

# Constraints Are Causes

Absurd Health Institute · Medical Concept Papers, Volume Three · Third editorial pass, 17 October 2026

**Article type:** Mechanistic research perspective · **Status:** Conceptual argument, not clinical guideline

**The missing cause may be the bottleneck, not the insult A constraint can be causally important even when it is neither the first insult nor the most visibly abnormal biomarker. For example, in tissue repair, oxygen delivery, immune resolution, substrate availability, blood supply, cell viability, and mechanical loading interact. A wound may be clean but fail to heal because perfusion is inadequate. The absence of necessary capacity is not mere “background”; it is part of why repair does not proceed. The thesis is therefore stronger than the conventional claim that disease has multiple causes: a limiting requirement can determine the effectiveness of every otherwise appropriate intervention.**

This can be stated with threshold logic. Suppose a tissue needs adequate perfusion and viable regenerative cells to restore integrity. Raising nutrient concentration does not resolve a severe perfusion deficit, and improving perfusion alone cannot reconstruct a completely absent cell population. When one requirement approaches zero, increasing another may yield little benefit. The result is a testable interaction rather than an invitation to treat all organs with an unspecified “terrain” protocol. The clinical question is which requirement is currently limiting the outcome.

**Proving a bottleneck is causal To demonstrate causation, investigators should show that the alleged constraint precedes impaired recovery, predicts treatment response, and that relieving it—where safe and feasible—changes the outcome. Study designs must distinguish a bottleneck from a marker of disease severity. Low circulating albumin, for instance, may track inflammation and prognosis without demonstrating that supplementing albumin reverses the disease process. A convincing bottleneck experiment identifies the step, measures it directly, and shows that manipulating it changes downstream flux.**

The implications reach beyond wound healing. In rehabilitation, motor learning may be limited by sleep disturbance, severe pain, or inadequate muscle function; in drug therapy, tissue access may limit the effect of a pharmacologically active molecule. A constraint-first medicine would ask what prevents the *known* treatment from accomplishing its expected effect. That is a sharper and more controversial challenge to molecular medicine than denying the importance of molecular targets. It requires a discipline of prioritization: one proposed bottleneck, one functional prediction, one measured response.

**When relieving one shortage reveals another A complex repair system may change bottlenecks over time. At the onset of tissue injury, bleeding control and contamination may dominate; during later healing, vascularization, matrix formation, or mechanical integrity may become limiting. The provocative extension is that the most important clinical constraint is phase-dependent. An intervention directed at yesterday's bottleneck can have diminishing effect even while the chosen marker continues to improve.**

A prospective wound study could define key milestones and repeatedly measure perfusion, infection indicators, tissue oxygenation, nutritional adequacy and structural healing. Investigators would estimate which factor precedes a slowdown and whether treating that factor restores the expected recovery slope. Changes due to ordinary healing must be distinguished from causal intervention effects. If measured perfusion explains no variation beyond wound size and infection, the proposed oxygen-delivery bottleneck would not be supported in that sample. The goal is a clinical discipline of identifying the current limiting step and revising that hypothesis as the organism changes, rather than applying a permanent label of “poor terrain.”

**Bottleneck identification is a competition among explanations Suppose wound healing stagnates despite good nutrition and normal circulating oxygen saturation. A bottleneck model might prioritize local perfusion, bacterial burden, mechanical loading, or tissue viability. Each predicts a different set of observations and a different likely response to treatment. A useful clinical paper should show how the options compete rather than presenting all possible limitations as though they were equally important. If measured oxygen delivery is adequate and vascular interventions fail to change healing, the perfusion hypothesis weakens, even if microcirculation remains biologically important in other settings.**

The same logic can guide experimental drug delivery: sufficient blood drug concentration may coexist with poor access to a poorly perfused tissue, but local measurement must establish the problem. The Institute's radical claim is that apparently secondary limitations can be *causally decisive*, not that every chronic disease is caused by invisible deficits. This requires a strong standard of proof: the proposed bottleneck should be measurable, should precede the failure, and should be relieved by an intervention that changes the relevant outcome.

**Identifying a changing limitation** The limiting constraint may move as treatment succeeds. Restoring perfusion, for example, might expose inadequate regenerative cell capacity or persistent infection as the next rate-limiting problem. That predicts a characteristic plateau: the first intervention improves one process, but further increases in its intensity produce diminishing returns while another measured deficit remains. A prospective investigation could document this sequence and compare planned stepwise responses with conventional management. If the supposed second bottleneck fails to explain the plateau, the model should change. The thesis earns clinical credibility by predicting a transition between measurable limitations, not by insisting that a hidden bottleneck exists whenever a patient stops improving. It is a theory about changing causes, not a fixed list of universal supplements.

### **Detailed considerations from the original investigation**

A constraint is a condition that limits the states a system can occupy. In biology, oxygen availability, microvascular perfusion, transport capacity, energy supply, membrane integrity and mechanical confinement can alter outcomes even without constituting the initiating disease. The thesis is that medicine often gains explanatory power by measuring these limiting conditions directly. The term “cause” must be used carefully: a constraint may be necessary, permissive, amplifying or truly sufficient for a particular outcome.

A myocardial cell with intact contractile proteins may still fail to perform under inadequate perfusion; a functioning neuron becomes unreliable when extracellular ion gradients are disturbed; normal digestive enzymes cannot compensate indefinitely for loss of adequate substrate delivery. Clinical deterioration is therefore not always a defective part but an unmet condition for a part to function. Interventions that restore oxygen delivery, circulation, nutrition or electrolyte balance are already important examples of constraint-directed treatment. The original contribution here is to make these causal roles explicit across disease models.

A patient with a reassuring hemoglobin concentration may still have exertional intolerance from cardiovascular or pulmonary disease. A patient with normal oxygen delivery can nevertheless have neuromuscular limitations. Both experiences illustrate that a normal component reading does not establish the adequacy of the entire process. The rate-limiting step must be identified rather than guessed from a general sense that the system is 'under strain'.

Constraint language could become an unhelpful catchall. If every clinical factor is renamed a “constraint,” no sharper diagnosis follows. A useful hypothesis specifies which variable has become rate-limiting, demonstrates that changing it alters downstream behavior, and rules out simpler explanations. Severe infections, structural lesions and genetic disorders often have causes that remain critical even when systemic context is measured.

Evidence could include dose-response relationships, rescue experiments, repeated measures demonstrating threshold behavior and interventions that restore functional output while the original

structural abnormality remains unchanged. Conversely, if modifying the supposed bottleneck does not alter function or prognosis, it was not decisive in the proposed context.

This paper encourages clinicians and readers to ask what conditions make normal physiology possible, rather than attributing every failure to intrinsic organ weakness. The practical result is more precise causal reasoning, not a universal alternative protocol.

An operative constraint limits possible performance even when the directly measured target is corrected. Constraints may be vascular, architectural, energetic or regulatory.

Correcting anemia can improve oxygen capacity while poor regional perfusion still limits exercise tolerance; alternatively, unresolved cardiac disease may dominate.

Demonstrate that the proposed limiting process mediates the response to a target-specific treatment and is not a coincident abnormality.

## **Selected scientific reading**

1. Kitano (2002), Systems biology: a brief overview, Science.

<https://doi.org/10.1126/science.1069492>

2. Barabási, Gulbahce & Loscalzo (2011), Network medicine: a network-based approach to human disease, Nature Reviews Genetics.

<https://doi.org/10.1038/nrg2918>

*Editorial source note: The inherited selected readings are retained from the source manuscript and have not all been independently verified. Newly checked evidence is identified separately. The mechanistic extensions are hypotheses except where explicitly described as established physiology.*