both downstream and driver simultaneously.

15. Trauma & Unresolved Emotional Burden

The psycho-emotional terrain that suppresses immune function in real time — distinct from epigenetics (inherited programming) and chronic stress (its physiological output). Trauma is the originating wound; unresolved emotional burden is what persists when it goes unprocessed; belief systems are the cognitive structures that perpetuate the wound state without requiring new traumatic events.

Adverse Childhood Experiences (ACEs) & PTSD

The ACE studies established dose-dependent relationships between childhood trauma and adult rates of autoimmune disease, cancer, heart disease, and early mortality. The immune system learns threat calibration in childhood — early experience of unresolvable danger sets a baseline of vigilance that persists neurobiologically into adulthood.

PTSD produces measurable, lasting changes in immune gene expression, cortisol rhythm, NK cell activity, and inflammatory tone. It is not merely psychological — it is a whole-body recalibration toward threat.

Unresolved Grief, Anger & Fear

Prolonged grief measurably suppresses lymphocyte function. Suppressed anger — the inability to set limits, to say no, to protect one's own boundaries — correlates with immune suppression in research and with chronic parasitic and fungal presentations in functional medicine clinical

experience. Fear held chronically in the body maintains the nervous system in a state of contraction that impairs every repair and regulatory process.

Belief Systems

Persistent belief structures that maintain a threat or diminishment state:

- "I am not safe" — maintains chronic sympathetic activation and cortisol elevation
- "I have no control" — learned helplessness directly suppresses NK cell activity in documented research
- "I don't deserve to heal" — unconscious resistance to recovery that can undermine even optimal physical treatment
- "I cannot say no" — the body may mirror an inability to expel what drains it relationally with an impaired capacity to clear what parasitizes it physically

The body does not distinguish between a threat in the environment and a threat held in the mind. Both activate identical neuroimmune cascades.

Some traditions would describe these as the contracts the soul carries — agreements, made consciously or not, about what one is allowed to have, be, or release. The mechanisms through which such patterns operate on immunity are now increasingly mappable in molecular terms.

16. Sleep Deprivation & Circadian Disruption

Sleep is not rest — it is the primary window during which the immune system performs maintenance, consolidates immune memory, clears cellular debris, and resets inflammatory tone. Chronic sleep deprivation (consistently under 6-7 hours) is an independent immune disruptor with measurable consequences distinct from those of stress or any other category.

Key mechanisms:

- NK cell activity drops measurably after a single night of poor sleep — the immune system's primary surveillance against viruses and aberrant cells
- Cytokine regulation is circadian: IL-1 β , IL-6, and TNF- α follow 24-hour rhythms that are disrupted by irregular sleep, shifting the system toward chronic inflammatory tone
- Melatonin — produced during darkness — is a potent immune regulator, antioxidant, and mitochondrial protector. Artificial light at night (screens, LEDs) suppresses melatonin production, impairing its immune functions regardless of total sleep duration
- Glymphatic clearance — the brain's waste-removal system — operates almost exclusively during deep sleep. Impaired clearance allows inflammatory debris and misfolded proteins to accumulate, driving neuroinflammation
- Immune memory consolidation occurs during sleep: T and B cell activation and long-term immune programming are sleep-dependent processes

Circadian rhythm disruption — through shift work, irregular schedules, artificial light exposure, and screen use — dysregulates immune gene expression on a systemic level even when total sleep hours appear adequate. The timing of sleep matters as much as the duration.

Sleep deprivation and circadian disruption are among the few Tier 1 factors that can meaningfully impair immunity within days of onset, making them both an acute and chronic root cause.

Many traditional healing systems place restoration and darkness at the center of recovery — not as comfort but as medicine. The science of sleep immunology is now catching up to what was long understood intuitively.

TIER 2 — Downstream Amplifiers

The following categories are consequences of Tier 1 root causes that then become additional burden — amplifying dysfunction and making resolution more difficult. They require treatment, but treating them without addressing upstream Tier 1 causes typically produces incomplete results.

1. Chronic Stress / HPA Dysregulation

The biological output of unresolved trauma and chronic threat states. Chronic cortisol elevation leads eventually to cortisol resistance — immune cells stop responding to cortisol's anti-inflammatory signaling, removing the primary brake on immune activation. Disrupted circadian cortisol rhythm impairs the repair and regeneration that normally occurs during sleep.

2. Limbic System Dysfunction

The limbic system — amygdala, hypothalamus, hippocampus — governs threat detection and survival responses. It can become stuck in a chronic threat state through two distinct but biologically identical pathways: unresolved psychological trauma, and pathogen-driven neuroinflammation.

Chronic viral or bacterial infection produces sustained pro-inflammatory cytokines (IL-1 β , TNF- α , IL-6) that cross the blood-brain barrier, activate microglia, and directly dysregulate the amygdala and hypothalamus. The body reads chronic infection as permanent danger — and cannot exit fight-or-flight regardless of the actual safety of the environment. These two pathways — psychological and microbial — compound each other when both are present, which they frequently are.

Limbic system retraining (through somatic therapy, DNRS, Gupta Programme, and related approaches) has produced documented improvements in chronic immune conditions — suggesting that the nervous system's threat calibration is a legitimate treatment target independent of physical interventions.

3. Vagus Nerve Dysregulation

The vagus nerve is the physical bridge between emotional and immune function — the primary pathway through which parasympathetic tone regulates inflammation. Vagal tone directly governs gut motility, the integrity of the gut-brain axis, NK cell activity, and anti-inflammatory reflex pathways.

Low vagal tone (impaired parasympathetic function) allows sympathetic dominance, worsens gut motility and dysbiosis, reduces the anti-inflammatory cholinergic reflex, and impairs immune surveillance. Trauma, chronic stress, and chronic infection all suppress vagal tone through overlapping mechanisms.

4. Mitochondrial Dysfunction

Downstream of heavy metals, chemical exposures, viral damage, and chronic inflammation — mitochondrial dysfunction impairs the energy supply that immune cells require to mount and sustain effective responses. Immune cells are among the most metabolically demanding in the body; energy-depleted immune cells are incompetent immune cells.

Mitochondria also regulate apoptosis (programmed cell death) — a process central to immune tolerance. Dysfunctional mitochondria impair the elimination of autoreactive cells, contributing to tolerance failure. Primary mitochondrial genetic disorders (Tier 1) aside, acquired mitochondrial dysfunction is almost always downstream of other root causes.

5. Hormonal Dysregulation

Chronic stress dysregulates cortisol, which suppresses thyroid function. Gut dysbiosis impairs estrogen metabolism through the estrobolome (the subset of gut bacteria that metabolize estrogens). Heavy metals and xenobiotics are direct endocrine disruptors. Chronic inflammation suppresses the conversion of T4 to active T3.

The sex hormone dimension is significant: estrogen upregulates immune responses (partly explaining why ~80% of autoimmune disease occurs in women); testosterone is broadly immunosuppressive. Hormonal imbalance shifts immune calibration toward reactivity. Thyroid dysfunction directly impairs every aspect of immune function through reduced metabolic rate and cellular energy availability.

6. Metabolic Dysfunction

Visceral adipose tissue is not inert — it is an active endocrine organ that continuously secretes pro-inflammatory cytokines (TNF- α , IL-6, leptin) in proportion to its mass. Insulin resistance produces chronic low-grade inflammation and drives glycation of proteins that the immune system may then target as foreign.

High blood sugar and high LDL cholesterol are markers of metabolic dysfunction, not root causes in themselves. They indicate an upstream problem — typically diet, stress, gut dysbiosis, or toxin burden — that requires addressing at its origin.

7. Failure of Immune Tolerance Mechanisms

The cumulative breakdown of the systems that prevent the immune system from attacking self: central tolerance (thymic selection, where autoreactive T cells are normally eliminated), peripheral tolerance (regulatory T cells that suppress escaped autoreactive cells), and immune checkpoints that prevent excessive activation.

This failure is almost always the final common pathway through which Tier 1 root causes produce autoimmune disease — not a cause in itself but the mechanism by which accumulated causes translate into clinical pathology.

8. Immune Dysregulation / Autoimmune Diagnosis

The named disease — lupus, multiple sclerosis, rheumatoid arthritis, Hashimoto's thyroiditis, IBD, psoriasis, and hundreds of others. These diagnoses describe the pattern of immune failure

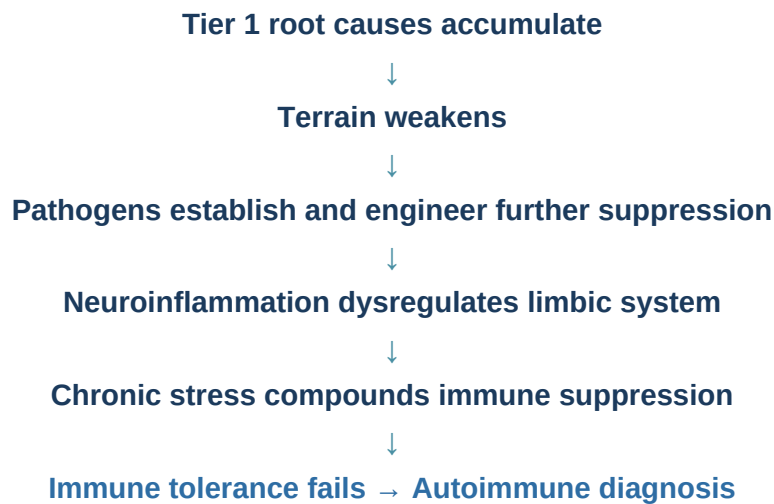
and its target organ, not the origin. They are the end result of accumulated Tier 1 root causes overwhelming immune tolerance over time.

Cancer belongs in this tier as well — representing a failure of immune surveillance (the immune system's ongoing clearance of aberrant cells) that accumulates through the same Tier 1 pressures. Like autoimmune diagnoses, cancer is an outcome of terrain failure rather than a root cause. Once established, both cancer and autoimmune disease actively suppress immunity to survive — becoming additional burden in a manner analogous to the chronic pathogens in Tier 1.

Lymphatic congestion — the accumulation of immune debris and metabolic waste in the lymphatic system — similarly belongs here. It results from chronic inflammation, sedentary lifestyle, and toxin burden, and then amplifies immune dysfunction by impairing clearance of the very debris driving the problem.

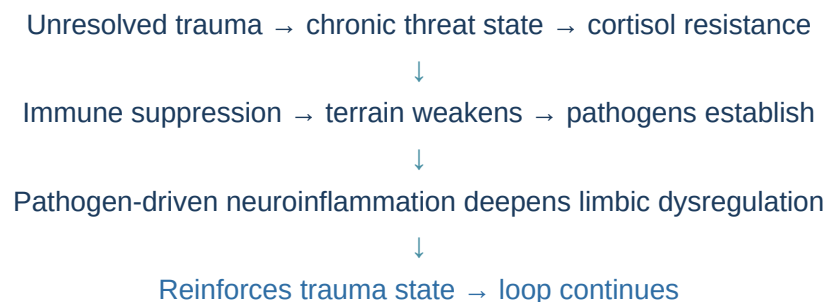
The Core Loop

Most chronic immune disease follows a recognizable cascade:



The Trauma Intersection

Unresolved trauma intersects at every level of the cascade and creates its own parallel loop:



Resolution requires working across multiple tiers simultaneously. There is rarely a single root cause to address — and addressing only physical causes while ignoring emotional terrain, or addressing emotional causes while ignoring pathogen burden and toxin load, typically produces incomplete healing.

Every map is a simplification of territory more complex than any framework can fully capture. This one is offered not as a definitive answer but as a more complete set of questions — a wider lens through which to look when the obvious approaches have not been enough.