The Emergence of New Diseases: Hybrid Methodological Approaches and the Case of CKDnt

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10. The Emergence of New Diseases: Hybrid Methodological Approaches and the Case of CKDnt

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In this paper, Glaser and Kierans provide an account of two closely aligned investigative trajectories reflecting new forms of kidney disease and how those trajectories have led them to propose an integrated framework for assessing and addressing these emergent epidemics. The authors show that the problem of kidney failure without warning or explanation cannot be addressed by single or unitary disciplinary approaches but requires genuine collaboration and alignment. Achieving this requires challenging disciplinary imperatives, entrenched biases and assumptions through investigations.

Introduction

The problem of kidneys failing without warning or adequate explanation constitutes a newly recognised but likely long extant problem across different global sites and settings, with new modes of hybridised investigative inquiry emerging in its wake. This paper provides an account of two closely aligned investigative trajectories, reflecting new forms of kidney disease linked to (a) working conditions in Central America and (b) sites of social and environmental degradation in Mexico and how those trajectories have led the authors to propose an integrated model for assessing and addressing these emergent epidemics, a challenge likely to increase in frequency due to human encroachment on fragile ecosystems and global warming. The nature of these problems are such that they cannot be addressed by single or unitary disciplinary approaches and require genuine collaboration and alignment. This is now already well-recognised across both the human and natural sciences, embodied in a growing array of inter and transdisciplinary approaches, *inter alia*: syndemics (Singer et al. 2017); biosociality (Seeberg et al. 2020); bioethnography (Roberts 2017); embodiment perspectives in epidemiology (Krieger 2005); more-than-human approaches (Tsing et al. 2017). How to achieve this is, however, far from easy without challenging already existing disciplinary imperatives, entrenched practices, ingrained biases, assumptions and epistemological starting points.

Uncertainty and Failing Kidneys

Rapid kidney failure without precedence is today shaping new understandings of the entangled relationship between health, society, work and the environment. The condition we are referring to is sometimes described as an epistemic problem with much contest over aetiology e.g. Chronic Kidney Disease of Unknown Origin (CKDu) or indeed Chronic Kidney Disease of Non-Traditional Origin (CKDnt) as lines of "evidence" and association are slowly built up. The condition is also described as a problem of place and population: e.g. MesoAmerican Nephropathy (MeN). Nomenclatures aside, this newly recognised variant, or indeed variants, of kidney disease is one where forms of knowledge production and contextual concerns critically matter. In this paper, we attend to their significance. We will use the Pan American Health Organisation (PAHO) designated acronym CKDnt (Wesseling et al. 2020) – as it best addresses alternative and multiple modes of CKD emergence beyond normative causal processes.

Photo 1: Former sugarcane worker Ramon Uriel Munguia, pictured at 27, now deceased from CKDnt, lost his father to the same disease. [Photo taken by Ed Kashi/VII]

As Wesseling and colleagues point out, CKDnt dispropotionately affects working age men, often as young as 25, and the mortality in affected areas of endemic countries is frequently >30/100,000. The average age of those in end stage disease at dialysis centers in El Salvador, for example, is 34 (personal communication with Hospital Rosales, San Salvador) and this grim number does not reflect the thousands who do not have acceess to care in overstressed health systems. CKDnt kills those in their prime earning years and this is exacerbated as the disease is largely asympotomatic and evades traditional kidney disease urinary screenings looking for proteinuria, until the advanced stages of disease. The disease is considered of epidemic proportions in Mesoamerica by PAHO and is potentially of pandemic proportion though surveillance among the populations identified at risk is still inadequate.

The two cases we describe raise many overlapping concerns despite having divergent investigative starting points and possibly differing aetiologies. They shed light on what research on this and similar challenges may look like by ensuring the needs of affected populations are kept front and centre. In what follows, we provide accounts of their respective trajectories of understanding, as work-in-progress, rather than offer after-the-fact reconstructions. This helps us to show what it means to follow a problem, as that very problem is being made. Our field-work trajectories are, therefore, fashioned as much by expedience, intuition and serendipity (Ginzburg 1979) as they are by disciplinary and professional logics. By paying attention to investigative practice, we also ask: what (as well as who) makes a disease?

Case Study 1 – Avoiding a Square in a Circle Hole: Puzzling Through the CKDnt Epidemic in Mesoamerica

Chronic Kidney Disease of non-traditional cause (CKDnt) affects millions of workers and impoverished communities in Latin America and South Asia (O'Callaghan-Gordo et al. 2019; Wesseling et al. 2020), resulting in early death for those affected. While initial studies occurred in the late 1990s and early 2000s (Trabanino et al. 2002), it wasn't until 2007 when I (Glaser) was making a documentary about the banana industry in Nicaragua that the issue began to gain international attention and resources were acquired for an integrated research strategy (Jimenez et

al. 2014). Protests had erupted in a nearby town decrying unprecedented levels of deaths among sugar cane workers at a local mill. Efforts to quell speculation by the local police, and subsequently the sugar mill's public relation firm (Burson Marsteller) created an impetus to coordinate with local academic researchers and a regional program with community and worker's health as the focus. With various partners, we founded La Isla Foundation which was later designated La Isla Network (LIN) and developed a research and advocacy organisation focused on addressing the needs of those affected with specific efforts aimed at preventative measures utilising the best available data.

How LIN Formed

When myself and the documentary team stumbled upon several young cane workers dying in sombre protest in hammocks in front of a sugar mill's company gates in 2007, we knew little of epidemiological statistics. I would certainly have struggled to explain what a confounder was, the fundamentals of logistic regression, or why it is important to designate exposures a priori and not dive into the sea of unresolvable biases that emerge from data dredges and research fishing expeditions. Today, the methodology of effective epidemiology and scientific investigation are thought of at LIN as tools, which have their limitations, applications and uses. They do not detract from fundamental and unrelenting realities of the exploitation inherent in commodities markets, the failures of development strategies that do not lift up the working poor but still manage to enrich their employers, or the banality of an international interconnected trade and development system that permits multiple permutations of abuse and brutality as part of nearly every relevant supply chain in the marketplace. Understanding dynamics while lacking the tools to assess and measure them makes for little more than angst and pontification. The film team, having been unimpressed by Jeffery Sach's (Sachs 2006) defence of the status quo were more inclined towards the assessment of development follies, particularly those relating to continued poor health and economic outcomes for those at the bottom of supply chains and social hierarchy, despite billions of investment. According to William Easterly (2007), this was in part driven by a lack of stakeholder engagement, and so I decided to inquire into who was working on the issue locally.

The team partnered with local advocates, who had helped to bring a complaint through the office of the Compliance Advisory Ombudsman (CAO) against the International Finance Corporation's investment in the sugar mill where so many young men had fallen ill, meaning the filmmakers connected with those suffering from the disease, families left behind, and local researchers who made up a network known as the Program for Worker Health and The Environment (SALTRA) operating through Central American Universities and funded by the Swedish government (Wesseling 2011). The early relationships with community members pursuing the CAO complaint, and the researchers looking into the issue were the foundation of LIN.

Mobilisation

The effort was energised by what several parties viewed as uninformed loan practices by the IFC and a subsequent CAO process that appeared to be a hand washing mechanism intended to clear the IFC's name from any responsibility for the identified kidney disease among workers. This dissatisfaction arose among local researchers, impacted community members and advocates driving them together to form what served as a critique of and counterweight to the official CAO process. Community leaders who through their local advocacy group, the Association of Chichigalpinos for Life (ASOCHIVIDA) had originally brought the complaint to the IFC now found themselves boxed out of the CAO process. The original ASOCHIVIDA leadership was pushed out by parties friendly to the company and convinced the CAO process would bring amelioration. In the case of researchers, a group from Boston University, most of whom did not speak Spanish and had limited experience in the field setting of Nicaragua, was chosen over local

researchers from SALTRA who had been working on the problem for years, due to claims by the sugar mill that local investigators would be biased. Community members that took part in the complaint were informed they would not get what they desired if the current ASOCHIVIDA board, which had advocated for and brought the original complaint, remained. Subsequently, they were replaced. The counsel from Washington DC's Centre for International and Environmental Law, which was representing the claimants, found such interference to be of little concern. Frustration built up and was compounded by policies like prohibiting claimants from participating in any non-mill sanctioned research, and pulling the provision of restitutions such as food stipends or housing from ASOCHIVIDA members who spoke to the press or engaged in independent research. Collectively, these actions drove a diverse group of actors together.

A pillar of the dissent to the CAO process centred around the dissatisfaction that little was done to improve the working conditions of those known to be at risk of CKDnt. The CAO's focus became almost entirely on those already ill or left behind by those who had succumbed. Both a precautionary principle-based intervention to improve current work practices, as well as aid and support, were needed but the CAO process only served the latter. Especially egregious was that aid arrived on the condition that recipients abided by the rules set by the CAO, the sugar mill and communicated to claimants by the new ASOCHIVIDA board.

The funding provided to Boston University to illuminate potential causes of CKD among the workforce was also entirely from the IFC or the company, with efforts to launder the money through a group known as the CDC Foundation (Lenzer 2015). This conflict of interest was repeatedly compounded by the deficit of timely pushback by BU researches when their work was misquoted and misused repeatedly by ISA or IFC.

The impact of CKDnt on the community, and the issues identified by LIN with the CAO process were eventually communicated to leading news outlets and reported on. This garnered interest from professors and students in the human rights issues highlighted, as well as the intrigue of a potentially addressable, but not well understood epidemic. It brought a large number of volunteers, interns and interested researchers to the issue. This amalgamation of community groups, researchers, and media helped to put the issue on the map, and provided focus through the lens of one community devastated by the disease.

Setting a Research Agenda; Building a Team

Listening to leadership and local researchers in affected communities, LIN began identifying what information was necessary to understand some of the upstream drivers that required amelioration, potential proximal causes that offered intervention opportunities, and provided some context for what this disease meant for people in terms of advocacy and associated economic considerations.

Due to limited resources we began with a local Knowledge Attitude and Practice study (KAP), and coordinated with researchers to carry out one of the earliest prevalence studies (Raines et al. 2014) which along with efforts from SALTRA (Torres et al. 2010; Peraza et al. 2012) later formed the basis for the standardised protocol that we developed to assess CKDnt globally, via **the Disadvantaged Populations eGFR Epidemiology Study (DEGREE)** (Caplin et al. 2017). Human rights and child labour reports ran in concert with these efforts, and as resources and risks were identified we began the first occupational cohort studies and interventions in the hope of mitigating identified risks, while exact causality was argued in the scientific literature. Utilising the data that built from simple cross-sectional to longitudinal research, we informed policy makers in the public and private spheres, where possible. This culminated in our thus far successful occupational health program, The Adelante Initiative.

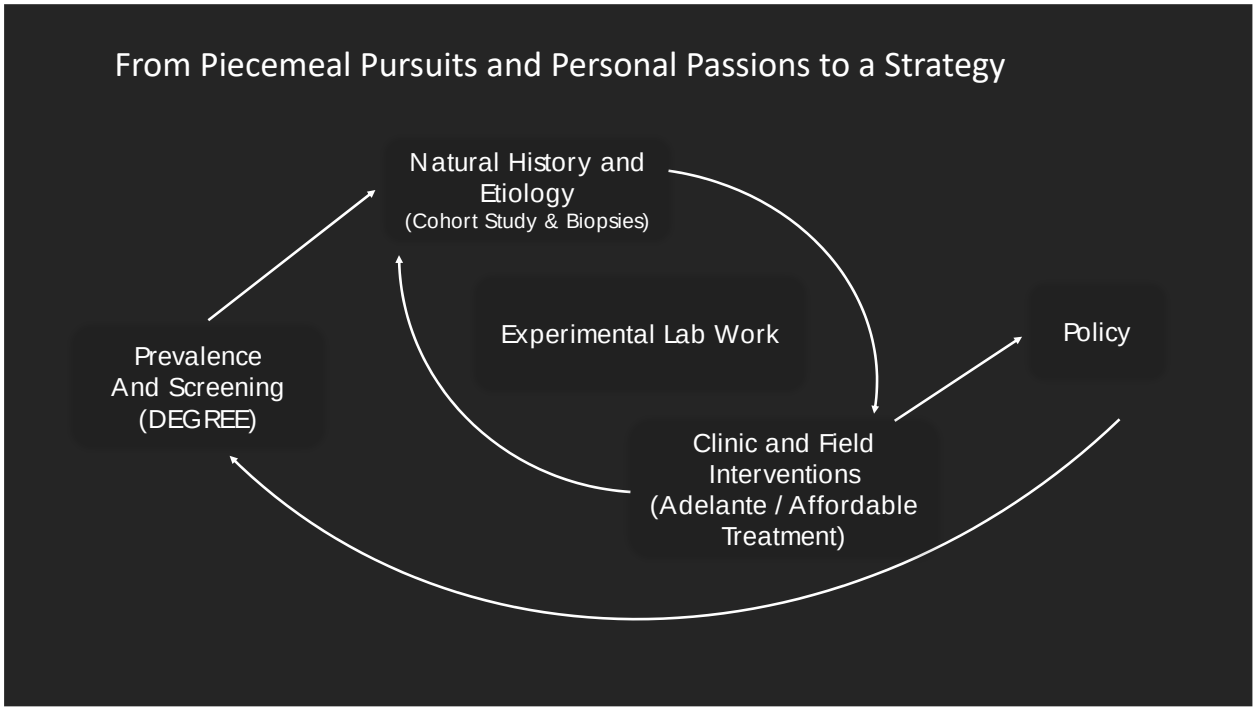

Figure 1: LIN conceptual framework of research strategy (2016).

Initially LIN wished to focus on the structural issues we felt, that if addressed, would render the proximal cause, or aetiology of the disease functionally irrelevant. If basic protections regarding heat stress, as well as toxin exposures were put in place – already mandated in regulatory systems across many countries – the incidence of the disease would plummet. Put simply, CKDnt does not happen among wealthy or middle classes or among management and supervisors living in the same towns or small cities where CKDnt exists. It specifically impacts the working poor, and those doing the most dangerous jobs. Consequently, we aimed to focus first on the context of the disease and the lived experience of those who were confronting it, and its devastation.

Economists, anthropologists, lawyers, and psychologists were of more interest than epidemiologists initially. However, aside from legal experts, the researchers who invested the time, and the energy needed to move publications and therefore credible data forward were a group of physiologists and epidemiologists. While this has been positive in the sense of understanding risks and where we might act in the fields to mitigate disease incidence, it has, until recently, left us with little in terms of understanding the true cost of the disease, economically, socially and otherwise. This has opened us up to academic quarrels over CKDnt aetiology which limits the ability to act on and improve working conditions that are already known to be dangerous, and contributing to the development and progression of CKDnt. Today we are finally incorporating the economists and anthropologists we believe would have helped frame the condition and provide insight early on.

Research Focus and Partial Reset

It was only by necessarily following the path of least resistance that we became part of the aetiology/causal debate by virtue of drawing on epidemiology and physiology. For LIN, causality has only been important in so much as it informs intervention. Meaning, we are most interested in mitigating identified and plausible risks that should be addressed anyhow. These include poor water quality, heat stress, dehydration, long working hours, and insufficient wages. By addressing

deficits in these categories, we hope to create conditions that allow a workforce to advocate for themselves on these issues and others.

Presently, we are most interested in data that can help us ascertain if an intervention reduces incidence of disease among a workforce, but also whether such efforts improve the economic stability and well-being of the affected population. Here we couple classic exposure assessment methods of epidemiology with socioeconomic questionnaires developed to assess the resilience overtime of stressed communities. Basically, this means providing a baseline that will allow for the assessment of community level and occupationally focused intervention efforts over time. This also provides us with, what is in effect, a partial reset and a return to our initial aims of addressing the context and upstream drivers in working with CKDnt. Today, with new research partners from the social sciences and humanities we can begin calculating the true burden of the disease on individuals, households, communities and how current political-economic conditions and other structural forces allow such phenomena to persist. With coordination of hospital and clinic data we can begin to paint the picture of what this disease means for health systems. With this data we can motivate an informed realignment in the development sector and pose the questions:

- How are development projects assessed for funding or financing?
- How is their success measured?
- What risk assessment processes can help improve current loan recipient practices and programs?
- How can we avoid missing issues like CKDnt?

The last question is especially relevant given that CKDnt appears to be one of the leading causes of death among those who constitute the working poor in the tropics and along the equator (Wesseling et al. 2020). In short, we question how sophisticated, well-funded development agencies can miss dire occupational and public health crises, and how they might be better positioned to sustainably address the risks and harms that consign people to lives of poverty. In parallel we are examining the structures in the private marketplace that allows such a condition to develop and persist.

While many papers assert that CKDnt is a new phenomenon, data from Costa Rica demonstrates it has been with us for some time. Costa Rica is one of the few affected countries with reliable routine data going back to the 1970s, and it is clear that CKDnt has been extant since the 1970s and is strongly correlated with the industrialisation of the sugar crop in its hottest and driest department, Guanacaste (Wesseling et al. 2015). This insight, brought about by epidemiologists assessing routine health and agronomy statistics, highlighted the need to integrate the history of agronomy in the region with climate data to lay the foundations for later Geographic Information Systems mapping that would help us understand the scope and primary exposures related to the disease (Hansson et al. 2021). Here we saw that as the industry moved away from small farms, operated by the farmers themselves, to a network of holdings worked by labourers, many of them migrants from Nicaragua, the incidence of mortality due to CKD increased as the land under sugarcane grew in hectacrage and was more intensively cultivated.

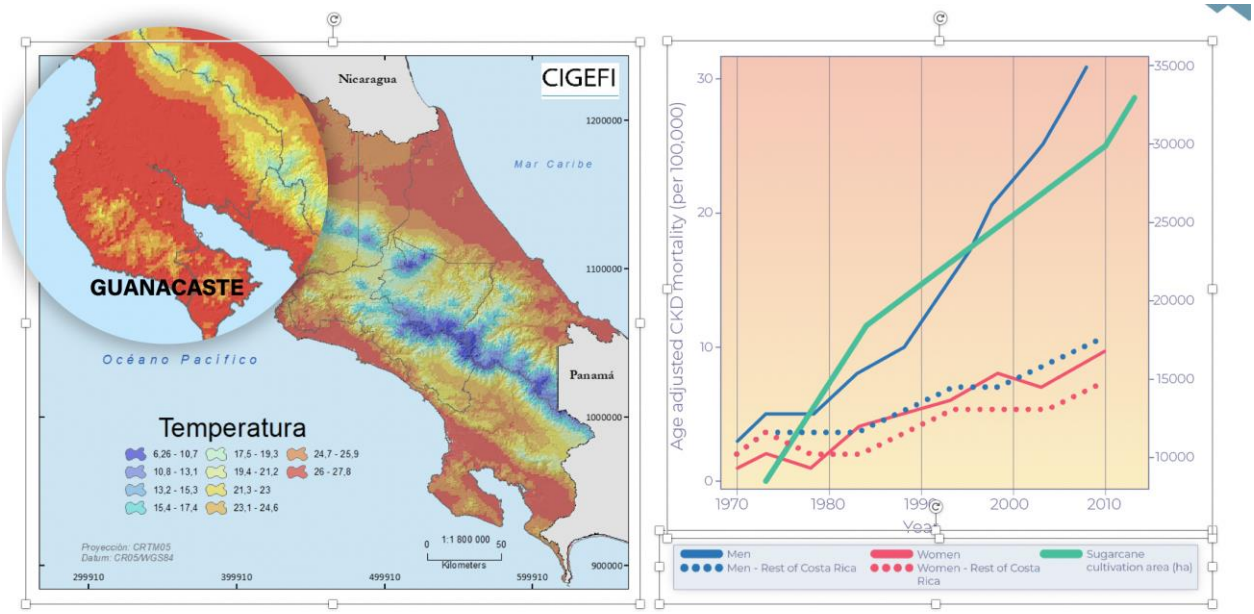

Figure 2: Costa Rica's NW province of Guanacaste is its hottest and driest, and home to an enormous intensification of sugarcane production that saw production move from small farmers working their land to larger holdings worked by labourers.

Strenuous manual work in extreme heat without sufficient rest and hydration is today considered a main driver for the epidemic in Central America (Glaser et al. 2016; Hansson et al. 2021; Glaser et al. 2020; Wesseling et al. 2020), where industrial agriculture is the most affected, especially the sugarcane sector (Hansson et al. 2019).

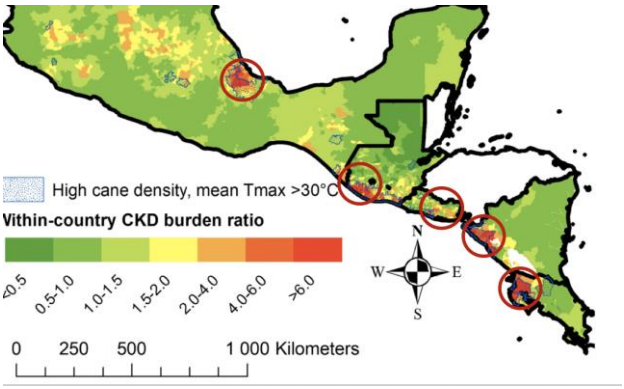

Figure 3: Intensive cane cultivation in hot lowlands is heavily associated with CKD burden in countries with reliable land use and patient data. Intensive cane in cool highlands, and low intensity cane in hot lowlands (both using pesticides) are not associated with CKD.

Case Study 2 – Reflections on the Conditions (as Distinct from Causes) of CKDnt Emergence around Lake Chapala, Mexico

The following case study – much less developed than the previous – emerged more recently in the context of conducting anthropological research on the political economy of kidney disease and healthcare in the state of Jalisco, west central Mexico (see Kierans 2019; Kierans and Padilla 2021). Colleagues and I (Kierans) noted that the patients we encountered at a public hospital for uninsured Mexicans in Guadalajara were presenting with a form(s) of kidney failure that did not

conform to established aetiologies for CKD more broadly. The patients in question had few symptoms even as their kidneys rapidly deteriorated and were comparatively younger than those presenting with more conventional forms of the condition. Many were told by their doctors they had *riñones chiquitos* (small kidneys) and as a result, were difficult to biopsy, analyse and diagnose.

As the condition was, and is, unexplained, one could not be sure it was the same as that encountered by Jason and colleagues in Central American sugar cane fields. To investigate, I led a small team of humanities and social science scholars working in dialogue with nephrologists and bioscientists. Having already established relations with affected patients, we decided to *follow* failed and failing kidneys from *clinic* back to *community*, specifically to the municipality of Poncitlán located on the northern shores of Lake Chapala, some 60 kilometres west of Guadalajara (Map 1). To date, no clinical nor epidemiological studies have been carried out in the municipality to characterise either the disease or the population suffering from it, however, data gathered from the public hospital in Guadalajara indicate that local children under 18 are 10 times more likely to experience kidney failure than the state average, with adults 4 times more likely (Garcia-Garcia et al. 2019). What is known is that high levels of the biomarker proteinuria, present in many in early stages of the disease in the Chapala area, are absent in the Nicaraguan population affected until much later. Our approach, in many respects, reflects a similar impetus found in Jason's work, i.e., to ask what is already known and to move forward with respect to available expertise, existing research and local relations. In our case, we started with a different constituency of disciplines – social science and humanities in the main – supported by clinical medicine and epidemiology. Our approach was thus driven by disciplinary and transdisciplinary expedience and serendipity (Ginzburg 1979).

Map 1: Municipality of Poncitclán (Mezcal, San Pedro Itzicán and Agua Caliente).

Poncitlán is home to 53,000 people, distributed among variably marginalised small towns and villages. They can be considered places of neglect and displacement; the consequence of colonial,

post-revolutionary, neo-liberal and neo-colonial histories. Those who live there – mestizo and indigenous – are part of Mexico's growing precariat reliant on the informal economy as contract labourers with local transnational agri-companies; as construction workers on building projects in nearby Guadalajara; as labourers on local farms or within the fishing industry, as domestic cleaners in nearby towns, and as subsistence cultivators of crops, primarily corn and chayote grown on their own small landholdings or gardens. As a potential occupational cohort, they do not easily map onto LIN's sugar cane cutters, but are, instead, constituted by fractured and overlapping modes of labour, shared histories of dispossession, exclusion and neglect, borne out by their health and the impoverished conditions of their lived environments.

In the absence of formal epistemic accounts of the unprecedented rise of CKDnt, our immediate priority was to empirically follow the condition by staying close to the "actors" themselves; documenting the condition as a vernacular concern, attending to their experiences and explanations and the everyday environmental encounters these experiences point to. Nonetheless, our methodological orientation was, to some extent, modulated by what was already known about CKDnt in other parts of the world, chiefly via LIN's work and also our own interdisciplinary sensitivities to health-environmental relations as slow moving effects (Nixon 2011). We, therefore, considered that present day articulations of CKDnt may well reflect prior pathologies (social, ecological and embodied). Our goal, however, was never to establish causal links but to examine the context and conditions of disease emergence and to consider the auxiliary elements – structural and infrastructural – where interventions might best or better be served, particularly in a context where access to healthcare for uninsured Mexicans was already profoundly problematic (Photo 2) (Kierans 2019).

Photo 2: On home dialysis in Agua Caliente. Lucero died of CKDnt, aged 22. Multiple members of her family have also been diagnosed with the condition. [Photo taken by Cesar Padilla-Altamira]

The methodological approach we mobilised was anthro-historical in character, and in dialogue with local clinical and bioscientific insights. We, therefore, intertwined three already closely aligned investigative approaches via a suite of pilot projects, publications from which are currently in process:

1. Ethnographic: to resituate CKDnt into its community settings, attending to the interrelations between livelihood (domestic; subsistence and waged), environment and health. 12 family cases were entry points and soon progressed to include others with a stake in the condition: family, friends and neighbours; health professionals; environmental activists; politicians, among others. With them, we mapped CKDnt emergence across a twenty-year period from 2000 to 2020 (Kierans and Padilla 2021).
2. Genealogical: a social history approach extended and expanded on issues raised in the ethnographic cases to produce inter-generational narrative accounts of CKDu emergence, in conjunction with social, political-economic and environmental change.
3. Historical Archival: health-environment relations were then followed back in time as functions of climate change, land use and water management.

As is the case with anthropologically anchored research more generally, our investigative approach is promiscuous, flexible, ethically reflexive and always empirically anchored. It was not about data collection as one-off moves (i.e., via discrete and bounded methods) but continual back and forth iterations that enabled relations to be traced between a locality, human experience and wider historical, environmental and structural processes. Despite the uncertainties that plague CKDnt as an epistemic and categorical problem, locals had little difficulty pointing out where they understood problems to lie – within *non traditional* origins, ultimately generating antinormative modes of reasoning. Sickness – far from the distinct entity amenable to clinical and bioscientific forms of reasoning it can be held up as being – is embedded in local forms of living and the relationships they hold between humans and more-than-human environments (Tsing et al. 2017). In other words, local interlocutors documented a catalogue of concerns bound to a wide range of exposures and infrastructural failures that profoundly shape livelihood and the practices of everyday living. They include, *inter alia* – widespread contaminations linked to: local wells used for everyday consumption; aquifers and hot springs used to bathe and wash utensils and clothes in (Photo 3); corroding pipes that carry local domestic water supplies; inadequate sewage and sanitation infrastructures; contaminated fish that are routinely caught and eaten; poorly irrigated soil for subsistence agriculture; the widespread use of unregulated agro-chemicals, which drain back into the hydrosocial cycles and also the complex shifting character of agri-work (made possible by extensive agrochemical use) which has facilitated synchronous work across both subsistence and industrial forms of agriculture – multiplying efforts and all manner of exposures. Each of these concerns constitute the threads we follow. In turn, they delimit the relations between failing health and failing environments opening up a space to rethink interventions as ways to mitigate structural and infrastructural harms. They demonstrate the range of risks, which have to be tackled, to promote safe, secure, healthy lives, out of which the emergence of CKDu is but one of many concerns. Our experience of this investigation has taught us that rather than put health problems (of which there are many) into direct competition with each other, as problems that independently require their own discrete causal modes of investigation and response, we ought to orient towards shared, in-common, interventions to produce the kinds of effects that may well have farther reaching consequences. Of course, this does not exclude the quest for discrete causality; it simply challenges its privilege, while recognising that kidneys do not stand alone. We should, therefore, exercise caution in affording primacy to discrete disease categories (Livingston 2019).

Photo 3: Washing clothes, Aqua Caliente. [Photo taken by Ciara Kierans]

To provide brief context to these threads and conditions: Chapala is Mexico's largest freshwater lake and one of the most endangered and polluted water systems in Latin America. It connects outwards to the heavily industrialised Mexican plateau via the Lerma River basin on one side, and on the other, to the Pacific via the Río Grande de Santiago. Industrial dumping, inadequate waste-water treatment, and intensive irrigation for farming have been implicated in the rising concentrations of contaminants in the lake and consumed through drinking water and eating fish (Trasande et al. 2010; Stong et al. 2013. Approximately 20 million people, live in the catchment area around the lake, all dependent on it for water, sanitation and land irrigation. When the first cases emerged in the early 2000s, the water levels of the lake were at their second lowest levels in history. Untreated waste discharged all along the Lerma basin. Environmental scientists raised concerns about heavy metal and pesticide accumulations and concentrations of lead, copper and mercury were reported in the muscles and liver tissue of fish. Fish stocks have rapidly decreased and the native species of catfish and pescado blanco, once a staple of local diets have all but disappeared. Stocks of charal and lamprey have also diminished. Carp, still widely eaten, is known to be contaminated by methylmercury and is the source of ongoing local controversy.

When the lake recovered, it flooded a newly constructed sewage treatment plant (Photo 4) – washing its contents up on to the shores of the Poncitlán villages – adding inadequate sewage treatment to the spaces of neglect and concern and multiplying problems with water. Household water supplies which draw from ground water aquifers and surface water via the lake have fared no better. The water is neither treated, nor cooled. It is intermittent and unreliable. It runs through pipes which corrode and break. For those houses connected to volcanic springs, it arrives hot into their homes. For those that can afford them, they purchase 20 litre plastic water *garrafones*; for those that cannot afford them, they use the local water supply. Concerns about health and water safety are perennial but severely neglected. The provision of local plastic water containers is unregulated.

Both tap and bottled water show contamination by coliform bacteria, including E. coli, fecal matter and arsenic (Smith et al. 2020).

Photo 4: Sewage reception tank and sump pump, San Pedro Itzicán. [Photo taken by Cesar Padilla-Altamira]

Uneven irrigation, climate change and the political economic consequences of NAFTA have increased reliance on a wide array of agrochemicals. Poorly regulated, mixed with little instruction and sprayed without protection by all, young and old, agrochemicals are the source of increasing concern with regard to ingestion, agri-run off back into the lake and in terms of food quality and safety. The widespread use of agrichemicals have lessened the time spent labouring outdoors in small-holdings, only to intensify labour across multiple employment sectors: construction sites, factory work and industrialised berry fields; pluralising occupational health concerns. CKDnt, furthermore, emerges in the contexts of comorbidities whose interactions are little known, though of significance. They include *inter alia,* malnutrition, congenital physical malformations, poor cognitive development, cancers, diabetes, chronic diarrhoea, the effects of violence, alcoholism and occupational harms, reinforcing the importance of interventions which elaborate structural and infrastructural conditions, rather than merely discrete causes.

Conclusion: Companion Methods and the Challenge of Hybridisation

That CKDnt has surfaced at the beginning of a new millennium at the margins of workplace and environmental harms suggests we need new ways of approaching novel health crises across global sites and settings. The above case studies have offered insights to doing so via our particular hybridising investigative methods as well as through explaining how such methods are made in

situ. In what follows, we reflect on some of the lessons we have learned as we begin to draw our lines of inquiry together. While the contexts, environments, pathophysiology and therefore precise aetiological elements may differ between the kidney diseases in Chapala and throughout the monoculture dominated lowlands in other parts of Mesoamerica, they share important similarities. Those who are affected are in precarious economic circumstances and unable to access treatment or readily advocate on behalf of themselves or their communities.

Context

Context matters. Descriptions of context – social, political-economic, environmental and historical – are critical to understanding and acting on CKDnt. This is achieved largely through ethnographic sensibilities, attributed to what the anthropologist Anna Tsing (2015) refers to as "acts of noticing" – i.e., attending to more than circumscribed lines of inquiry, by being open and amenable to new questions and directions, iterations and feedback loops. Situating CKDnt in context is impossible to accomplish from a unitary disciplinary perspective; it necessitates a "collaboration of hands" (Goffman 1979). This also enables concerns of relevance to arise for other modes of disciplinary inquiry – from toxicology to nephrology to structural engineering and ecology, in addition to the work of anthropologists, historians, economists, epidemiologists and so on. In other words, attending to context prepares the bioethnographic ground of and for collaboration without prescribing in advance how they ought to fit together.

With regard to case study one, contextualised approaches help ascertain what environmental and occupational exposures merit investigation, ideally eliminating the tendency for epidemiological and medical specialists to merely *apply* their disciplines, specific specialities, and interests to new puzzles. They help curb the proximal exposures traditionally the domain of medical and epidemiological research methods and with that the decontextualised consignment of complicated pathophysiology to discrete *causal* determinants. The search for discrete determinants too often become the focus of protracted research and years of inquiry and debate before consensus is reached and subsequent action is taken. There is much to be said in favour of elaborating the conditions – as distinct from merely the causes – not only to link so called "down-stream" effects to "upstream" structural mechanisms but importantly to "midstream" intervening and mediating concerns (Yates-Doerr 2020), particularly those that shape everyday engagements between human populations and their environments (ecological, social, political-economic and cultural). Investigating structural and infrastructural mechanisms moves us beyond a strict biomedicalisation of disease to incorporate sustainable forms of intervention and prevention, e.g., improving work practices through policy and implementation reform; the provision of clean water and sanitation; access to health services and welfare – all critical to eliminating or reducing proximal exposures and ensuring protections and prevention for at-risk populations. If such efforts eliminate the outcome, then the precise pathophysiology of a disease remaining unknown is a modest trade for the health of impacted populations. Elaborations of context allow for alignments and collaboration with affected populations to set the framework for aid and ameliorations while causal processes are further investigated. They also create space for economic methods, among others, to provide significant baselines from which the success of later interventions can be measured, often well before they get off the ground. In the context of case-study one, proceeding thus, would provide not only much needed data, but opportunities for analytical comprehensiveness. For case study two, the capacity to work in collaboration with epidemiologists and bioscientists provides a significant pathophysiological and population-base to anchor and elaborate social, cultural and historical insight.

Drawing both case studies together, we advocate for a dialogical investigative approach, one which requires iterative feedback loops to be an essential part of project building and may, depending on

circumstances, require a mix of phased and synchronous methods, for example, it may be pertinent to establish the context in which a health crisis is occurring prior to integrating models of epidemiological, environmental and social research.

Epistemic Cultures

We recognise what we propose is not straightforward, and that efforts to hybridise inquiry have ontological and epistemological implications. Such efforts produce all manner of challenges for epistemic cultures. Our case studies have taught us much about where the pitfalls of investigative processes lie, particularly when approaches are overdetermined by methods that produce results, which are themselves artefacts of those methods, professional vision or indeed ambition. While we have been careful to not fall into a trap of setting out to prove what we already believe, the tendency to apply specific expertise and held beliefs to a new problem have permeated much of CKDnt research in Mesoamerica. Hybridisation, as we see it, in no-way dissolves disciplinary expertise and insight, but puts bias and bedrock assumptions on the table, such that investigations are driven by the nature of the problem in question (rather than methodological conflict and competition) – and with the needs of affected communities to the forefront – avoiding as Jason refers to in Case Study 1, attempts to force a square peg into a circular hole.

While many causes have been proposed for the wider pandemic as well as local epidemics of unexplained or non-traditional CKD, they have not emerged due to a process of methodological pluralism, but due to the efforts of experts in different disciplines and specialties applying their own entrenched expertise to perceived and/or actual holes in the puzzle. Instead of looking at the pieces surrounding that hole and evaluating what piece or approach may best fit the situation, the approaches to-date have frequently been ad hoc and dependent on a principal investigator's former successes or interests. Differing opinions have led to contentious and unproductive exchanges leading to dysfunction in the research community instead of collaborative action, potentially adversely affecting the populations and impacting the pace of policy change and intervention efforts that could mitigate identified risks such as heat stress or dangerous toxins. This is wasteful. It entrenches beliefs and biased unthinking, creating "tribes" that attack each other in the pursuit of limited funding resources and ensuring disagreement will never be worked out in academic journals or conferences.

Meanwhile, the populations who require clarity of thinking, collaboration, informed investigative methodology and precautionary principle-based interventions are left as subjects, not participants, in research too often carried out by elite researchers, be they local or foreign.

Investigating novel diseases at society-environment intersections requires a paradigm shift. Here we echo already existing conversations held, *inter alia*: by social scientists in challenging the privileged status of the lone worker ethnographer in deference to wider ethnographic alignments (Tsing et al. 2017; Boyer and Marcus 2020); by critical epidemiologists who challenge discrete causal processes in favour of a focus on mechanisms, processes and relationality (Krieger 2011; Breilh 2021); by science and technology scholars challenging the implications of hierarchical, extractivist research, rarely aligned with community interest and with little capacity to exact sustainable change (Liboiron 2021). We critically need, therefore, to recognise and account for the politics of evidence and the capacity to handle and work with multiple truths.

Collaboration

Hybridised investigative methods are by necessity and design collaborative and this can and does mean multiple things to multiple people and sometimes all at once. Positively, it can offer novelty

and innovation: opportunities to provide new ways of representing old problems, generating bold new kinds of research; new information infrastructures that yield new ways of writing and dissemination; the capacity to generate new kinds of conceptual and analytical work (Boyer and Marcus 2020). Perhaps cynically, there is always the danger of simply putting old wine in new bottles, particularly if hierarchies of evidence and control of research processes remain intact, and where socially focused disciplines remain as under-labourers to the bio and health sciences, ostensibly where the status quo remains unscathed (Adams 2016). Hybridised investigative inquiry ought to reflect the nature and character of the partnerships they mean to connect and pull together and so, we cannot be overly prescriptive here. Our efforts to draw together the approaches reflected in the above case studies are in their infancy and in progress. Our commitment, however, is to generate research methods that are flexible and promiscuous, that seek to keep lines of inquiry open rather than shut them down in advance. Our objective is to minimise the kinds of erasures that can mask the emergence of novel forms of disease and harm. Doing so rests on other values that we have also learned the benefit of while doing: trust, transparency and intellectual curiosity.

Adaptive and Comparable Methodologies

Reports emerging from SE Asia, South America, the USA, West and Northern Africa show that what was once thought to be a localised epidemic is in fact a pandemic affecting a large percentage of the global precariat. While other aetiologies aside from heat stress have been posited, epidemiological evidence is absent for most, if not all of them. Heat stress has been shown to be an exposure with a well described and supported pathophysiology as well as the possibility of successful intervention efforts. Without improved preventative efforts through occupational safety and health and wider public health and healthcare interventions, the pandemic is likely to accelerate due to climate change. Increasing temperatures, for example, put more workers at risk of exertional heat stroke and subsequent acute kidney injury, therefore predisposing many to developing chronic kidney disease. However, other exposures should also be assessed, especially with ongoing environmental degradation due to industry and extractive capital, decreasing precipitation in drier agricultural regions, and use of pesticides and other toxins, which concentrate at higher levels in the environment.

This raises issues regarding the possibilities for scaling investigative efforts and how we might reconcile problems which are simultaneously local and global in character. As our research moves to encompass CKDnt as a multi-sited global concern – by examing the actually existing possibilities for comparability, particularly in the context of heat stress driven kidney disease – holding true that many populations may simultaneously or independently be affected by other risk factors is critical. We therefore need to consider toxin related environmental degradation which could lead to localised epidemics of CKDnt, as well as the CKD pandemic related to metabolic syndrome. Given that toxin exposures and preexisting metabolic syndrome are likely to interact with heat stress and subsequent dehydration, it is essential that we reconcile such interactions as a potential feature of the condition. In our view, they *should not drive polarisation between proposed aetiologies*. One approach to describing the differences and similarities among kidney diseases affecting disadvantaged communities lie in the development of comparable protocols:

The ongoing Disadvantaged Populations eGFR Epidemiology Study (DEGREE) (Caplin et al. 2017) provides one such basis for creating an integrated and transdisciplinary set of protocols, that draw from the disciplines across epidemiology, physiology, climatology, the medical specialties, to further include the social sciences and humanities. In doing so, we can identify commonalities and differences in the different permutations of unexplained kidney diseases affecting vulnerable communities. By including the socioeconomic context, lacking in current efforts, we would allow

future investigations into kidney disease among disadvantaged communities to provide insight as opposed to the confusion and conflict that erupts when methodological approaches are disparate. Such efforts would allow for improved understandings of CKDnt driven by heat stress in areas recognised as affected and where it is suspected. Equally importantly it would identify and contextualise several forms of kidney disease, and their potential interaction with one another, be they due to heat stress, traditional metabolic drivers, or specific toxic or infectious agents, affecting the precariat in low resource settings.

Proceeding thus, local and global scales operate as guides to each other's respective concerns – continually linking effect and affect to different mechanisms and processes (if not necessarily causes). The global is directly encountered and embodied via the local, something clearly illustrated by sugar cane cutters intimate connection with global capital or climate change or indeed the Lake Chapala residents encounter with colonial and neo-colonial forms of neglect.

How to Think Prevention in an Unequal World?

Our goal is to create aligned and adaptive investigative research processes that put the needs of the participant population first, and focuses on addressing the risks, if not outright causes, related to their concerns. We hope that such processes would inform precautionary principle-based interventions in the community and occupational setting, produce information for advocacy for access to care and requisite treatment and contribute to translational work that empowers those affected to advocate for themselves. In other words research processes ought to emerge through a genuine effort to "people critique" – to ensure a "conscientious empiricism is wedded to a radical analytical openness" (Biehl and Locke 2017). It is therefore essential that research in disadvantaged and neglected communities is non-extractivistist in character particularly when access to the human body and its practices are at the forefront of inquiry. Genuine forms of local partnership and collaboration are not simply desirable, but critical to meeting the kinds of challenges that CKDnt poses as well as calling into question who has the power to make a disease.

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