White Paper
Redox Collapse: A New Diagnostic Frontier for Chronic Disease

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Executive Summary

Modern diagnostics are late to the fight. They wait for organs to break down, for scans to show damage, or for symptoms to finally scream loud enough to trigger a response. But chronic disease doesn't start there—it starts at the molecular level, when the redox system loses control and oxidative chaos begins to spread.

That tipping point is redox collapse: a measurable breakdown of redox balance that marks the irreversible shift from adaptive stress to biochemical degeneration.

OXO isn't guessing. We measure it.

Our Redox Collapse Score quantifies this breakdown using urine biomarkers—4-HNE-MA, 8-OHdG, pyroglutamate, and creatinine—to deliver a single number that flags systemic dysfunction *before* conventional labs show anything.

This isn't early detection. It's **pre-disease surveillance**.

1. The Problem: Structural Tests Come Too Late

- Most diagnostics detect the aftermath of disease, not its origin.
- Imaging and labs like LDL-C or A1C report on damage after it's happened.
- But chronic fatigue, cardiovascular failure, neurodegeneration—these begin with **metabolic instability**, not plaque or lesions.
- We need tools that reflect **ongoing biochemical stress**, not legacy damage.

2. The Hypothesis: Redox Collapse as Early Breakdown

- Redox collapse is the failure of oxidative control—the degradation of cellular systems due to unneutralized reactive species.

- Lipid peroxidation triggers cascading chain reactions that generate reactive aldehydes like **4-hydroxynonenal (4-HNE)**.

- 4-HNE forms covalent adducts with nucleophilic sites on proteins, enzymes, and DNA bases, altering structure and function.

- **8-hydroxy-2'-deoxyguanosine (8-OHdG)** is a direct result of ROS attacking guanine residues in DNA—implicating nuclear and mitochondrial genetic damage.

- These signals precede phenotypic pathology. They flag collapse *at the molecular level*. Numerous studies have shown that elevated levels of 4-HNE and 8-OHdG are found in patients with cardiovascular disease, neurodegenerative conditions like Alzheimer's disease, and cancer. For example, 4-HNE has been detected in atherosclerotic plaques and is implicated in endothelial dysfunction (Zarkovic, 2003). Elevated 8-OHdG is consistently reported in Alzheimer's disease brain tissue and urine (Lovell & Markesbery, 2007; Mecocci et al., 2002), and correlates with oxidative DNA damage in multiple chronic pathologies.

> Collapse is not a metaphor. It's a biochemical inflection point measurable through metabolite flux.

3. The Innovation: The OXO Redox Collapse Score

To move from concept to quantification, the OXO Redox Collapse Score aggregates normalized concentrations of oxidative biomarkers into a single index using a weighted composite formula. The core model:

OXO Score = $[w_1(HNE) + w_2(OHdG) + w_3(Pyro) + w_4(GSSG)] / Cr$

Where:

- **HNE** = urinary 4-HNE-MA concentration (µg/g creatinine)

- **OHdG** = urinary 8-OHdG concentration (ng/g creatinine)

- **Pyro** = urinary pyroglutamate (mg/g creatinine)

- **Cr** = creatinine normalization factor (g/L)

- w_1, w_2, w_3, w_4 = empirically determined weighting coefficients derived from literature and internal pilot data, reflecting each biomarker's contribution to oxidative burden and redox system failure

The score is scaled and stratified into percentiles (low, moderate, high oxidative burden) based on population baselines and clinical relevance.

This transforms complex biochemical volatility into a clinically useful signal, delivering early insight into redox imbalance and systemic stress load.

We quantify collapse using five key urinary biomarkers:

- **4-HNE-MA** – A conjugated metabolite of 4-HNE processed via glutathione and mercapturic acid pathways; reflects total lipid peroxidation burden.

- **8-OHdG** – A marker of oxidative DNA damage, filtered through the kidneys and excreted in urine.

- **Pyroglutamate** – Indicates dysfunction in glutathione recycling via the gamma-glutamyl cycle, a key redox buffering system.

- **Creatinine** – Used for normalization of excretion to account for kidney function and hydration status.

- **GSSG (oxidized glutathione)** – Reflects redox buffering capacity and oxidative pressure; elevated GSSG is a signal of depleted antioxidant reserves and glutathione system overload.

These are integrated into the proprietary **OXO Redox Collapse Score**—a unifying index of oxidative instability and biochemical stress load.

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4. Applications and Markets

- **Hospitals**: Predict readmissions by quantifying unseen oxidative stress prior to discharge.

- **Clinics**: Identify mitochondrial collapse in patients presenting with nonspecific symptoms like fatigue, neuropathy, or brain fog.

- **Performance Health**: Track redox adaptation under extreme physiological loads (athletes, executives, military).

- **Payers**: Integrate oxidative stress scoring into preventive risk stratification models.

4.1 Redox-Informed Clinical Interventions & Illustrative Cases

The following case studies are fictionalized, illustrative examples based on emerging patterns observed in pilot data and published literature. They are intended to demonstrate how the OXO Redox Collapse Score can inform clinical decision-making and anticipate dysfunction ahead of conventional diagnostics.

The OXO Redox Collapse Score doesn't just measure dysfunction—it informs action. When oxidative biomarkers indicate biochemical instability, clinicians can intervene using redox-targeted IV protocols. These therapies are matched to biomarker profiles and address mitochondrial overload, glutathione depletion, and systemic oxidative damage.

Redox-Targeted IV Interventions:

Glutathione System Restoration:

- **IV Glutathione (GSH)** – Replenishes depleted intracellular glutathione pools

- **N-acetylcysteine (NAC)** – Boosts endogenous GSH synthesis

- **Alpha-lipoic acid (ALA)** – Regenerates oxidized GSH and neutralizes free radicals

Mitochondrial Repair & Energy Restoration:

- **Coenzyme Q10 (CoQ10)** – Enhances mitochondrial electron transport and ATP synthesis

- **PQQ & Taurine** – Support mitochondrial biogenesis and membrane stability

Free Radical Scavenging & Redox Buffering:

- **High-dose Vitamin C** – Direct antioxidant action and immune modulation

- **Magnesium sulfate** – Stabilizes mitochondrial membranes and supports ATP processes

- **Trace minerals (Zinc, Selenium)** – Cofactors for antioxidant enzymes and detoxification

Patients with **elevated GSSG** may be prioritized for glutathione-replenishing protocols. Elevated GSSG signifies redox system exhaustion—where the body's buffer capacity is depleted, and intervention is critical to halt biochemical collapse.

These interventions are administered under medical supervision and informed directly by redox biomarker profiles.

The following cases illustrate how the OXO Redox Collapse Score enables personalized intervention—well before conventional diagnostics detect dysfunction:

Case 0: Redox Collapse Predicts Readmission Risk

> "She looked stable. Her labs said normal. But her redox score was 95th percentile. Eight days later—readmitted."

- A 73-year-old female discharged after heart failure exacerbation appeared clinically stable.
- BNP, ejection fraction, and blood pressure normalized at discharge.
- OXO Collapse Score on day of discharge: 95th percentile
    - 4-HNE-MA: 3.8 µg/g Cr
    - 8-OHdG: 11.4 ng/g Cr
    - GSSG: elevated
- 8 days later, she was readmitted with acute dyspnea and hypertensive urgency.
- Intervention post-readmission: Implementation of redox-based discharge protocol including IV GSH, CoQ10, and anti-inflammatory nutritional support.
- Repeat OXO Score at 4 weeks: dropped to 68th percentile
- Commentary: Despite appearing clinically stable, the elevated redox collapse score identified unseen biochemical instability predictive of readmission.

Case 1: Hidden Cardiovascular Risk in a Post-Discharge Patient

- A 68-year-old male with prior CABG presented with fatigue and shortness of breath 10 days post-discharge.
- Standard labs (LDL-C, CRP, BNP) were within normal limits.
- OXO Redox Collapse Score: 87th percentile
    - 4-HNE-MA: 3.1 µg/g Cr
    - 8-OHdG: 9.2 ng/g Cr
    - Pyroglutamate: 16.7 mg/g Cr
- Intervention: Targeted antioxidant therapy (CoQ10, NAC), omega-3, and lifestyle overhaul
- Follow-up: Score dropped to 61st percentile in 6 weeks; patient reported return of energy and reduced inflammation markers

Case 2: Elite Athlete Under Performance Collapse

- A 34-year-old triathlete reported declining endurance despite normal VO2 max and clean cardiac panels
- OXO Score: 93rd percentile
    - Notably elevated 8-OHdG and pyroglutamate
- Analysis: Evidence of mitochondrial strain, redox dysfunction despite no overt disease
- Resolution: Adjusted training load, incorporated targeted redox support (alpha-lipoic acid, PQQ, taurine)
- Result: Score reduced to 70th percentile; energy and endurance returned within 3 weeks

Case 3: Preclinical Neurodegeneration in Midlife Executive

- A 52-year-old female with subjective cognitive decline but normal MRI and labs
- OXO Score: 91st percentile
    - High HNE and 8-OHdG, borderline pyroglutamate

- Referral: Neurologist confirmed mild cognitive impairment (MCI); initiated early-stage intervention protocol

- Commentary: OXO panel flagged redox collapse **prior** to structural/clinical confirmation

5. Scientific Foundation

- 4-HNE impairs mitochondrial complex I, II, and IV, directly inhibiting ATP production and promoting membrane permeability (Zarkovic et al., 2013).

- 8-OHdG levels correlate with disease severity in cancer (Valavanidis et al., 2009), atherosclerosis (Wu et al., 2004), and neurodegenerative disorders (Mecocci et al., 2002).

- Pyroglutamate is elevated in conditions of glutathione depletion, oxidative stress, and chronic inflammation (Jones, 2006).

- Redox collapse is not speculative—it is **the energetic footprint of failure**, long before organ dysfunction manifests.

6. What Makes OXO Different

- We don't infer damage from downstream markers—we quantify upstream biochemical chaos.

- Redox collapse offers **pre-disease resolution**: we detect dysfunction before structural biomarkers light up.

- Urine-based, non-invasive, repeatable, and already validated in existing literature.

7. Go-to-Market Strategy

- Pilot studies with cardiometabolic and integrative clinics

- Partner with CLIA labs for certified sample processing

- Launch practitioner-facing software with interpretive scoring

- Scale access through strategic D2C and institutional partnerships

8. The Ask

Redox collapse is measurable, actionable, and clinically urgent. We are seeking early partners—investors, clinicians, and lab networks—who see the opportunity to redefine preventive diagnostics.

This is not just a new test. It's a new **lens** on disease—grounded in physics, biology, and clinical reality.

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