

# Counterfactual Medicine: Can Comparative Physiology Test Our Causal Models?

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**Counterfactual organisms can test whether a causal model is genuinely general** When a medical explanation is developed entirely within one population, the investigator may confuse a local correlation with a general biological necessity. Comparative physiology offers a way to test the explanation against organisms with different anatomical and metabolic designs. The Institute's proposed counterfactual medicine asks: if our causal model were correct, what would we expect in a species that solves the same physiological problem with different structures? The key is to generate predictions before observing the comparison.

For example, oxygen transport must satisfy cellular demand, but species differ in respiratory architecture, blood pigments, temperature regulation, and activity patterns. A simplistic hypothesis that one human biomarker alone determines oxygen sufficiency might fail when confronted with those differences. Such failure does not invalidate the human measurement; it reveals that transport performance depends on the relationship among demand, delivery, extraction, and environmental conditions. The general mechanism survives when expressed at the right level.

**Natural experiments and their limitations** Researchers can compare related species with different traits, or unrelated species with convergent adaptations, while controlling as much as possible for body size, environment, and evolutionary relatedness. Phylogenetic methods are essential because species are not independent randomized observations. Evolutionary adaptation also reflects multiple tradeoffs: a trait's presence does not prove it is optimal for longevity or disease resistance. Counterfactual reasoning should therefore focus on sharply specified predictions rather than storytelling about what nature “intended.”

The clinical value lies in making hidden assumptions visible. If a proposed human mechanism collapses when its anatomical implementation changes, the theory may be narrower than claimed. If the same causal constraint recurs through different biological designs, confidence in its generality increases. This is not a proposal to extrapolate animal treatments directly to people. It is a method for testing whether an explanation concerns a real physiological requirement or only a coincidental feature of one species' measurement system.

**A successful counterfactual prediction must be made before the comparison. Comparative physiology can become post hoc storytelling if investigators search across animals until they find a trait that matches a favored thesis. A stronger method specifies a mechanistic constraint, predicts how a different anatomical solution should meet it, and tests the prediction with independent observations. Species related by evolution are not independent experimental replicates, so phylogenetic relationships and ecology must be considered. Convergence is suggestive but not automatically proof of optimal design.**

The Institute's idea would be most powerful when an apparently indispensable human biomarker turns out to be one implementation of a general physiological requirement. The researcher must then restate the causal model at the level of delivery, balance or adaptation rather than a species-specific measurement. That move is not a retreat; it makes the model more general and more vulnerable to counterexamples. Comparative medicine becomes a way to refine causal explanations rather than merely decorate them with unusual animals.

**Counterfactual failure is as valuable as cross-species success. A causal model proposed from human physiology should generate predictions in other organisms, but the comparison may reveal that a supposedly essential human feature is merely one implementation among several. That is an opportunity to refine the model at a deeper functional level. Physiological equivalence does not imply anatomical identity, and a trait shared across species may reflect common ancestry rather than independent convergence.**

The research therefore needs phylogenetic controls, careful definition of environmental constraints and predictions specified before data inspection. It should ask whether alternative designs solve the same transport, regulation or repair requirement. If they do, the underlying cause may be a systems constraint rather than a particular molecule. If they do not, the explanation may need to be limited to the human context. That vulnerability to comparative counterexamples is precisely what makes the method scientific.

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

Counterfactual biological reasoning asks what would be expected if a known physiological process operated under different size, environment, anatomy or evolutionary history. The dinosaur book proposes using extreme cases to test whether medical models are genuinely mechanistic or merely fitted to familiar human baselines. The useful insight is that physical constraints can generate bounded predictions, even when direct clinical trials are impossible.

An animal with exceptional body mass changes surface-area-to-volume relationships, load-bearing demands and the geometry of circulation. Air-sac respiration in avian lineages introduces different ventilation considerations from mammalian lungs. A fossilized bone lesion can be compared with

known tissue responses across living archosaurs, but preserved morphology does not by itself reveal the organism's symptoms, immune history or clinical prognosis. Counterfactual modeling can expose hidden assumptions in human-centered physiology: for instance, whether an explanation depends on body size, posture, metabolism or a specifically mammalian organ system.

A giant sauropod and a modern bird differ in size, ecology and often anatomy, yet both exist under fundamental physical constraints. A comparative model may use those constraints to narrow possibilities without pretending to observe extinct physiology directly. This is useful reasoning, but it cannot be elevated to a treatment manual in the absence of living reference populations.

The main danger is analogical overreach. Modern birds and crocodilians are not interchangeable representatives of extinct lineages; dinosaurs varied enormously over time. A model may fit a vivid story while remaining underdetermined by sparse fossils. Claims about psychological distress, gallbladder physiology, therapeutic dose or detailed infection timelines in extinct species would usually exceed the available evidence.

A credible counterfactual paper states which parameters are known from fossils, which are borrowed from living taxa, what mathematical or mechanical assumptions are used, and how predictions change across plausible parameter ranges. Competing reconstructions should be carried through the analysis rather than suppressed. The method is weakened when it generates no observation capable of distinguishing alternatives.

For Absurd Health Institute, the broader lesson is transferable: explanatory models earn credibility by surviving difficult cases, including cases unlike those from which they were first developed. That is an argument for disciplined inference, not certainty beyond evidence.

Cross-species thought experiments test the portability of causal explanations, not the literal treatment of extinct patients.

An explanation based solely on body-mass index fails when anatomy and life history differ radically across species.

Write competing biomechanical and metabolic models and judge them against comparative data rather than imaginative plausibility alone.

Suppose a theory claims that obesity, temperature regulation or prolonged fasting has the same effects in every vertebrate because it affects a supposedly universal metabolic pathway. That assertion can be investigated by comparing organisms with sharply different feeding ecology, adipose storage, thermoregulation and reproductive strategies. The existence of a conserved pathway does not guarantee an identical whole-organism outcome: network connections and selection pressures may differ. A valid counterfactual therefore specifies both conserved mechanisms and expected divergences. Studies in extant species could ask whether the same manipulation alters performance in a similar direction after accounting for body size, physiological temperature and developmental stage. The theory would fail as a universal account if those measured outcomes systematically reverse in well-chosen comparative cases. The purpose of the extinct-animal scenario is to force precision about generality, not to generate medical advice for humans from imaginative zoology.

## 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>
3. Bailleul et al. (2019), Dinosaur paleohistology: review, trends and new avenues, PeerJ.  
<https://doi.org/10.7717/peerj.7764>

*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.*