



Chronic Kidney Disease and Scientific Uncertainty, a Way Forward.

Good friends challenge you. They help you be your best self. For nearly 25 years, Carolyn Raffensperger has been a very good friend to me. When she asks me to do something, I know I will be challenged. And every time, I am better for it.

March is [World Kidney Month](#). Because I study an epidemic of chronic kidney disease in Central America, Carolyn, and Kayhla Cornell, asked me to write something for the [Networker](#) about my research and how it relates to the principles of SEHN.

The last time I wrote a piece for Networker, it was because Carolyn asked me to write about the connection between a [Danish-style consensus conference on the topic of biomonitoring](#), and music. In that piece I referred to Zimbabwean musician, Oliver Mtukudzi, known by his fans as Tuku. Tuku was one of my favorite musicians and I was fortunate to see him perform more times than I can count. Last month Tuku shocked his fans by dying at the age of 66. The cause? Complications of diabetes.

[Diabetes is one of the primary causes of chronic kidney disease.](#)

Chronic kidney disease (CKD) is the gradual decline of kidney function. Our kidneys filter all the blood in our body approximately every 30 minutes, removing toxins and waste (excreted in urine), keeping the blood clean as it is pumped by the heart and circulates through the body.

In the case of diabetes, the inability of the body to process sugar results in excess glucose in the blood. Over time, the glucose being filtered by the kidney causes damage to the cells in the kidneys-- it is toxic. The damage accumulates, cell by cell, until kidney function declines.

It is normal for kidney function to decline over time; the job of filtering our blood takes a toll on even the healthiest of kidneys. Along with diabetes, age is a major risk factor for chronic kidney disease. Other causes of kidney disease include autoimmune diseases (e.g. Sjogrens Syndrome and Lupus), medications (e.g. NSAIDs and chemotherapeutics), exposure to heavy metals (lead and cadmium), and other chemicals that contaminate drinking water supplies.



Three aspects of SEHN's work have fundamentally influenced my approach to research, my study of kidney disease, and importantly, my decisions about where I work and with whom: The precautionary principle, ecological medicine, and the public trust doctrine.

"As public health professionals, the precautionary principle challenges us to act for the benefit of public health even when the science is uncertain."

The **precautionary principle** is rooted in the German principle of foresight. In the US, SEHN co-hosted the conference in January 1998 that led to the [Wingspread Statement on the Precautionary Principle](#). At that time, I worked for a nonprofit organization whose mission was to democratize science and technology (we are still working to accomplish that mission...). The executive director, Dick Sclove, was a signatory on the statement, as was David Ozonoff, who I would work for three years later as a graduate student at [Boston University School of Public Health](#) (BUSPH). The precautionary principle has several critical elements, the first being the duty to take precautionary action in the face of uncertainty. As a graduate student and now an environmental health scientist, this element of the precautionary principle affects how I think about study design and conduct. No matter how good a study is, people will criticize it. Science rarely speaks for itself. As public health professionals, the precautionary principle challenges us to act for the benefit of public health even when the science is uncertain. It is also fundamentally an acknowledgement that science does not generate universal proof, it does not tell us what is true or false in such a manner that all will agree (think about evolution v. creation, round or flat world), nor is any single study likely to be the impetus for action.

As a student at BUSPH, and still today, I helped to create a book, along with SEHN and other contributors, a [Guide](#) for communities thinking about health studies. The *Health Studies Guide* is essentially written to help community groups affected by environmental health hazards and/or illnesses think about the pros and cons of initiating a study to address their concerns. As Dick Clapp, a contributor to the *Guide*, once pointed out, epidemiology is by definition anti-precautionary; by the time we are studying associations between exposures and disease, there is already disease. This is a major limitation of our approach. I am working on a study now that follows people over time, essentially waiting for them to get sick so we can then examine what exposures were experienced by those who became ill versus those whose kidneys stayed healthy (a prospective cohort study). Etiologic studies don't stop disease. But so often, people with disease look to scientists for answers, and the tools we have to provide them are dull; our answers often plagued with caveats and uncertainty.

The chronic kidney disease (CKD) I am studying affects primarily young men (under age 45) in El Salvador and Nicaragua. These men are not old, nor do they have diabetes or any of the known traditional causes of CKD- therefore, it has been given the name CKDu (CKD of unknown etiology). Other names are:

- CKDnt (non-traditional etiology)
- Mesoamerican Nephropathy, focused on the geographic concentration of affected communities in Latin America
- Chronic Interstitial Nephritis of Agricultural Communities (CINAC), which tells you more about the area of the kidney that is thought to be the origin of injury and the rural nature of affected communities
- Kidney Disease of Unknown Cause in Agricultural Laborers (KDU CAL), which describes the occupation of the population that is primarily affected.

These last terms, CINAC and KDU CAL are used in Sri Lanka and India which are also highly affected areas of the world. What the disease is called, and if it is the same disease, is the topic of discourse among investigators (see this [Letter to the Editor](#) of the *American Journal of Kidney Disease*, for example).

The [Boston University Research Group for the Study of CKD](#) formed after workers in the sugar industry filed a complaint with the World Bank against their employer. In a mediation process, the employer and the worker organization agreed on questions they wanted to have studied by outside researchers. Our team got that contract. The conditions were less than ideal for doing a study, but many of the lessons in the *Health Studies Guide* and from the precautionary principle informed our work and communication.

We found [evidence](#) that occupational heat exposure is associated with the decline of kidney function. The evidence was not strong enough to suggest that the entire epidemic is caused by heat, but BU made recommendations to the company for reducing heat stress among the workers, including that breaks be required for workers to rest in shade. We also recommended that heat stress training be given to all workers- including information on recognizing the symptoms of heat stress, and the importance of hydration. The BU team felt this was important information for preventing illness of any kind, even though we were (and are still) not certain it is responsible for the CKDu epidemic.

Additionally, in our preliminary studies early on, although we found no evidence of pesticide exposures that would explain the epidemic, we knew no evidence of effect does not mean evidence of no effect. We continue studying pesticides and heat exposure, and as with heat exposure, the team recommended improvements in pesticide use and handling practices. A more [recent publication](#) in the journal *Kidney International* summed up this perspective with the following conclusion, “Proper agrochemical regulations and environmental controls may substantially reduce disease appearance or progression. Hence, in accordance with the precautionary principle, they must be implemented, regardless of hypothesis or understanding of causation or mechanisms.”

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Pesticides are an especially vexing exposure to study due to the fact that chemical policies in the US are *anti*-precaution. Chemicals are innocent until proven guilty, and policies that protect industry trade secrets prevent researchers (and even the federal government) from knowing the chemical composition of many widely used agrichemical products. SEHN's advocacy for more transparent chemicals policies and right-to-know laws is essential for public health research and disease prevention. For the vast majority of public health researchers, our goal is to prevent disease, which is a second element of the precautionary principle: Set goals for health protection.

Finally, although I personally spend most of my research time these days on trying to understand the occupational health exposures that contribute to disease, I do not believe this disease is *primarily* occupational. I know that there are young people who have never worked and who also get CKDu. So, the occupational exposures are part of the larger story, and to fully understand the complete picture requires collaboration with people looking at different aspects of the disease, and different life phases. Our BU team refers to this as a life course approach, looking at early life exposures, workplace exposures and genetic susceptibility that may be inherited.

Last week many of us studying CKDu convened at the [Third International Conference Chronic Kidney Disease of Unknown/Non-Traditional Etiology in Mesoamerica and Other Regions](#). As it has been written elsewhere, the precautionary principle does not mean we need less science before making decisions. On the contrary, the best decisions would be made with more and rigorous science, ultimately reducing our uncertainty to the extent possible.



"Ecological medicine draws on knowledge of ecosystems as a practical metaphor. It is a reminder that the human body is a complex system, within a complex system, and we are interdependent."

Ecological medicine is a term coined by Carolyn in 2001 naming the concept that human health is dependent on ecological health. While this is essentially the foundation of what I do, environmental health science, ecological medicine draws on knowledge of ecosystems as a practical metaphor. It is a reminder that the human body is a complex system, within a complex system, and we are interdependent. Biological systems often have a threshold, a tipping point.

Chronic kidney disease is often not diagnosed until damage has taken a substantial toll. We have two kidneys, essentially a built-in back-up system. By the time decline in kidney function is symptomatic, the damage is pretty bad. Damaged or diseased kidneys can lead to heart disease, stroke, anemia, and increased occurrence of infections. A member of my own family went to the hospital with symptoms of a heart attack, only to learn that the kidneys were first to fail.

One of the big research questions for people studying CKD, and a question discussed at the earlier mentioned conference last week is, can we identify a more sensitive, earlier indicator of kidney dysfunction so that we can foresee and forestall decline sooner (back to the precautionary principle)?

In 2002 a committee convened by SEHN and the [Collaborative on Health and Environment](#) drafted a [statement on ecological medicine](#). Two concepts that define ecological medicine and resonate most with my research are Reconciliation and Interconnectedness.

Reconciliation refers specifically to health care,

“Individual health care services should be economically sustainable, equitable... of high quality, noncommercial and readily available to all. Societies should build and maintain infrastructures that assure all citizens the capability to meet basic needs such as health, nutrition, family planning, shelter, and meaningful work while minimizing harm to the Earth.”

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The BU CKD research team includes physicians and nurses who are incredible researchers, and for whom treatment and care are fundamental. This is not true of many epidemiologists who simply are not trained in medicine or health care practice. As we see more people die of disease and get sick during our studies, the imperative to stretch human and economic resources to their limits, and be creative about care becomes more urgent. CKDu appears to be a disease of the poor. The most affected populations are often the poorest, in poor countries with health care systems not equipped to provide dialysis to everyone in need, and where transplants are not legal or possible. Of course, even in the US, one of [the wealthiest countries in the world](#), there are [disparities in disease and access to care](#). Indigenous Americans have been especially vulnerable to kidney failure; [Five times more likely to experience kidney failure](#) than their White counterparts. Ecological medicine requires coming to terms with unequal, unsustainable, and often culturally inappropriate health care, and committing to its improvement.

As per Interconnectedness, ecological medicine suggests that the chronic strains on ecosystems due to climate change may likely result in less predictable patterns of disease. Due to weather patterns and rising temperatures creating environments that are hospitable to disease transmitting vectors (ticks, rodents, lice, bacteria, etc.), infectious diseases are most certain to appear in places where they were not previously experienced. But what about chronic diseases that appear to have no direct relationship with climate? It is not known that CKDu is caused by heat or even a widely accepted hypothesis. However, an entire area of the US is called the kidney stone belt to the high rates of kidney stones. Research suggests the [kidney stone belt is creeping north](#) as temperatures rise, and temperatures more characteristic of the Southern US move north. In regions of the world where potable drinking water is scarce, could [CKDu also be a disease of climate change?](#) Regardless, over time, prevalence of chronic kidney disease and attributed mortality is [increasing globally](#). Some fraction of this increase is attributed to the obesity epidemic, and to diabetes. Ecological medicine would ask, What interconnected variables together explain these epidemics? More recent studies of endocrine disrupting chemicals indicate that poly- and perfluoroalkyl substances known collectively as PFAS, are both kidney toxicants and [obesogens](#). In other words, they are toxic to the kidney *and* they interfere with metabolism, resulting in more fat. PFAS, and other endocrine disruptors, also interfere with hormone production. In addition to filtering our blood, kidneys secrete hormones that are essential for controlling our blood pressure, fat regulation and bone density. Similarly, some endocrine disruptors simultaneously [destroy bone, and make fat](#). Is this interconnectedness a coincidence? I think not.

"One failure of medicine and public health is our ability to act on entire complex systems, or even to understand them."

One failure of medicine and public health is our inability to understand and act on entire complex systems. Viewing CKDu through the lens of ecological medicine might suggest we examine patterns of ecosystem poverty and disease, and not just the usual suspects. Some studies identify the prevalence of depression being [“3 to 4 times higher in patients with CKD and \[end stage renal disease\] compared with the general population and 2 to 3 times higher compared to individuals with other chronic illnesses.”](#) The reasons for this are complex and not the same for everyone. Some attribute the depression to grief related to the loss of kidney function, and indicate that it is also mediated by other factors including social support, loss of employment and income, and financial costs. These impacts are also not experienced equally. The kidney disease and depression also take a toll on family members of CKD patients, and caregivers who are often one and the same. In our research, one of our investigators who is a nurse says she is able to garner support for our studies by engaging the participants’ wives and family members. They are key to any solutions.

Finally, one problem that many face in addressing CKDu, is that people often don’t want to know if they have the disease. Treatment is poor, physically inaccessible, or astronomically expensive relative to their income, that there is no solution. There is also stigma- some have compared the situation today with AIDs in the 1980s. The diagnosis is deadly, people don’t want to marry into families with the disease, nor have children. Ecological medicine requires that we consider this aspect of context when thinking about research and solutions.

Which brings me back to Oliver Mtukudzi. He sang about AIDS in a song titled, “What shall we do?” [In his own words](#), Tuku described the song as “full of questions with no solution at all. And all those questions started making people talk about the disease and try and take the stigma away from it.” He asked the questions with music. Public health researchers ask the questions in the context of science. I think we share goals.



The **public trust doctrine**. I first learned about Tuku in 1989, when I spent six months during high school living in Zimbabwe. This was the year the Berlin wall came down, and before Nelson Mandela was released from prison. Apartheid in South Africa was alive and well, and AIDS was a rapidly growing problem.

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When I came home, back to Cape Cod, I was horrified to see the evidence of one of the biggest construction booms in my lifetime along the salt marsh and shorelines where I had previously walked freely. When I returned and walked along the shorelines, instead of being surrounded by fields, I felt the vacant stare from the windows of empty second homes. One of my big thrills during the summer was walking on beaches right in front of these often huge, newly constructed homes with Private signs posted on the beach. I knew that the tidal area in front of the home was public- even if it was just feet from their big porch or sliding glass doors, and all attempts at intimidation. I did *not* realize that this was due to the Public Trust Doctrine protecting public access to the shoreline, described by [Massachusetts](#) as dating back to "ancient Roman law." The Science and Environmental Health Network has been [building on the Public Trust Doctrine](#), kind of bringing it up to-date. Young people are using this same idea to hold governments accountable to future generations, leaving school to demonstrate that the public commons must be protected (the air we breathe, the water we drink, the land we sow,). [What is government for, after all](#) (if not to protect these things)? This question was asked Peter Montague in last month's Networker.

We humans studying CKDu are walking in places where the tides are changing rapidly. We are having to shift and update our thinking about boundaries, because the physical landscape, our shores, are changing faster than the policies to protect us or them.



Finally, several SEHN staff and board members have been directly touched by kidney disease in their family. When she was 30, board member Benno Friedman's wife was told that she had PKD (polycystic kidney disease). Now, 37 years later, she's in need of a kidney transplant. Because the disease is hereditary, neither of her sons are able to donate a kidney. If you are inspired to help her, or learn more about her situation, please visit <https://www.findstefakidney.com/>

I do not know if Tuku died of kidney failure, or if his kidneys were affected by his diabetes. I do know, however, that he was voice for people who had no voice under apartheid in Southern Africa. He gave people courage through his music. He moved people to get on their feet, to stand up. To dance.

SEHN does this too. And so does my friend Carolyn Raffensperger.

In honor of world kidney month, and in honor of SEHN.



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