BeyondMold

CLINICAL PRIMER

CDR / ISRMT PHENOTYPE SERIES · NO. A

The Stuck Alarm

Phenotype A · Stuck Alarm

Quieting an active CDR1 danger signal — the anti-inflammatory, pro-resolution, mast-cell, and barrier agents that turn the alarm down, and the autonomic work that retrains it.

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ORIENTATION · HOW TO READ THIS PRIMER

Quieting an alarm that is still firing

This is the Phenotype A companion to the Beyond Mold phenotype series. It assumes the reader works inside the CDR/ISRmt model and the four-phenotype classification — A Stuck Alarm, B Drained Battery, C Worn-Out Defender, D Closed Gate — and that the staging baseline has been run. Its job is to lay out, in clinical detail, the agents that **turn down an active CDR1 danger signal** and help it finally resolve.

Each agent is presented the same way: mechanism, a practical dosing summary, the caution profile, and a plain statement of where it fits and how strong the evidence is. Agents are grouped by the lever they pull, not by drug class, because in this phenotype the lever is what matters.

THE CARDINAL RULE OF PHENOTYPE A

Do not silence an alarm that is still accurate. Phenotype A is, by definition, often *still receiving a real danger input* — ongoing exposure, an unremediated environment, a persistent infectious or food-antigen driver. The first and most powerful intervention is to **remove the input**; anti-inflammatory agents layered over a live exposure will disappoint. Confirm the environment before reaching for anything below. And do not deploy the gate-opening neuropeptides of Phenotype D (VIP) here — an alarm that is still firing is not a closed gate.

01 · THE PHENOTYPE

What CDR1-Dominant actually is

Phenotype A is **active CDR1** — a sustained innate-immune alarm that has not resolved. The hallmark mechanism is persistent purinergic signaling: extracellular ATP acting on P2X7/P2X4 receptors maintains MMP-9 release from neutrophils, macrophages, and mast cells, activates the NLRP3 inflammasome, and perpetuates a reactive neuroinflammatory state. The mitochondrial compartment is engaged but not yet arrested — GDF15/FGF21 are normal or only mildly elevated — and the neuroendocrine all-safe signal is stressed but not yet depleted.

The single most useful clinical sign is **location dependence**: symptoms worsen at the exposure site and partially improve away from it, reflecting CDR1's dependence on continued danger input. Fatigue is reactive rather than post-exertional; the nervous system feels "electric" or "vibrating" rather than psychologically anxious; sleep is hyperarousal insomnia.

The A2 sub-pattern — the conditioned alarm

In **A2 (neuroimmune / limbic)**, the CDR1 alarm has become limbically encoded: mast-cell hyperactivation, multiple chemical sensitivities, and neuroinflammation persist *even after the original trigger is removed*, because

the nervous system itself has become a perpetuating input. TGF-β1 may be elevated. A2 is where the psychological and autonomic arm (Section 07) carries much of the load — agents quiet the periphery, but the conditioned circuit must be retrained.

Laboratory signature

Domain	Phenotype A pattern
Trigger panel	Positive — mycotoxins, tick-borne/herpesvirus, food-antigen IgG/IgA, or stool dysbiosis still supplying danger input.
MMP-9	Elevated (>332 ng/mL) — the innate-response-persistence marker; the alarm is still firing.
GDF15 / FGF21	Normal or only mildly elevated — ISRmt not yet dominant (distinguishes from B/C).
CD3 / CD4 / NK	Normal — immunity intact (distinguishes from C).
VIP / α-MSH	Low-normal, not critically depleted — the gate is not yet closed (distinguishes from D).
HRV	Acutely reduced (sympathetic dominance), not structurally collapsed.

02 · STRATEGY

The logic of quieting the alarm

Phenotype A opens to four reinforcing levers, applied on a foundation of confirmed exposure control:

- **Remove the input** — remediation/relocation, trigger clearance, infection and food-antigen control. This is the cardinal move and the prerequisite for everything else.
- **Quiet innate & purinergic signaling** — damp NF-κB, NLRP3, microglial/TLR4 activation, and the leukotriene/COX arms.
- **Stabilize mast cells** — central to the A2/MCAS overlap.
- **Actively resolve** — supply specialized pro-resolving mediators so inflammation switches *off* rather than merely being blocked, and repair barriers. Then retrain the conditioned/limbic alarm.

03 · PREREQUISITES

The gate you must earn

Before layering anti-inflammatories, confirm that the alarm is no longer simply *correct*:

Entry conditions for Phenotype A treatment

- **Exposure hunted & controlled** — ERMI/HERTSMI-2 in range; no second uncontrolled environment (home, work, vehicle).
- **Active drivers addressed** — binders run if biotoxin load present; MARCoNS/occult infection and dominant food antigens managed.
- **A1 vs A2 clarified** — if symptoms remain tightly location-bound, finish source control (A1) before assuming a conditioned alarm (A2).

The treatment target is a falling MMP-9 and receding symptoms once the input is removed; a persistently firing alarm in a confirmed-clean environment is the signature that the work has shifted to A2 retraining.

04 · LEVER 1

Quiet the innate & microglial alarm

Low-dose naltrexone (LDN) RX · MICROGLIA / TLR4

Mechanism. At 1–4.5 mg, naltrexone acts largely outside classical opioid antagonism: it antagonizes TLR4 on microglia, damping the activated-glia state that sustains neuroinflammation and central sensitization, and lowering IL-1β, IL-6 and TNF-α; a transient opioid blockade drives an endorphin rebound.

Dosing. Start 1.5 mg qHS; titrate by 1.5 mg every 1–2 weeks to a usual 3–4.5 mg qHS. Morning or split dosing if sleep is disrupted. Compounded for low strengths.

Cautions. Vivid dreams and transient early sleep disturbance; occasional headache. Precipitates withdrawal in anyone on opioid agonists — a true contraindication. Otherwise well tolerated and inexpensive.

Where it fits. A low-risk background that quiets microglial danger signaling early; especially useful in A2. Evidence: B

Curcumin (bioavailable) NATURAL · NF-KB / NLRP3

Mechanism. A polyphenol that inhibits NF-κB activation, the NLRP3 inflammasome, and both COX-2 and 5-LOX arms, lowering the core innate-inflammatory drive of CDR1.

Dosing. 500–1000 mg curcuminoids 1–2×/day in an absorption-enhanced form (phytosome, e.g. Meriva; or BCM-95). Take with food/fat.

Cautions. Generally well tolerated; GI upset; mild antiplatelet effect (caution with anticoagulants); inhibits CYP3A4/2C9 and P-gp (check interactions); can stimulate bile flow (caution with obstruction).

Where it fits. A first-line natural anti-inflammatory background; pairs well with boswellia. Evidence: B

Boswellia serrata (AKBA) NATURAL · 5-LOX / LEUKOTRIENES

Mechanism. Boswellic acids — chiefly AKBA — selectively inhibit 5-lipoxygenase, reducing leukotriene-driven inflammation that COX-targeted agents miss; complementary to curcumin.

Dosing. Standardized extract (30–40% AKBA), ~300–400 mg 2–3×/day.

Cautions. Generally well tolerated; mild GI; theoretical CYP interactions; limited pregnancy data.

Where it fits. The leukotriene-arm complement to curcumin in the innate-inflammation background. Evidence: C

Nrf2 / redox support NATURAL · OXIDATIVE DRIVE

Mechanism. Sulforaphane (broccoli-sprout extract) and related Nrf2 activators, with NAC for glutathione, lower the oxidative load that helps keep innate inflammation and the eIF2α kinases engaged.

Dosing. Sulforaphane per product; NAC 600–1200 mg 1–2×/day.

Cautions. Well tolerated; NAC may cause GI upset or sulfur odor; rare bronchospasm at high doses.

Where it fits. Low-risk background redox support beneath the specific anti-inflammatories. Evidence: C

05 · LEVER 2

Stabilize the mast cell (A2 / MCAS)

Quercetin NATURAL · MAST CELL / NLRP3

Mechanism. A flavonoid that stabilizes mast cells, inhibits NLRP3 and NF-κB, and lowers histamine release — directly relevant to the MCAS overlap common in A2.

Dosing. 500 mg 1–2×/day; absorption improves with a phytosome or bromelain co-formulation.

Cautions. Generally well tolerated; inhibits CYP3A4/P-gp (check interacting drugs); theoretical renal/thyroid-peroxidase concerns at high chronic doses.

Where it fits. A foundational mast-cell agent; combine with luteolin/PEA. Evidence: C

Luteolin NATURAL · MAST CELL / MICROGLIA

Mechanism. A flavone with mast-cell-stabilizing and microglia-quieting activity; crosses into the CNS compartment better than many flavonoids, addressing the neuroinflammatory side of A2.

Dosing. ~100 mg 1–2×/day, often in a liposomal blend with quercetin/rutin.

Cautions. Well tolerated; mild GI; the same CYP cautions as other flavonoids.

Where it fits. The neuro-mast-cell complement to quercetin. Evidence: C

Palmitoylethanolamide (PEA) NATURAL · ALIAMIDE / GLIA

Mechanism. An endogenous fatty-acid amide that down-modulates mast-cell and glial over-activation (the ALIA mechanism) and damps neuroinflammatory and neuropathic signaling without immunosuppression.

Dosing. 300–600 mg 1–2×/day, micronized or ultramicronized; effects build over weeks.

Cautions. Very well tolerated; minimal interactions.

Where it fits. An excellent, low-risk anchor for the neuro-mast-cell axis in A2. Evidence: B

Prescription mast-cell agents RX · MCAS

Mechanism. Where MCAS is prominent, clinician-directed H1 and H2 antihistamines, the mast-cell stabilizer cromolyn (oral for gut, intranasal for sinus), ketotifen, and a leukotriene-receptor antagonist provide stronger, titratable control.

Dosing. Per standard MCAS protocols, uptitrated to effect.

Cautions. Sedation (antihistamines), GI (cromolyn); standard agent-specific cautions.

Where it fits. Layer in when natural mast-cell agents are insufficient. Evidence: B

06 · LEVER 3

Actively resolve & repair the barrier

Blocking inflammation is not the same as ending it. CDR1 that will not resolve often reflects a *resolution deficit* — too little of the pro-resolving signaling that actively switches inflammation off. Supplying that signal is mechanistically apt for a “stuck” alarm.

Specialized pro-resolving mediators (SPMs) NATURAL · ACTIVE RESOLUTION

Mechanism. Resolvins, protectins, and maresins derived from EPA/DHA actively terminate inflammation — clearing neutrophils, promoting efferocytosis and M2 polarization — rather than merely blocking a single pathway. They address the resolution failure that defines a stuck alarm.

Dosing. ~2–3 mg SPM blend (e.g., 1–3 softgels) daily, often pulsed higher during flares.

Cautions. Well tolerated; mild GI; the antiplatelet caution of the omega-3 family.

Where it fits. A targeted resolution agent layered onto adequate omega-3 substrate. Evidence: C

Omega-3 EPA/DHA (high-dose) NATURAL · RESOLUTION SUBSTRATE

Mechanism. High-dose marine omega-3 supplies the EPA/DHA substrate from which SPMs are synthesized and is broadly anti-inflammatory and membrane-stabilizing.

Dosing. 2–4 g/day combined EPA+DHA, with food; verify purity/oxidation.

Cautions. Mild GI/reflux; antiplatelet effect at high dose (caution with anticoagulants/surgery).

Where it fits. The substrate foundation beneath SPM supplementation. Evidence: B

KPV (Lys-Pro-Val) PEPTIDE · A-MSH PROXY / BARRIER

Mechanism. The C-terminal tripeptide of α-MSH; it enters cells and inhibits IKK→NF-κB, damps the inflammasome and MAPK signaling, and strengthens epithelial barriers — carrying the α-MSH "stand-down" message without pigmentary or appetite effects.

Dosing. ~200–500 µg/day orally (orally bioavailable); topical/SubQ routes also used.

Cautions. Very well tolerated in available data; human data limited (mostly preclinical).

Where it fits. A gentle anti-inflammatory and barrier primer; useful for gut/skin overlap. (Note: here it is an adjunct, not the gate-opening step it represents in Phenotype D.) Evidence: C

BPC-157 PEPTIDE · BARRIER / REPAIR

Mechanism. A "body-protective" peptide promoting angiogenesis, nitric-oxide signaling, and gut and connective-tissue repair; relevant where gut-derived load and barrier loss feed the alarm.

Dosing. ~250–500 µg 1–2×/day, oral (gut-centric) or SubQ; compounded.

Cautions. Limited human data; mild injection-site/GI effects; off-label/compounded.

Where it fits. An adjunct for barrier repair once active drivers are controlled. Evidence: D

07 · LEVER 4

Calm the conditioned alarm & autonomic tone

In A2 the alarm is partly maintained by the nervous system itself, so peripheral anti-inflammatories are necessary but not sufficient. This is where the *psychological & behavioral arm* of the resilience primer does its work, and it is biology: vagal tone gates the cholinergic anti-inflammatory pathway that lowers the same NF-κB-driven cytokines as the agents above.

- **Limbic retraining & trauma reprocessing** — for the conditioned environmental alarm (DNRS/Gupta/Primal Trust; clinician-led EMDR for the A2 lesion). See the resilience primer, Psychological Arm.
- **Down-regulation & HRV** — resonance breathing, extended-exhale work, vagal toning, and HRV biofeedback to lower the sympathetic dominance that defines A.
- **Oxytocin (gentle, optional)** — intranasal ~10–24 IU adds a social-safety/vagal, anti-inflammatory signal; use as an adjunct, not a primary anti-inflammatory.

Sequence note. Pair the peripheral agents with autonomic and limbic work from the start in A2. Quieting the periphery while the conditioned circuit keeps firing — or retraining the circuit while mast cells are still flaring — each disappoints; together they compound.

08 · THE ROADMAP

A sequenced approach

Stage	Do	Exit gate
0 · Earn it	Hunt and control the exposure; run binders if indicated; address occult infection and dominant food antigens.	Environment verified; MMP-9 falling on serial draws; symptoms less location-bound.
1 · Quiet	LDN background + curcumin/boswellia + Nrf2/NAC; begin HRV/vagal work.	Innate-inflammatory tone receding; patient tolerating background agents.
2 · Stabilize	Add quercetin/luteolin/PEA (± Rx mast-cell agents) where MCAS features persist.	Mast-cell reactivity and flares settling.
3 · Resolve	Layer omega-3 + SPMs; KPV/BPC-157 for barrier; intensify limbic retraining in A2.	Resolution evident; conditioned triggers loosening; MMP-9 normalizing.
4 · Re-phenotype	Reassess at ~12 weeks. If MMP-9 normalizes but VIP/α-MSH fall and HRV collapses, consider transition to Phenotype D.	Stable resolution, or a clear re-phenotyping decision.

A flare is information. If a stage flares the patient, step back a stage and re-secure it — almost always a missed exposure or moving too fast, not an ineffective agent.

09 · AT A GLANCE

Master summary

Agent	Lever	Mechanism (one line)	Dosing	Ev.
LDN	microglia/TLR4	TLR4 antagonism damps activated glia; endorphin rebound	1.5→3–4.5 mg qHS	B
Curcumin	NF-κB/NLRP3	Inhibits NF-κB, NLRP3, COX-2/5-LOX	500–1000 mg 1–2×/d	B
Boswellia	5-LOX	AKBA inhibits leukotriene synthesis	300–400 mg 2–3×/d	C

Agent	Lever	Mechanism (one line)	Dosing	Ev.
Quercetin	mast cell	Mast-cell stabilizer; NLRP3/NF-κB	500 mg 1–2×/d	C
Luteolin	mast cell/glia	Mast-cell & microglial quieting	~100 mg 1–2×/d	C
PEA	ALIAmide	Down-modulates mast-cell/glial over-activation	300–600 mg 1–2×/d	B
SPMs	resolution	Resolvins/protectins actively end inflammation	~2–3 mg/d	C
Omega-3	substrate	EPA/DHA substrate for SPMs; anti-inflammatory	2–4 g/d	B
KPV	α-MSH proxy	IKK→NF-κB inhibition; barrier repair	~200–500 µg/d oral	C
BPC-157	barrier/repair	Angiogenesis; gut/connective repair	~250–500 µg 1–2×/d	D

10 · EVIDENCE, SAFETY & SOURCING

Honest framing

The anti-inflammatory mechanisms here are well grounded; their application to CDR1 biotoxin illness is mechanistically reasoned and, for the naturals, supported chiefly by pain/inflammation rather than mold-specific trials. Only LDN (adjacent indications) and high-dose omega-3 reach good human data; the flavonoids, SPMs, KPV and BPC-157 rest largely on mechanistic and preclinical support.

- **Monitor** the markers that defined the phenotype — MMP-9 trend, hs-CRP/NLR, and symptom location-dependence — plus tolerance of each agent. Direction of travel matters more than any single value.
- **Hold in view** opioid agonists with LDN; antiplatelet/anticoagulant interactions with curcumin, omega-3, and SPMs; CYP3A4/P-gp inhibition with the flavonoids.
- **Off-label & compounded** peptides (KPV, BPC-157) from reputable compounding pharmacies with documentation.

*This document supports clinician decision-making and education within the Beyond Mold CDR/ISRmt framework. It is a clinical synthesis, not a guideline: it is not individualized medical advice, does not establish a standard of care, and does not replace prescriber judgement, informed consent, or appropriate monitoring for the individual patient. Many agents are used off-label and several peptides are compounded; source from reputable compounding pharmacies with potency and sterility documentation, and apply standard monitoring. Evidence grades are deliberately conservative: **A** RCT-level in this or a closely adjacent indication · **B** good human data, extrapolated here · **C** mechanistic + preclinical, limited human · **D** mechanistic / experimental only. Not a substitute for clinical judgement.*