Ecological medicine: Complex systems, health, and disease

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Oct, 2006

At the beginning of the 20th century, the Flexner Report, commissioned by the Carnegie Foundation, concluded that medical practice was not sufficiently informed by science and that medical education should be designed so that physicians would be well-grounded in science and the pathophysiology of disease. The report exerted strong influences on the direction of medical research, education, and practice in the decades that followed. We're all aware of major advances that have grown out of an increasingly large medical-industrial complex. But the advances have come at a steep price. Health care-related activities now comprise about 16% of the GDP and health care institutions are increasingly interested in the bottom line, capturing market share, units of service, and productivity. Flexner himself said just 15 years after issuing his report that "scientific medicine in America—young, vigorous, and positivistic—is today sadly deficient in cultural and philosophic background."

It is not entirely coincidental that during the 20th century the paths of medicine and public health diverged. Despite recent repeated calls for re-integration by the Institute of Medicine, the NY Academy of Sciences, and others, medicine and public health continue to live largely, though not entirely, in separate worlds.

Let me now add yet another thread to this story. During the past 100 years humans have brought unprecedented change to the earth—to the soil, oceans, lakes, rivers and streams, coral reefs, forests, climate, the troposphere, and even the stratosphere. Biodiversity has precipitously declined throughout the world, the world's fisheries are severely depleted, and worldwide people and wildlife are contaminated with industrial chemicals. In a reciprocal fashion, these changes have in turn, exerted profound influences on human health. We will be hearing about some of these today though many will not be mentioned because of time constraints.

These and other unprecedented changes in planetary ecosystems are authoritatively described in the United Nation's Millennium Assessment—published in 2005 and readily available on the web for those who have not seen it. It also warns that many ecological systems are stressed to the point that they are increasingly likely to cross thresholds and undergo rapid, surprising, non-linear, and irreversible change.

It seems clear to me that the need for integration goes beyond medicine and public health. There is a sense of urgency to the need for more fully developing the concept of ecological health. Ecological health embraces the deeply fundamental complex interrelationships that collectively influence human and environmental health. Ecological health recognizes the undeniable interdependence and connectedness of all living and non-living things in the planet's biophysical systems. The natural, social, and built environments are intimately interconnected without discrete boundaries. I have come to imagine a kind of nesting of medicine within public health within ecological health. Viewed in that way, inter-relationships, connections, and patterns become more apparent.

Using this as context, here are a few basic questions: What is health? What is environmental public health? Do we know it when we see it? What are we looking for? If you ask these questions of people in clinical medicine, public health, or ecology, you are likely to get different answers. And, we might wonder why.

At a somewhat superficial level, we might simply say that clinical medicine tends to focus on the individual, public health on communities, and ecologists on ecosystems and let it go at that. But I think there's more. I'm going to address three topics that I believe to be relevant.

1) First, there is considerable evidence that how we view the world or "how the world works" is socially and culturally determined. As a result, there are profound differences

in world-views wherever there is social and cultural heterogeneity. Moreover, the way we view the world influences the metaphors that we use to describe what we see. In turn, the metaphors that we use influence the way we view the world—a kind of self-reinforcing circularity.

2) Second, how we view the world influences how we study the world and explain what we think we see.

3) Finally, how we view and study the world influences how we respond—what we decide to DO—as individuals, and collectively, through public policy.

Worldview:

I am convinced that most people in the US think of "the environment" as "out there".

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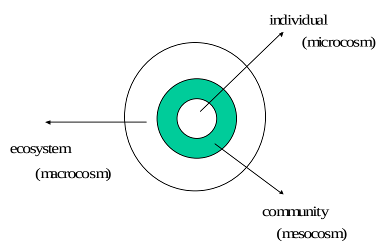


It is other than me. I am here, and it is out there, even though it surrounds me. Inherent in this idea is that I am somehow separate from "it". But this image is challenged when I'm told that a similar mixture of industrial chemicals can be measured in house dust or rainwater and my blood or urine. It is challenged by the trillions of bacteria in my intestinal tract on which my health (or illness) depends, or the quality of air in my lungs. It is also challenged by my increased risks of morbidity and mortality if I am born into poverty. It's not really "out there". It's "in here."

But we soldier on. We talk about external "events" or "forces" that act on us as individuals or communities that individually, or in some kind of additive way, influence our health or well-being. These metaphorical terms reflect how we view the world—that we are the "recipients" of forces from "outside".

There are of course other popular metaphors. But their use varies considerably and it seems to me important to understand why and what the consequences might be.
As George Lakoff and Mark Johnson put it in their essay, "Metaphors We Live By":

"The concepts that govern our thought are not just matters of the intellect. They also govern our everyday functioning, down to the most mundane details. Our concepts structure what we perceive, how we get around in the world, and how we relate to other people. Our conceptual system thus plays a central role in defining our everyday realities."

In a number of fascinating experiments described in a series of papers and in his book, "The Geography of Thought", Richard Nisbett (University of Michigan) identified important cultural differences between Asians and Westerners that may be relevant to this discussion.

Among the major findings:

- When presented with a complex scene, Asians are more likely to see a whole picture rather the various parts
- Westerners are more likely to insist on using formal logic, while Asians are willing to live with more contradiction
- Asian languages are rich in verbs, while Western languages are rich in nouns, and this affects how children relate to the world
- The Western style is to state things clearly and directly so that no misunderstanding is possible, while the Asian communication style is less direct (and less clear to Westerners)

This suggests to me that there may also be important cultural differences in how we study the world and attempt to explain what we see:

Science, of course, has rapidly progressed over the past 150 years using primarily a reductionist approach in which complex systems are taken apart into individual pieces in order to try to understand more and more about smaller and smaller parts.

That approach has undeniably been useful and in medicine has helped to advance understanding of the pathophysiology of many diseases. It is also an approach that is commensurate with a view of the world comprised of a collection individual “things”.

But the consequences and limits of this approach are increasingly apparent. Clinical research tends to focus on proximate causes of disease. Social structural causes of disease, whose mechanisms may be indirect, circuitous, and difficult to study, are either relegated to second class status or believed to be the responsibility of someone else.

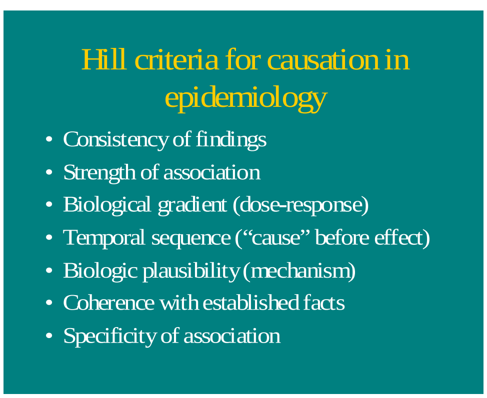
Beyond that, for years, ecologists have known and told us that complex systems have emergent properties that cannot be predicted from examining individual components. By now, we should know that this is right but our training and disciplinary structures and isolation get in the way of figuring out how to address system interactions and emergent properties.

Today, systems biologists painstakingly attempt to understand the emergent properties of biological systems by studying reassembled pieces of cells and tissues. Unfortunately, this still leaves us quite some distance from whole organisms, communities, and ecosystems.

The 17th and 18th centuries saw the beginning of systematic attempts to explain the world mathematically, to remove faith, values, and emotions from reason that was equated with science, to break the world up into smaller objects of study, and above all, to keep Humanity apart from Nature—“in a world by itself”. (One thoughtful account of this story is by Stephen Toulmin in his 1990 book—Cosmopolis, The Hidden Agenda of Modernity).

People have wondered for a long time how to explain what we are seeing when someone is sick. What is the cause of her illness? Why are so many people dying in this community? People have always struggled with the concept of “causation”. Scottish philosopher David Hume said, “We do not see causation. We observe events in the world and we infer causation”. In the 19th century, Robert Koch laid out his criteria for judging whether a given bacterium is the cause of a given disease. His criteria brought much-need clarity to the field of infectious disease. But we know now that rigid criteria can lead us astray when dealing with most non-infectious diseases where we are more likely to be dealing with multiple factors interacting in complex ways. Moreover, we also now know that the causes of individual disease may be quite different from the causes of the pattern of that same disease in a population.

Modern epidemiology has been strongly influenced by Bradford Hill’s criteria for establishing cause and effect relationships since he published his influential paper on causation in 1965. (SLIDE)



Kenneth Rothman has been another important influence. He uses a “causal pie chart” that ascribes various sized slices to component causes of a disease and lays out differing sufficient causes of disease.

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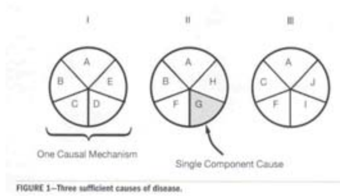

Rothman, AJPH, 2005

Rothman emphasizes that a given disease can be caused by more than one causal mechanism, and every causal mechanism involves the joint action of a multitude of component causes. This approach gets us thinking metaphorically about causal webs of disease rather than single causes—single outcomes linked together in predominately linear relationships.

But we can also see how this metaphorical approach can be misleading, since we have a tendency to think that collectively, the slices of the pie should add up to the whole pie—to 100%. But that is often not the case. The sum of the fractions attributable to each component cause of a particular mechanism may actually add up to more than 100%. This is because individual factors do not act in isolation from each other but often interact—interact biologically—to increase (or decrease) the risk of disease.

There is yet another concern with the metaphor of the causal web. In 1994, epidemiologist Nancy Krieger published a paper called, “Epidemiology and the Web of Causation: Has anyone seen the spider?” (Soc Science and Med. Vol 39, 1994) She claimed that the metaphor of a web of causation traps us in a particular way of viewing the world that leaves out important considerations.

Why, she asked, were some strands included in the causal web model while others were left out? What might explain the entire web that the mathematical models attempt to describe?

She proposed an eco-social model that could accommodate the influence of numerous environmental influences—physical, biologic, social, cultural, economic—at each level of biological organization—from DNA to the individual to the entire population.

Krieger has spent much of her career addressing the influences of gender, race, and income on health outcomes. Her research shows how they also shape the strands and structure of causal webs of disease.

When epidemiologists look for the main effect of some environmental factor on health—for example the impacts of lead exposure on brain development in children, or pesticide exposure on cancer risk—they often use multivariate regression models that attempt to "control" for gender, race, and income as if they are "confounders".

But there are problems with this approach. First, models that represent these variables simply as male-female, black-white-Hispanic, or absolute income fail to recognize an entire cascade of their more nuanced influences on multiple strands of the causal web over lifetimes.

Race is more than being black or white or Hispanic. Racism, or how a person actually experiences being black, white, or Hispanic, has strong influences on health in multiple ways and may vary dramatically from one place to another.

Income is more than an absolute monetary number. In a given community, income inequality, regardless of absolute income level, is also an important determinant of adverse health outcomes. And gender bias may vary from one community to another and influence the biology and life experience of individuals in multiple ways.

Racism, poverty, and gender are not variables to be "controlled for" as confounders. Rather, they are frequently "effect modifiers". Effect modifiers alter the magnitude of the association between an exposure and an outcome across the strata of some other factor—such as race, social status, or gender.

Effect modifiers influence the biology of organisms and communities in ways that make them more or less susceptible to other environmental factors such as exposure to chemical environmental contaminants or nutritional deficiencies.

In the October issue of EHP, Bernie Weiss and David Bellinger discussed the importance of effect modifiers when studying the impacts of neurodevelopmental toxicants. They put it this way:

"We contend that a true evaluation of toxic potential and neurobehavioral consequences is inseparable from the ecologic setting in which [neurodevelopmental toxicants] act. The ecologic setting creates unique, enduring individual vulnerabilities **that warrant the same status as genetic predispositions and are imprinted as forcefully. "**

They went on to say: "We tend to assume that the potency of the neurotoxicant is invariant regardless of the social ecology within which it occurs. Such a bold assumption is appealing in its simplicity but almost certainly wrong."

Let me give just a few examples to illustrate the point:

Lead, iron deficiency, and social circumstances.

[Effects of lead, iron deficiency, separate, together. New model.]

Many other studies in animal models show that various combinations of maternal stress, lead exposure, and dietary manipulations can influence the behavior and learning capacity of offspring, with permanent alterations in brain architecture, neurotransmitter levels, and gene expression.

Mercury and dietary fatty acids

In September, at the annual neurotoxicology conference in Little Rock, Phil Davidson from the University of Rochester reported the latest findings from the Seychelles Island study of the impacts of methylmercury on brain development in children.

[Many of you are probably familiar with that study but briefly: It is a long term, longitudinal study of the neurodevelopmental impacts of methylmercury exposure during fetal development. Maternal methylmercury exposures are largely from fish consumption. Maternal hair levels of mercury were measured during pregnancy and their children's neurological development has been assessed periodically. As you may be aware, up until now, no impacts of methylmercury at these levels of exposure have been detected, though other studies in the Faroe Islands, New Zealand, and Brazil have detected adverse impacts from ambient exposures in their study groups.]

But the Seychelles Island group has now added a nutritional arm to the study. In 282 children, all of whom are well nourished, they have measured levels of iodine, choline, the omega 3 fatty acid DHA (docosahexanoic acid), the omega 6 fatty acid, arachidonic acid, iron, and total fish intake as well as maternal mercury levels during fetal development.

They have constructed two different models for examining the data. Looking at the data in this way, they learned that the 30 month PDI (psychomotor development index) is influenced by the combination of mercury and DHA levels. Increased DHA levels improve performance on the PDI. When corrected for DHA, however, increased exposures to mercury led to decreased performance. Put another way, as mercury exposures increased in this population, increased levels of DHA were necessary to maintain the same PDI score.

This is the first time that adverse impacts of mercury were detected in the Seychelles cohort at these levels of exposure. Uncovering the impacts depended on knowing detailed information about individual nutritional status—information that is missing from the vast majority of epidemiologic studies examining for the impacts of toxic environmental contaminants.

There are many other examples of interactions between exposures to toxic substances and nutritional status. Very briefly, here are two more.

A few human and many more animal studies show that relatively common micronutrient deficiencies (such as zinc deficiency in women of reproductive age) increase the risk of having a child with a birth defect after exposure to a teratogen. But most studies looking for environmental causes of birth defects never attempt to examine the combined influence of exposure to potential teratogens AND maternal micronutrient status, although it appears that these interactions are extremely important.

One final example: In rodent studies, a maternal diet that is high in omega 6 fatty acids relative to omega 3 fatty acids alters breast development of female offspring so that they have a higher risk of breast cancer as adults when exposed to a carcinogen. In humans, there is considerable support for the idea that dietary factors influence the age of thelarche, puberty, and breast cancer risk. But I know of no human study that has taken a detailed look at dietary factors as a risk modifier for breast cancer in the setting of subsequent exposure to potential carcinogens. Such a study would of course be difficult to design and implement, but it would come closer to representing the real world than ignoring these important interactions.

I could go on but time does not permit. It brings me to my final question:

How are we to respond to an ecological view? In research? In public policy? In clinical practice?

There is, I think, an urgent need to refine our metaphors and models. Many of the terms that we use imply external sources acting on us individually. In reality, there are few external sources but rather ecologic circumstances, discoverable within each of us, bound up our DNA and tissues.

Whatever metaphors we use, they should be consistent with the strong interdependent and co-evolutionary relationships among individuals, communities, and ecological systems. Change is inevitable, but the qualities and directions of change result from dialectic relationships among parts and whole.

Most current epidemiologic studies include measurement of individual-level or family-level factors but rarely consider the importance of neighborhood, community, and cultural characteristics. Even more rarely are such factors evaluated as effect modifiers as well as potential confounders.

New study designs, models, and statistical techniques, perhaps drawing on lessons from ecology and the social sciences, are likely to deliver more informative epidemiologic research.

Much of this will open up new territory for physicians and health care professionals who are usually "prisoners of the proximate." (I'm not sure who coined that phrase. I first heard it from Paul Farmer but have also heard it attributed to the epidemiologist Tony McMichael.)

Here's what it means to me. We tend to concentrate our efforts on well-established proximate causes of disease about which there is little uncertainty, rather than more distal structural causes.

We are also imprisoned by disciplinary boundaries—not only between medical specialties, but many conclude that corporate, social, economic, and political forces that influence health are not in the realm of medicine but are the responsibility of others.

How does this play out? Health care professionals may provide gastric bypass surgery for obesity but fail to address the root causes of obesity in their communities—including their own hospitals, which often serve calorie dense-nutrient poor food in cafeterias or lease space to fast food restaurants serving similar food elsewhere on the premises. (It's important to acknowledge exceptions to this at Kaiser Permanente, Catholic Healthcare West, other hospitals in the Bay Area, in Portland OR, in the Midwest, and New England where these connections are beginning to be seen and new practices initiated)

We treat various kinds of cancer, fertility problems, and neurological disorders in our health care institutions but nearly always fail to address systemically the strong weight of evidence that implicates pesticides and other industrial chemicals in their origins.

How do we grapple with the urgent message delivered in the UN's Millennium Assessment, which tells us in no uncertain terms about the need to confront the unprecedented decline of ecological systems throughout the world? The implications for human health are profound. Health professionals from any discipline cannot continue to ignore this important empirical analysis even though mainstream media gave it little prominence.

It would help to learn how to design interventions to address multiple factors rather than addressing one risk factor at a time in isolation. Might we design institutions and interventions that address lead exposure, iron deficiency, and poverty in an integrated way? How do we restore the fisheries, get the mercury out of fish, AND enhance dietary omega 3 fatty acids in our children's diets?

In social ecology, the attributes of resilience, adaptability, and transformability determine the future trajectories of systems. <u>Resilience</u> is the capacity of a system to absorb a disturbance and reorganize while undergoing change so as to retain essentially the same function, identity, and feedbacks. <u>Adaptability</u> is the capacity of members of the system to influence resilience. Transformability is the capacity to create a fundamentally new system when ecologic, economic, or social structures make the existing system untenable.

It is likely to be useful to emphasize building resilience in individuals and communities; to use adaptive management techniques to explore interventions that solve multiple problems without creating new ones; and to seriously examine the kind of transformation necessary to address the realities of today's world.

Here are a few principles that we might consider when designing strategies:

- Consider the natural, built, and social environments in all decision making—at the individual, community, regional, and national levels
- Consider scale (both time and space)—if something is good, is more necessarily better? What is the reach of an activity in time and space?
- Consider relationships and not just data points
- Consider proportion. Ratios matter—often more than absolute values.
- Consider diversity. One size does not fit all. Appropriate solutions are usually context specific.
- Consider justice and fairness. The distribution of benefits and risks
- Consider future generations

A few examples of strategies to consider:

- Adopt individual and institutional purchasing policies that give preference to products whose ingredients are easily identifiable and that do not contain hazardous chemicals.
- Support reform of our current flawed chemical regulatory policy that allows untested and unsafe chemicals into the marketplace where they contaminate virtually all people and wildlife and into the workplace where workers are injured;
- Support new and existing regulatory policies that protect vital planetary life support systems, including air, water, and climate.

- Adopt dietary interventions and institutional purchasing policies that support the production of nutritious food raised in ecologically sustainable and socially just ways.
- Support fundamental transformation of agricultural policies that predictably result in inadequate or inappropriate nutrition, diabetes, obesity, increased risks of birth defects, cancer and other chronic diseases, and severe degradation of entire ecological systems. These are ecological health issues.
- Support revision of social policies that fail to address root causes of poverty and other sources of social stress like racism that predictably result in increased morbidity and mortality

- And as a long term goal in support of a long term vision, support transformation of the material economy to one that is right-sized and commensurate with the workings of the earth's biophysical systems. This is a far reaching goal, but seems essential so that future generations can survive with lives of quality.

There are of course many others.

When Bradford Hill published his classic paper on causation in 1965, he also said:

> "All scientific work is liable to be upset or modified by advancing knowledge. <u>That does not confer upon us a freedom to ignore the knowledge that we already have, or to postpone the action that it appears to demand at a given time</u>."

In an ecosocial model of health and disease, based on the best available science, medicine and public health inescapably share membership with the planet's ecosystems upon which life depends. Each individual and organization needs to examine what it believes its roles and responsibilities are in disease prevention as well as disease treatment—preserving and restoring life-sustaining ecological functions—and engaging with other sectors in a more integrated approach to environmental public health.