Swiss Medical Editorial

Clinical Judgment in Cold Agglutinin Disease: The Art of Timing

Moving beyond algorithms to treat based on clinically meaningful harm.

BASED ON THE CLINICAL INSIGHTS OF WILLIAM AIRD

The Tension Between Risk and Morbidity

In Cold Agglutinin Disease (CAD), knowing when *not* to treat is as important as knowing how to treat.

Treating Too Early

Treating too early exposes patients to unnecessary risk and toxicity.

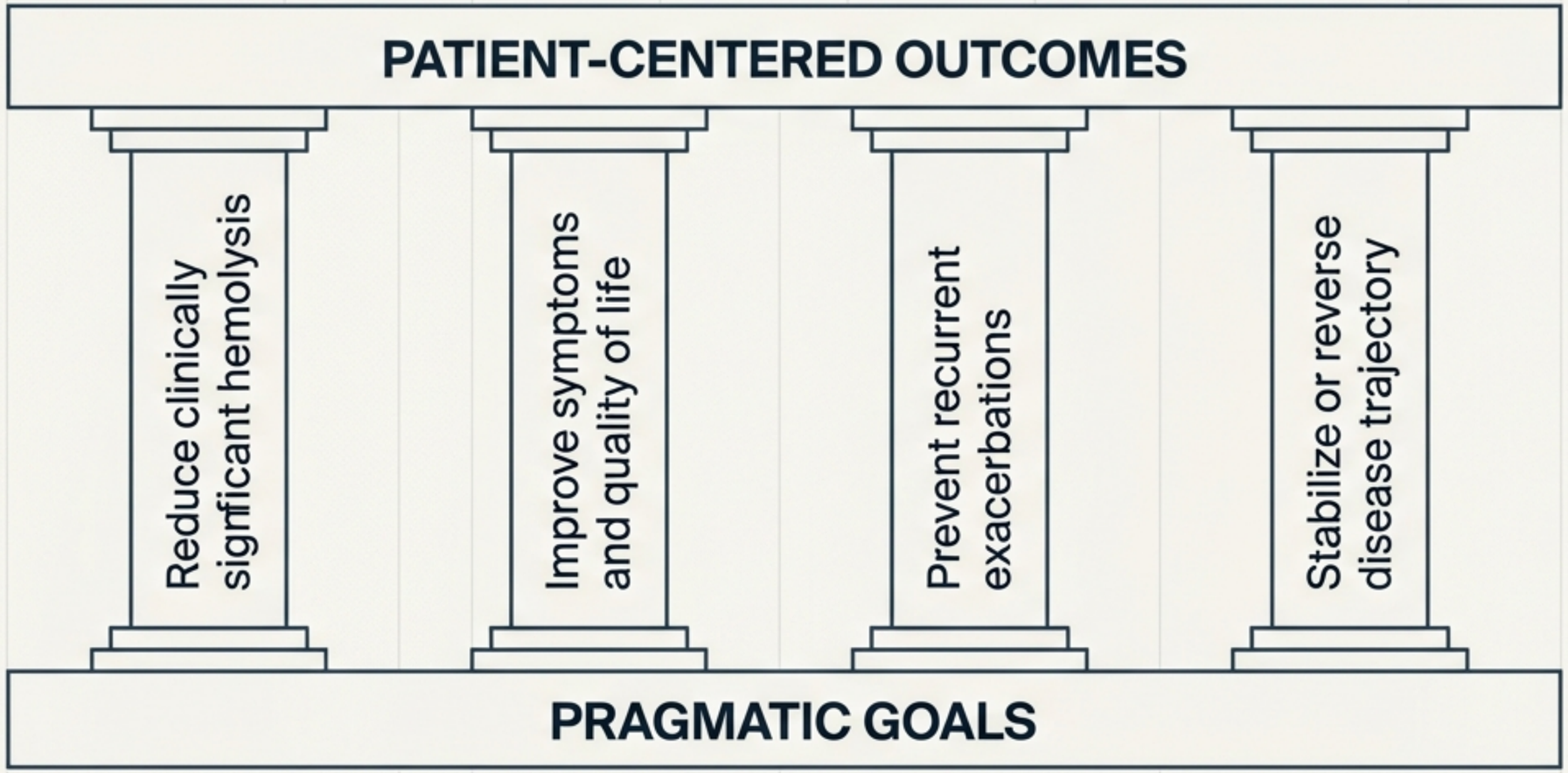
Treating Too Late

Treating too late prolongs avoidable morbidity and functional decline.

Key Insight: There is no single hemoglobin threshold, antibody titer, or laboratory value that that dictates treatment. Decisions must be judgment-based, not algorithmic.

Defining the Goal of Intervention

Treatment is aimed at reducing clinically meaningful harm, not normalizing numbers in isolation.

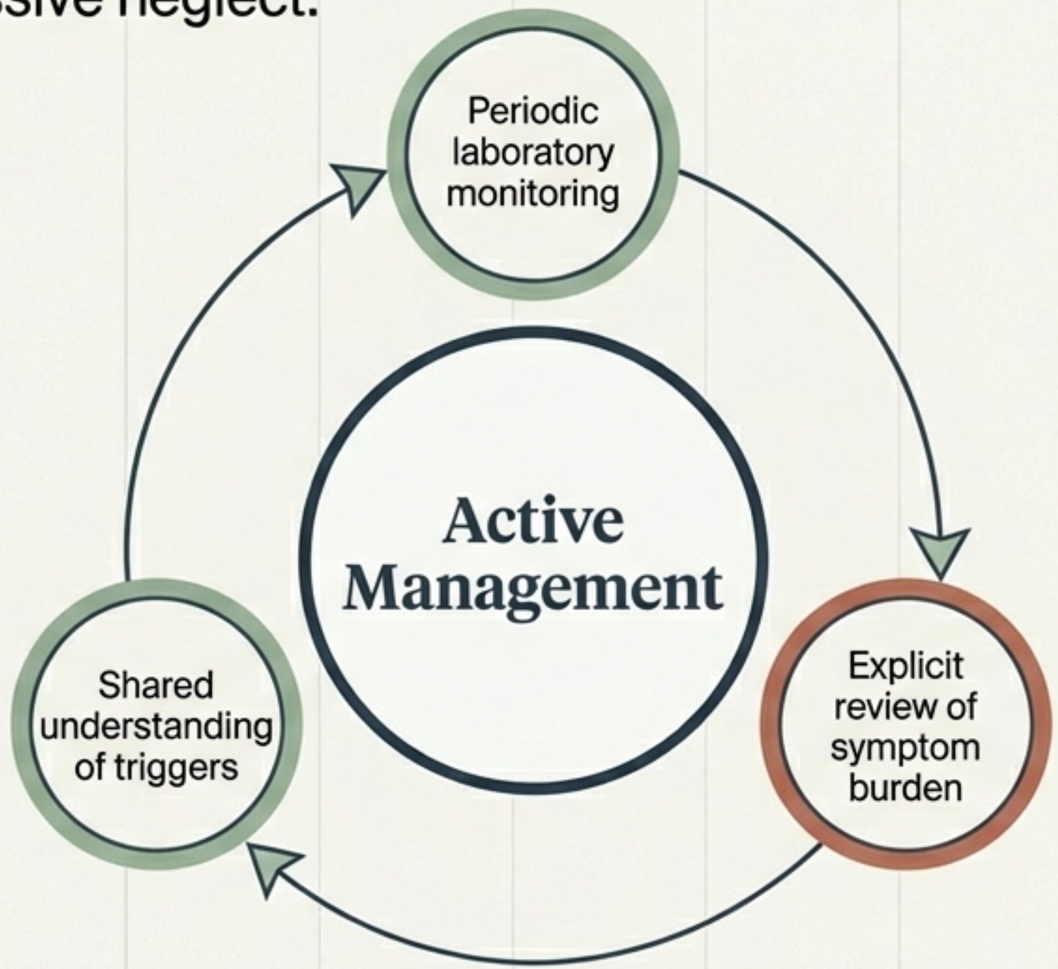


The outcomes must be ones the patient actually feels.

Observation Is An Active Strategy

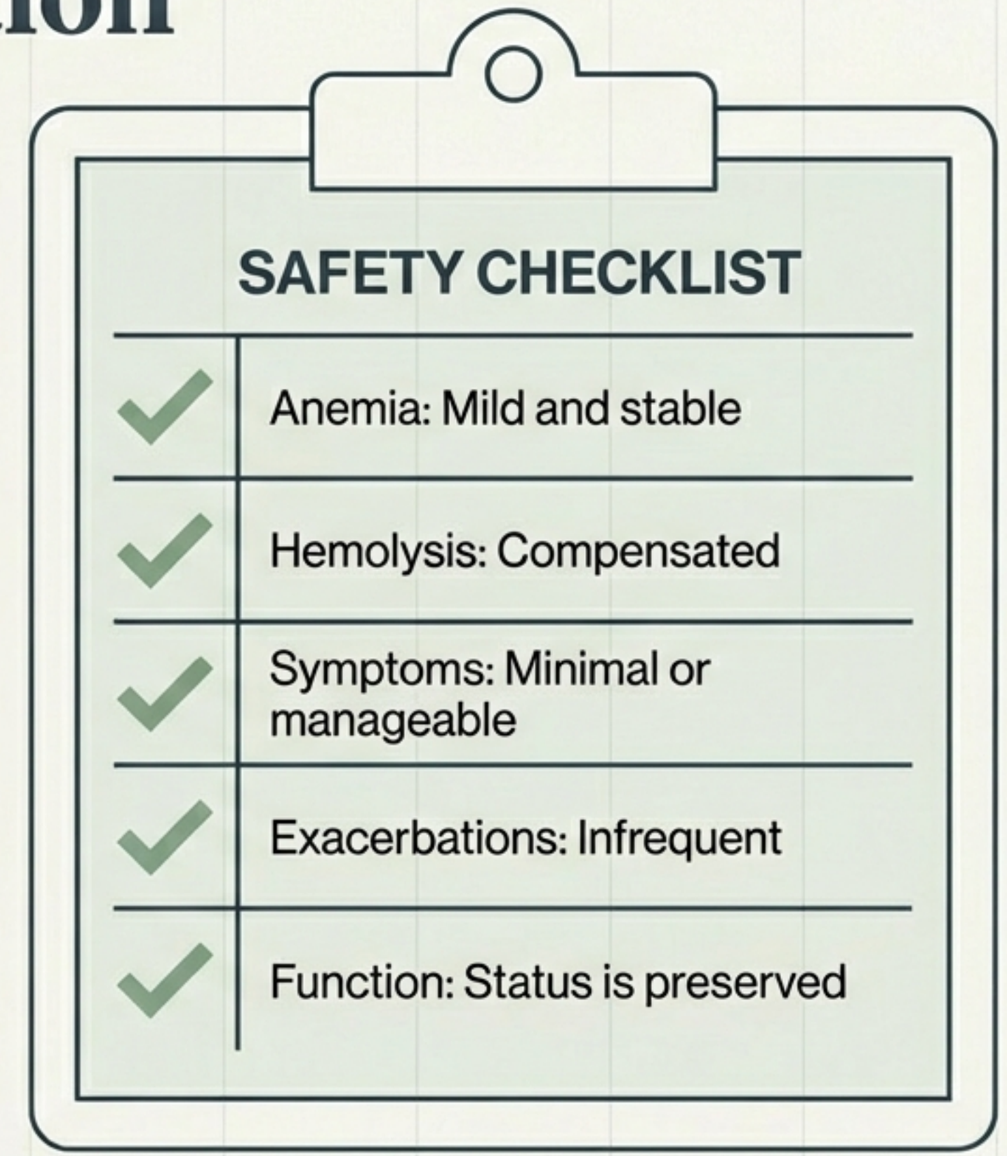
Many patients do not require immediate disease-directed therapy. However, observation is not “passive neglect.”

“Active management requires follow-up, symptom assessment, and reassessment over time.”



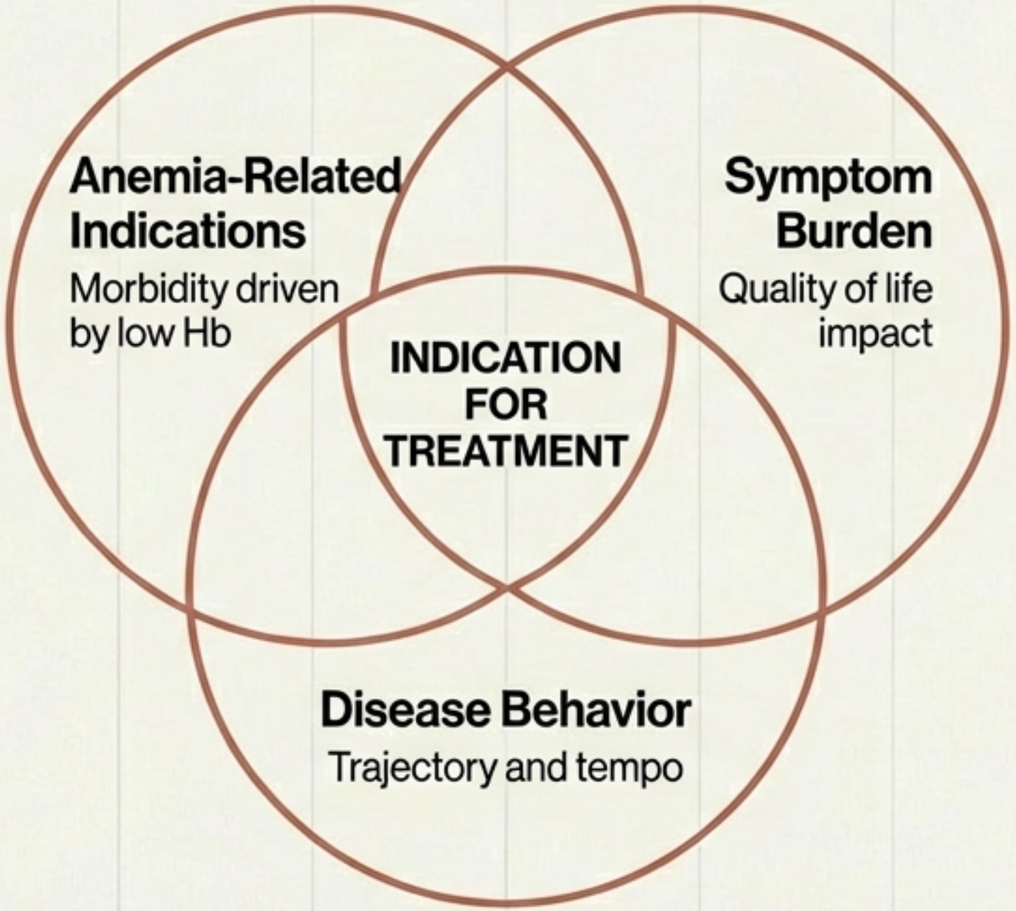
Criteria for Safe Observation

Observation is reasonable and appropriate when the disease impact is limited and stable.



The Three Pillars of Clinical Harm

Treatment should be considered when CAD produces clinically meaningful harm.
No single domain is sufficient on its own; look for the intersection of these factors.



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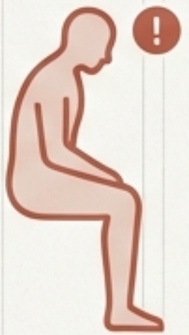
Anemia Severity Is Not the Whole Story

Hemoglobin level alone is an unreliable trigger. Context is king.

8.0 g/dL

Patient A:
Tolerates low Hb well.
Asymptomatic.



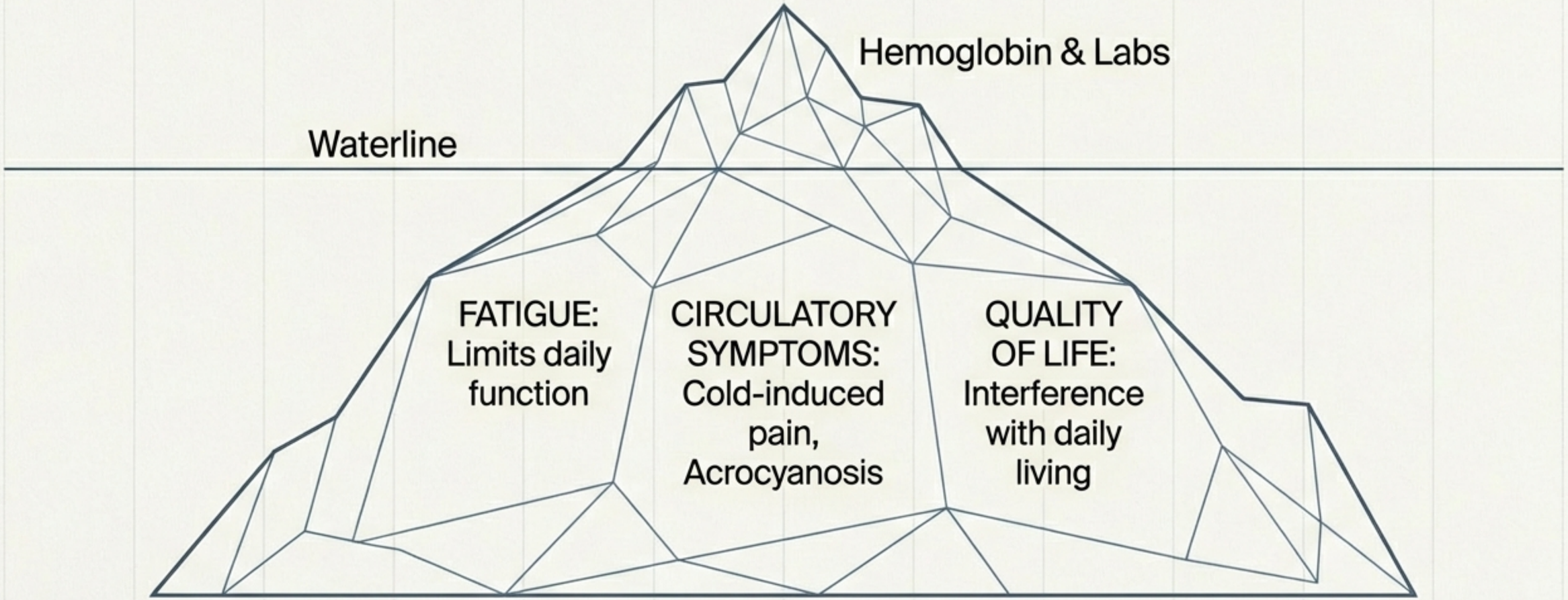
Patient B:
Profoundly
symptomatic.
Functional decline.

When Anemia Justifies Treatment

- Symptomatic anemia (breathlessness, palpitations)
- Progressive decline in hemoglobin
- Transfusion dependence

The Hidden Burden of Symptoms

Symptoms matter even when laboratory abnormalities appear modest.
Burden frequently exceeds what laboratory markers predict.



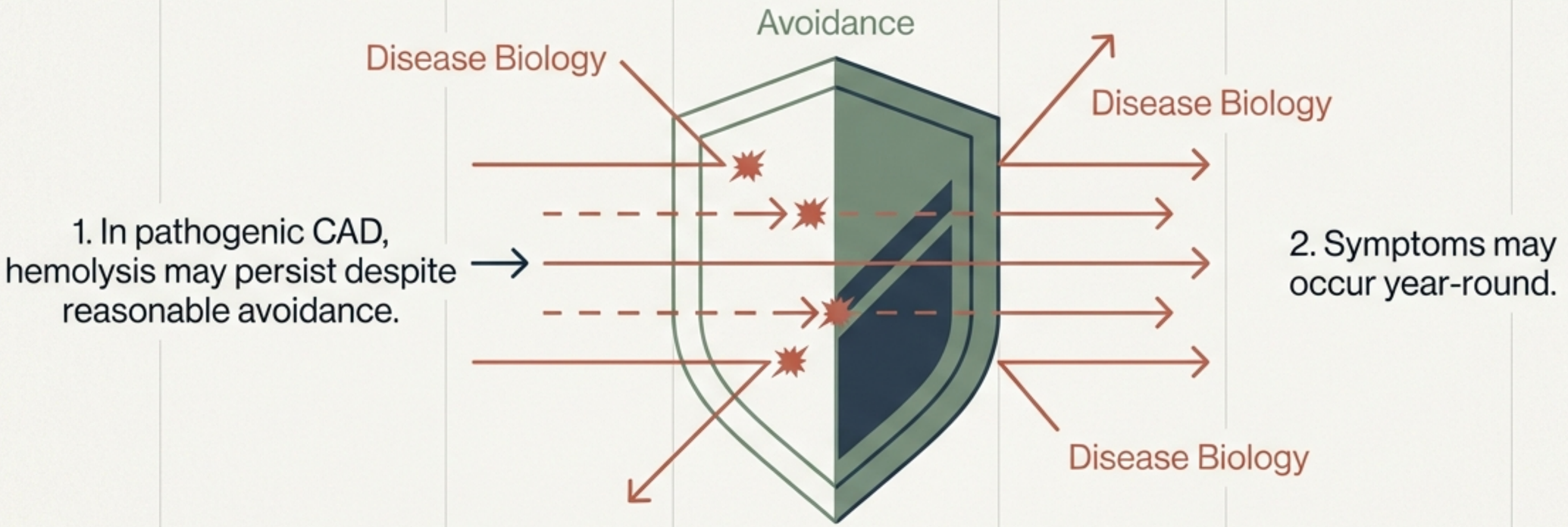
Trajectory and Tempo

Disease behavior over time often matters more than snapshot severity.

Tempo matters. Rapid decline requires accelerated decision-making, though urgency should not replace judgment.

Cold Avoidance Is Not a Litmus Test

Cold avoidance is a preventative measure,
not a diagnostic or therapeutic test.



Crucial Point: Failure of cold avoidance does not imply poor adherence.
It implies disease biology that requires therapy.

The Trap of Underestimation

Why treatment is often postponed inappropriately

Normalization

Labeling anemia as “mild” despite high symptom burden.

Misattribution

Attributing fatigue to “getting old” or cold weather rather than biology.

Metric Fixation

Over-reliance on modest hemolysis markers while ignoring functional decline.

False Comfort

Mistaking uncertainty for benignity.

The Trap of Premature Action

When biological context is misunderstood.

Triggers for Error

- **Misdiagnosis:** Mistaking an isolated cold agglutinin for CAD.
- **Confusion:** Assuming transient post-infectious hemolysis is chronic disease.
- **Anxiety:** Treating asymptomatic laboratory abnormalites out of fear.

Reminder: Not every patient with CAD needs therapy.

Managing Uncertainty Without Paralysis

Deciding when to treat often requires acting without perfect information.
This is not indecision; it is disciplined restraint.

Best Practices

→ Revisit assumptions as the disease evolves.

Best Practices

→ Match treatment intensity to disease behavior, not diagnostic labels.

Communicate uncertainty
→ honestly to patients.

Reframe the Critical Question

~~THE OLD QUESTION~~

Is the hemoglobin low enough to treat?

THE NEW PARADIGM

Is this disease currently harming the patient in a way that treatment is likely to meaningfully improve?

This shift aligns treatment with benefit rather than numbers.

Disciplined Restraint

Do not treat laboratory abnormalities in isolation. Treat patients whose disease meaningfully interferes with health, health, function, or stability.

Mastery of CAD is less about memorizing criteria and more about learning to recognize impact, trajectory, and burden over time.