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Article

Chronic Ambient Poisoning

Beth Alderman

Medical Philosopher and Methodologist, Future Medicine LLC, Ashland, OR, United States
medphil@evolvemedicine.us

Abstract: As of now, anthropogenic habitat injury via dissemination of manufactured chemicals is injuring the world's ecosystems, but doctors have yet to recognize its consequences to humans. Recognition of overt toxicity due to chronic low-dose exposure will open the door to diagnosis, sequential elimination studies, and prescriptions for preventive cure that represent a first step in preventing escalating chronic diseases. This paper offers a diagnostic construct for such use: chronic ambient poisoning. Incorporating it into clinical practice can reduce misdiagnosis of gastro- and near-toxicity that doctors and patients presently suppress rather than remove, and reduce patient co-dependence with proton-pump inhibitors, anxiolytics, and antidepressants—and the thriving "alternative" health industry. This diagnostic elephant-in-the-room is presently missed for reasons of habit (when an ailment is not recognized, it cannot be included in the differential diagnosis) and of poor conduct and interpretation of non-clinical research studies that are taken to mean an absence of evidence is evidence of absence. Moreover, modern methods fail when: the exposure comprises a "daily cocktail" of poisons acting additively, interactively, and cumulatively over a lifetime; when there is no normal, unexposed comparison group; and when absence of a robust etiopathogenetic model disallows inapt statistics. Only patient-led, consultant-informed sequential elimination studies can "peel the onion" of toxicity and its recognition and "preventive cure". Clinical use of the chronic ambient poisoning diagnosis can thus open the door to stemming and reversing anthropogenic epidemics.

Keywords: ubiquitous exposure; diagnosis; research design; quality of health care; habitat injuries; discovery

Key Messages

- **What is already known on this topic** – Provisional diagnostic labels have enabled doctors and patients to discuss emerging "silent epidemics" via terms such as fibromyalgia, "mito", CFS/ME, and so on; however, there is no actionable diagnostic construct based on contextual etiopathogenetic models.
- **What this study adds** – This study offers a working diagnosis that integrates new and mysterious chronic ailments under the construct "chronic ambient poisoning", and offers a working etiopathogenetic model for development via research and intervention that begin with sequential N-of-1 elimination trials, which lend themselves to qualitative aggregation and eventual creation of one or more gold-standard diagnoses.
- **How this study might affect research, practice or policy** – Clinicians can use this working diagnostic construct to: collaborate with literally uncountable patients in avoiding life-long suffering with early disability and onset of structural diseases; contribute to global efforts to restore the health of habitats; and aid in arresting onrushing extinctions and co- creating a living future.

1. Introduction

Cases of new "silent" epidemics such as myalgic encephalomyelitis cannot be counted accurately or precisely—in part because neurological or gastrointestinal toxicity

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goes unrecognized and unacknowledged in patients presumed to be unexposed to toxins. Other systemic obstacles include fatalism about the rise of chronic diseases, misinterpretation of uninformative negative studies as "ruling out" effects, immurement in false efficiencies that preclude personalized care, and being content to leave patients to providers and researchers with no grasp of diagnosis. The end result is that doctors miss exposures to ubiquitous toxins that are impactful at unexpectedly low doses, and so neurological and gastrotoxicity remain absent from differential diagnoses even when a patient is severely disabled. To address this diagnostic error, it is key to go back to the necessary art of formulating a clinical gold standard that abstracts biomedical reality without obscuring it.

2. Habitat Injuries as Context

At the present time, life on earth is immersed in a protean cocktail of poisons for which only insects and microorganisms can rapidly evolve resistance in nature. At the same time, species are disappearing and chronic illnesses in humans are escalating. *Homo sapiens* cannot keep up with the consequences of its actions, nor can the trees that outlive us (and that may not show signs of poisoning for a century). Even engineers ensconced in virtual realities question the reckless adoption of untested technologies (1) that are falsely perceived as desirable and therefore "safe" (2).

The ubiquity of synthetic chemical exposure is now sufficient for long or peak exposures to become symptomatic through toxicity aggravated by end-organ susceptibility, loss of tolerance, or both. While the tendency of the human mind is to dissociate the "silent epidemics" of mysterious ailments such as myalgic encephalitis from the seemingly slow-motion catastrophe of the modern era, we have noted poisoning of indicator species such as pollinators, amphibians, and pinnipeds, and are now documenting the progress of the Sixth Extinction (3). It is time to overcome the age-old illusions of human separation (4) and human exceptionalism. Humans, too, are an indicator species of damage to the biome and reveal the chronic sublethal effects of ambient exposures to chemicals such as those widely used in industrial agriculture.

3. Biomedical Complexity as Context

Busy doctors immured in over-systematized, over-engineered institutions have become over-reliant on data and statistics and overloaded by extraneous information. As a result, the "computerized" medical database assumes the role of oracle rather than fallible social consensus. The magic of statistics is not preferable to the practice of medicine, and the practice of medicine has become dominated by the practice of technology. Models comprising two "main effects" and an interaction term are too simplistic to penetrate the *in vivo* biomedical reality, which is that everything is connected (4). At and above the organ-system scale exist a myriad of influences related to organ function (e.g. liver enzymes), end-organ susceptibilities, concurrent exposures, and cumulative effects over time. Disregarding that complexity in favor of simplistic modeling is scientism, the dogmatic counterpart to true science, and goes hand-in-hand with under-utilization of clinical knowledge, wisdom, and street smarts. Ultimately, engaging with clinical complexity can only be done by fully-trained doctors who are free to listen to, observe, and collaborate with their patients while employing the close, informed, contextualized, and iterative experiential learning characteristic of Hippocrates.

4. Proposed Working Gold Standard

The new diagnosis Alderman syndrome, or chronic ambient poisoning (CAP), is based on the twenty-year self-study of the author, who was prepared by a career as an academic physician epidemiologist and specialist in Public Health and Preventive Medicine, and further "favored" by her own case of myalgic encephalomyelitis. This diagnosis is intended for eventual extension from the human scale to the biome by allopaths who

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draw upon our profession's two-and-a-half millennia of experience to serve as "doctors of life."

Figure 1 and Figure 2 illustrate the acute and chronic consequences of consuming a protean "cocktail" of poisons in and over time. Figure 3 profiles a lifetime of cumulative exposure, toxicity and detoxification, and loss of tolerance due to CAP. Figure 4 shows four hypothetical courses of human poisoning in the context of habitat poisoning. Note that this model offers the opportunity to "re-see" mental illness as neurotoxicity until proven otherwise.

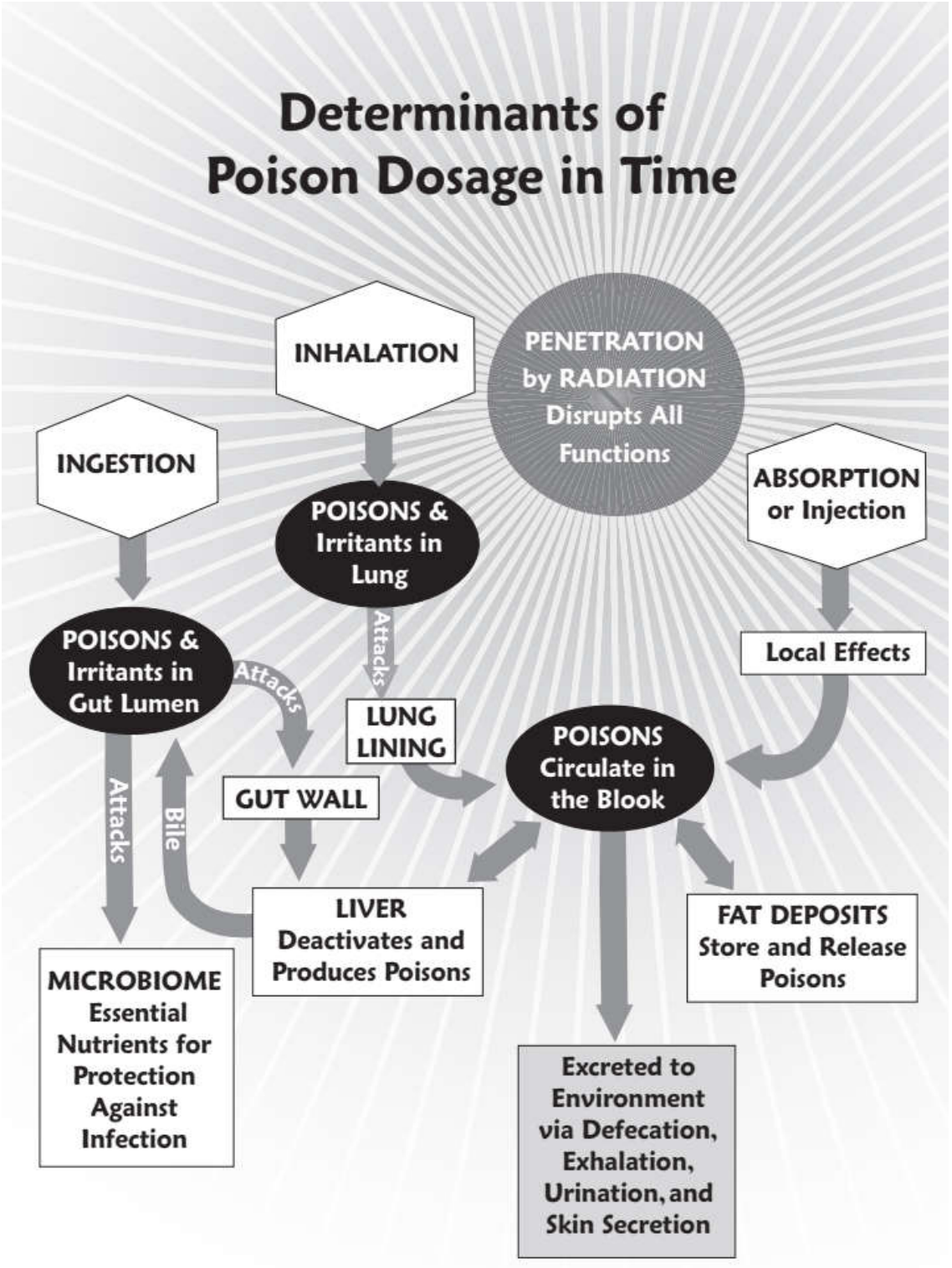

Figure 1. A diagram of poison metabolism and dosages in Alderman syndrome.

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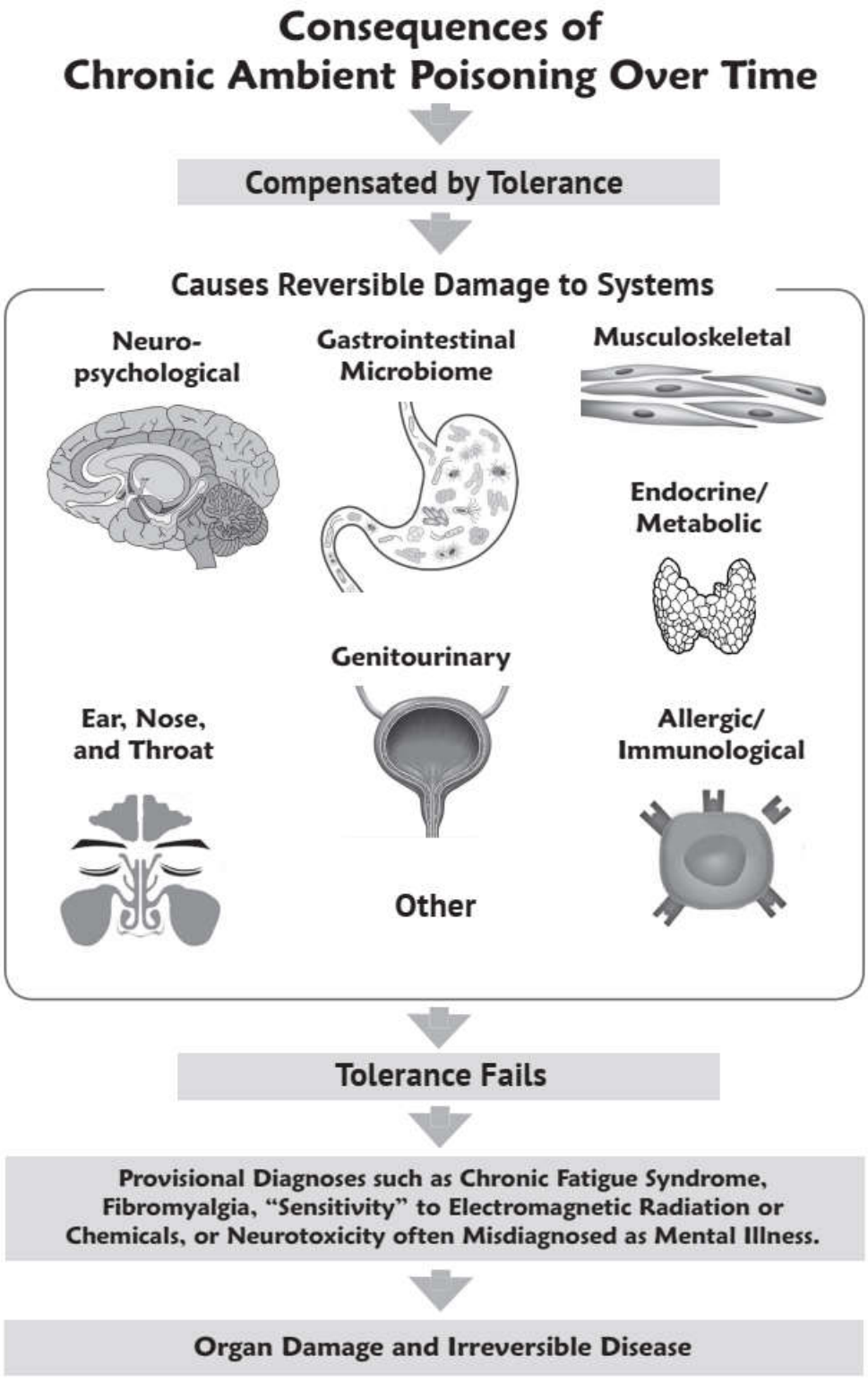

Figure 2. Consequences of chronic ambient poisoning over time.

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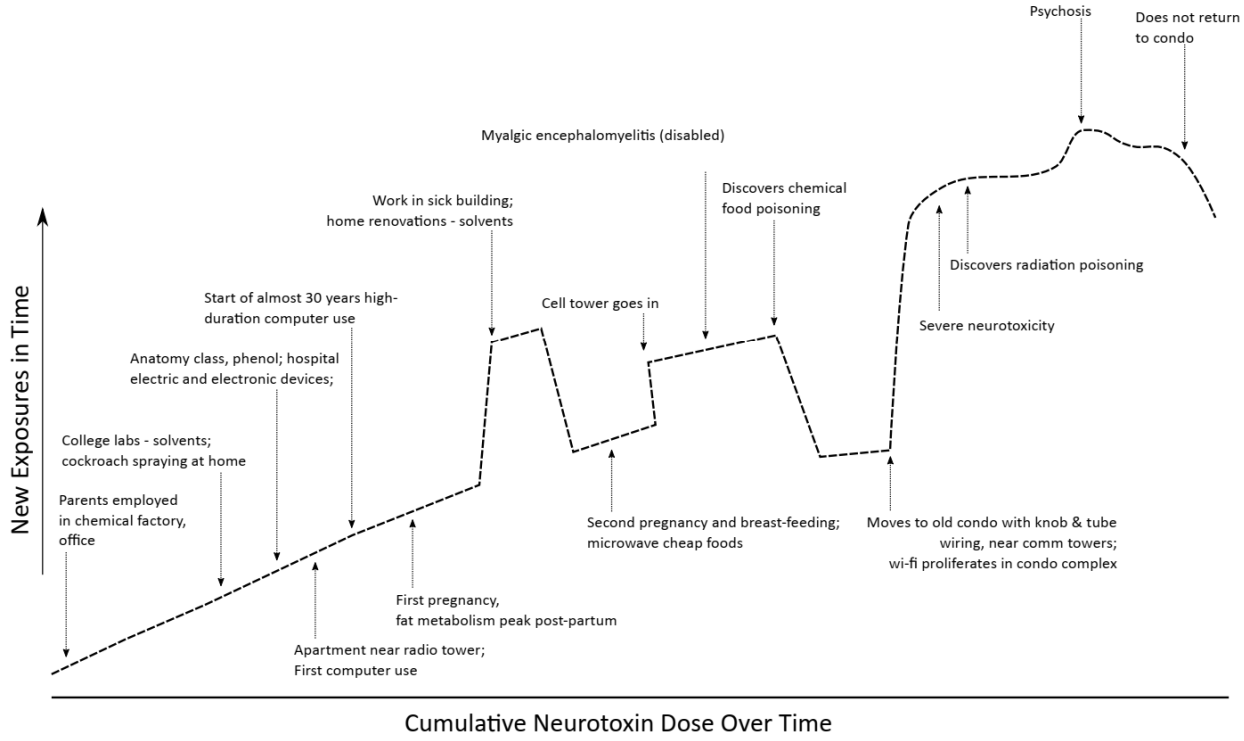

Figure 3. Representative individual neurotoxin profile accumulated over a lifetime.

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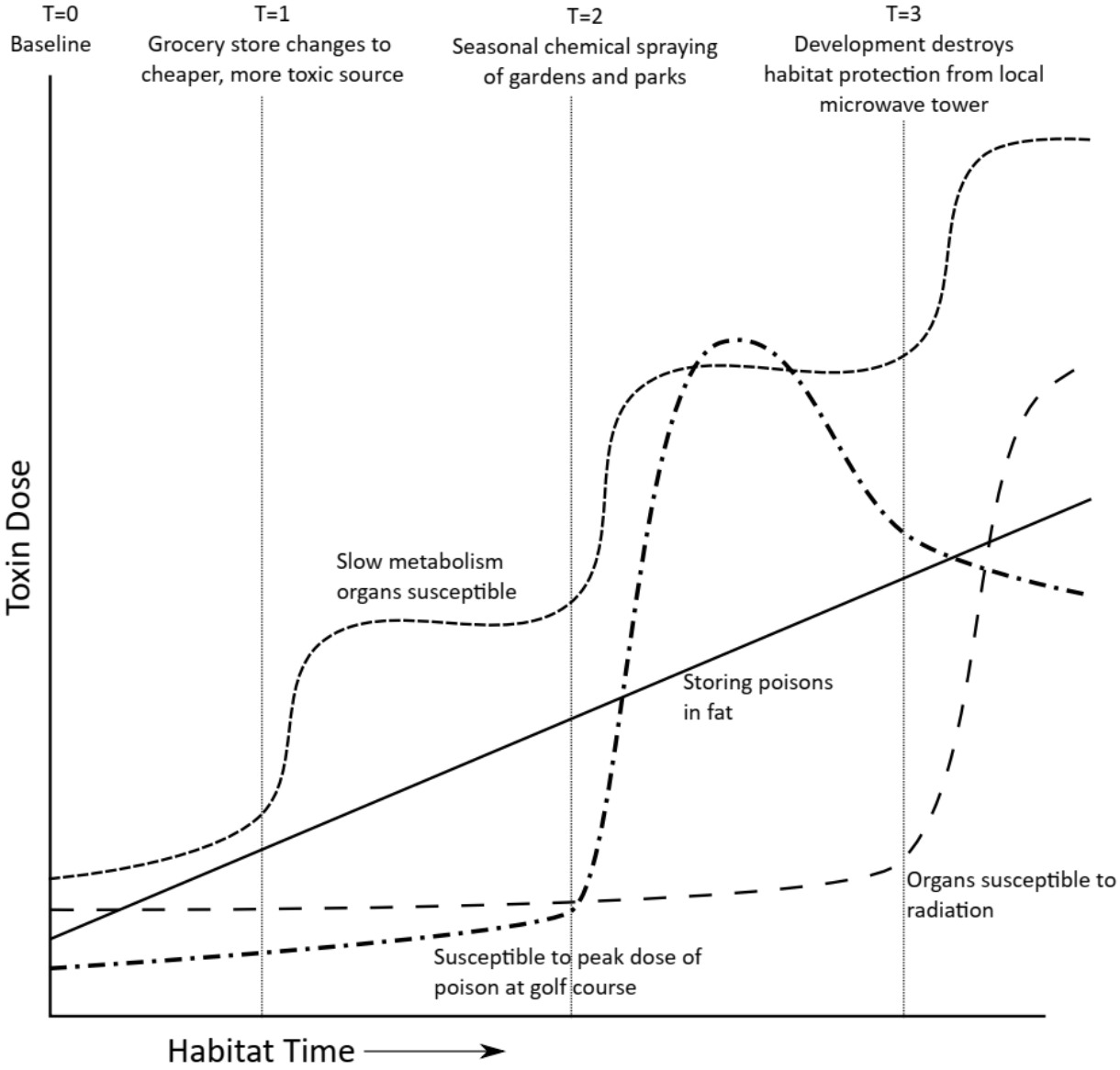

Figure 4. Examples of four distinct individual profiles of toxicity given a sequence of neighborhood events.

This diagnostic model obviates modern methods that cannot help but fail in the absence of a clinical gold standard, in which circumstance no diagnostic test nor risk factor can be evaluated by Bayesian methods that reveal predictive values and false positives and negatives (5). If cases cannot be counted and relevant exposure is not yet characterized, no analysis is the right analysis, and placing faith in AI will not change that (6,7). Moreover, in the case of CAP, until discovery of toxicity through sequential elimination has yielded the experiential group learning required to organize an effective response to this new-to-medicine diagnosis, there may be no valid legal or economic proxy test or consensus on "efficient" or effective treatment protocols.

5. Implications for Studies of "Environmental Factors"

Review of the four figures above will reveal some of the sources of noise that can explain negative results in conventional studies; such studies tend to so misclassify outcome and exposure as to obscure any signal, and represent premature social "science" analysis of provisional diagnoses. The figures can also provide a basis for reconsidering

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the assumptions typical of late-modern studies and the practice of statistical p-hacking, which are ripe for constructive disillusionment (8).

Table 1 displays untenable explicit or implicit assumptions alongside proposed emergent assumptions. Once a robust clinical gold standard for symptomatic CAP has been worked out through discovery (below), early detection and prevention—i.e. "cure" of chronic exposure—may become feasible. Then, rational "lumping and splitting" of cases will be feasible and reductionist analyses may be of use.

Table 1. Untenable to provisional assumptions.

Subject Lead-in	Untenable	Proposed
Poisons in the food supply…	…are safe and can be ignored.	…may cause leaky bowel, food allergies, microbiome injury, loss of liver/kidney function, and end-organ damage.
p-hacking is…	…an acceptable side-effect of present best standards.	…aggravates noise and overload in the literature and obscures advances.
Hazards are confirmed by…	…statistical modeling.	…elimination studies, personal and clinical.
Organ systems for evaluation are…	…identified via pathology gold standards or technological methods.	…selected via clinical evaluation at earliest stages of injury as possible in support of cure.
Studies of a single exposure and outcome in the general population are…	…accepted as definitive.	…discouraged as likely to waste time, money, and resources that could be used for restoration clinics.
The unseen, intangible, and subjective are…	…irrelevant.	…essential to active patient participation and to patient-doctor collaboration for care, cure, and discovery of the new.
The carefully-selected comparison group is likely to…	…be unexposed and "normal".	…be exposed from the womb to a dynamic "cocktail" of ambient poisons variously metabolized by liver and kidney and of changing dosages that may include "peaks" of etiopathogenetic importance; be evolutionarily abnormal for intergenerational, experiential, and concurrent reasons related to anthropogenic dissemination of toxics.
The patient or participant's natural life-giving habitat can be…	…ignored.	…the source of urgent, declining aspects of health such as evolved immune function.
Determination of dosage may be…	…short-term and limited to the parameters of interest.	…impossible due to dissemination of toxins that may or may not be metabolized into less-toxic forms and may be stored in fat, bone, and/or other tissues.
Chemicals can be deemed safe if…	…they do not cause the endpoint under study; if the study is negative; if the methods were deemed acceptable; or if the study is large and negative.	…never, because negative studies mean very little and *p*-hacking proves nothing.
Statistics are essential to…	…generalize results and prove significance.	…scientism, i.e. the appearance of science, which is lost in the gap between biomedicine and math.
In situations wherein exposure cannot be plausibly calculated across toxins for the lifetime, or the full spectrum of harm cannot be assessed…	…it is good enough to do the best possible study.	…no conventional study should be attempted as it will yield disinformation.

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6. Exposure Assessments

In risk analyses used for regulatory purposes, dose-response relationships tend to be non-linear, and short-term high-dose exposures may prove as damaging as chronic ones with respect to cancer occurrence (9). In other words, "dose assessment" is not yet clear even for studies of cancer risk, which is a well-understood and precise outcome relative to CAP. Medical science cannot depend on frequentist modeling when the substantive knowledge on which mathematicians depend is lacking.

With CAP, there is no reason to believe that evolutionary "normal" levels of exposure exist for late modern risks, or that any threshold of toxicity can be defined. In terms of risk, the presence of fixed aggravating factors such as slow or toxifying metabolism may appear to be more important than toxicity itself. Therefore, at present, doctors and patients are best positioned to identify relevant and remediable personal exposures via deterministic reasoning informed by a broad knowledge base of medical diagnosis and free discussion.

7. Discovery Process

In the decades after publication of Rachel Carson's book *Silent Spring*, Professor Mervyn Susser wrote a book that attempted to apply ecological thinking to epidemiology (10); Alvan Feinstein wrote an article on the lack of utility of publishing small odds ratios that were likely to be unimportant (11); and Thomas Chalmers, originator of the meta-analysis, advocated the N-of-1 patient trials proposed by David Sackett and colleagues (12). Their efforts remain in the literature like dangling conversations, reminding us that the acquiring of experiential wisdom (i.e. clinical acumen) is all but precluded by the false efficiency of scientism. Diagnosis remains an art unattainable by algorithm, as the developers of "INTERNIST-1" confirmed (6) and as the investigators of complex systems at the Santa Fe Institute (13) ceded upon replacing the mathematical term "emergence" with the artistic word "creativity".

Fortunately, Drs. Luria and Sacks sustained long narrative case studies based on keen observation of phenomenology, as per Dr. William James; field biologists such as Diana Beresford-Kroeger and Bernd Heinrich continued to observe species *in situ* over time; and case series like that of Dr. Grace Ziem (14) and policies like those of the ACOG (15) continue to inform and protect the species.

Such examples of direct learning and the history of medical discovery from Hippocrates to the dawn of interventionist medicine informed the author in undertaking a discovery process that some now use in biotech. It comprises sequential theorizing, observation, elimination, and pivoting to iterate in a new direction when a theory does not prove useful. The object of this process is learning rather than "proving." It is responsive, resilient, relatively rapid, reliable, flexible, and clinically valid. It is suited to the early, strategic seeking of cure, and as such is suitable to the present challenge of addressing problems caused by the rapid degradation of our living context, such as CAP.

Employing discovery and putting their patients first, the author's personal physicians learned directly from clinical experience, and—despite paying the social and financial price for being mavericks—were successfully able to help reduce neurotoxicity and increase patient efficiency in self-care (for more, see Web Extras and long narrative case study (16)). Note that allowing time for elimination trials of sufficient length to suit the suspected toxin and the rate and route of exposure is key.

8. Discussion

Now, modern subliminal assumptions about Nature are failing. She is not infinite; the human-caused Sixth Extinction is killing her. But while leaders form action programs like "Making Peace with Nature" (17) and Project TENDR (18), biomedical scientists have yet to engage the "Living Paradigm" or Living Futures (19). We physicians must scramble to deconstruct our modern failures and to construct views, frames, constructs, and methods able to sustain life on earth—including habitat-aware and re-integrated humans (20).

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As the UN Decade for Biodiversity ends in failure (21) and the Decade for Restoration dawns (22), it is time to accept that the new normal is no evolutionary normal, that habitat degradation and sublethal environmental poisoning affects humans alongside the bees, birds, salamanders, seals, and other species besides, and that doctors must step up and aid in the process of restoration and recovery.

It is ironic that Bayesian probability revision, which is key to grasping quantitative differences in the utility of proxy gold standard diagnostic tests, risk factors, and biomarkers, is ignored by doctors while black-box frequentist modeling abounds—and obstructs biomedical reasoning. The doctor is left with skepticism, which is not a method and does not scale. As such, mentioning any aspect of CAP to a clinician can elicit a blank stare or what might euphemistically be called an unscientific response. One reason is that the adaptive unconscious trained by long habit or by databases is not amenable to rational system-two (2) thought or to careful critique of studies that sustain conventional errors. Uncoupling the term "evidence-based" from p-hacking could reduce error and stimulate discovery.

By learning with patients in clinic, allopaths can hone their acumen and construct useful and prudent hypotheses with their patients, and so emerge from the late-modern era of top-down data and information bondage and develop restorative practices suited to the moment. Critical to collaboration will be toxic patients who carry labels such as: myalgic encephalomyelitis, chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivities, chronic Lyme disease, mitochondrial dysfunction, insomnia, mood or thought disorders, leaky bowel, small bowel intestinal overgrowth, gastrointestinal reflux, immune dysfunction, or irritated bowel syndrome.

As fuel for future theorizing, it may be pertinent that many pesticides target the evolutionarily-stable potassium pump (23), and that *KCNJ15* and *Kir4.2* may be candidate genes for susceptibility to non-ionizing radiation poisoning, *Kir4.2* through its interaction with polyamine levels (24). In the interim, neurotoxic patients should be advised to limit ongoing radiation exposure to one milligauss as per the Austrian Medical Association and German Institute of Building Biology, or at most to four as per the Israeli Ministry of Environmental Protection. Finally, a practical approach to restoring patients with their habitats would be to upgrade spas or lightly-damaged habitat reserves to include habitat restoration clinics and communities; these could affiliate with specialists ranging from plant pathologists to physicians, as per the One Health programs but located in safe habitats and infrastructures.

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in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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