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ORIGINAL ARTICLE

Cancer in the tropics: geographical pathology and the formation of cancer epidemiology

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Abstract Researchers have long been concerned with cancer in what has been called the tropics, developing world, and low- and middle-income countries. Global health advocates' recent calls to attend to an emergent cancer epidemic in these regions were only the latest effort in this long history. Researchers, known as geographical pathologists, sought to determine the etiologies of cancer and other non-infectious diseases between the 1920s and the 1960s by comparing their occurrence across different environments. The geographical pathologists used the concept of the environment to analyze the influences that natural and artificial surroundings had on health. While the international network of geographical pathology fostered medical thinking about environmental health in the early and mid-twentieth century, the very meaning of environment, alongside the scientific methods for studying the environment, changed in this period. In the 1960s, epidemiology, previously used for the study of infectious diseases, displaced geographical pathology as the cohesive framework of cancer research. This signaled a shift in research focus, from one dedicated to diagnostics and the environment to one centered on population and statistical studies. This article shows that it was not the lack of knowledge about cancer in the developing world but rather specific configurations of knowledge that shaped which cancer interventions in the developing world researchers and public health officials conceived.

I confirm that the manuscript is comprised of original material that is not under review elsewhere, and that the studies on which the research is based has been subject to review by the Committee on the Use of Humans as Experimental Subjects (COUHES) of the Massachusetts Institute of Technology.

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Global health advocates have recently called for the expansion of cancer care and control in low- and middle-income countries, arguing that cancer, "once thought to be a problem almost exclusive to the developed world," was now becoming a leading cause of death and disability in poor countries (Farmer et al. 2010, p. 1186). However, medical researchers have thought intensely about cancer in the developing world for a long time. In the early and mid-twentieth century, geographical pathologists hoped that their studies would not only reveal the patterns and causes of cancer in the tropics but culminate in a general theory of cancer causation. While geographical pathology ultimately fell short of this ambitious goal, the field played a pivotal role in the formation of cancer epidemiology.

This paper examines geographical pathology from the 1920s to the 1960s, the period in which the field flourished. In the 1920s, pathologists in Switzerland and Germany built an international research community that systematically studied etiologies by comparing disease occurrence and forms around the globe. This conceptual framework for the study of disease was not new; it had been articulated by physician August Hirsch in the 1850s and others before him (Hirsch 1859). Unlike Hirsch, who relied on existing literature, the geographical pathologists of the 1920s set out to collaboratively record disease occurrence in different places according to uniform methods of pathological diagnosis on the microscopic level of tissue structures. At conferences, the scientists compared their diagnostic classifications and observations to discern which, if any, geographical factors were decisive for the divergent distribution and frequency of a disease, thereby explaining etiology. The International Society for Geographical Pathology (ISGP), which the Swiss and German pathologists founded for this purpose, was soon comprised of more than 260 members from 36 countries. After World War II, the community, reconstituted to include physicians from specialties other than pathology, continued to develop a methodology for the etiological study of "degenerative" or non-infectious diseases. The researchers considered their approach to be especially suitable for explaining the causes of cancer, which was becoming a major health concern in the postwar years. In the 1960s, geographical pathology began to lose its role as a cohesive framework for cancer research. Epidemiology, previously reserved for the study of infectious diseases, became the predominant term. This also signaled a shift in research focus, from one dedicated to pathological diagnosis and environmental relations to one centered on population studies and statistical analysis.

In the 1920s, geographical pathologists popularized and operationalized the concept of the environment (*Umwelt*) to describe the influences on health by natural and also artificial surroundings that society, industry, customs, and politics created. Previously, Hirsch and other physicians had used terms such as milieu, geography, or external factors. Putting the environment at the center of analysis enabled the geographical pathologists to vary the scale of their study areas from cities to regions

to countries and to conduct investigations across the temperate and tropical regions. Everyone in every group was always surrounded by an environment.

My analysis of geographical pathology centers on the usage and measurement of the environment in the publications and correspondence of geographical pathologists in Europe, Kenya, South Africa, and the United States. I describe the scientists' conceptual apparatus as well as the institutions they built to study these concepts, attending to the interaction between knowledge and social and political organization (Jasanoff 2004). I analyze how liver cancer as a disease became a structuring factor for geographical pathological research, and which kinds of etiology became perceptible (Rosenberg and Golden 1992; Murphy 2006).

This article shows how the very meaning of environment changed in this period alongside scientific methods for studying the environment. The hitherto untold history of geographical pathology adds a crucial element to our understanding of environmental health science and epidemiology in the twentieth century. Medics had ruminated on influences of "airs, waters, and places" on health since antiquity, but the rise of germ theory in the late nineteenth century, historians of medicine in the United States have argued, decentered such ruminations until their reemergence within occupational health in the late twentieth century (Sellers 1997; Nash 2006; Rosenberg 2012). This article argues that thinking about environmental health continued in international networks, such as that of geographical pathology, in the early and mid-twentieth century. This network formed a nucleus of the epidemiology of non-infectious diseases. While the epidemiology of infection had been studied in the Epidemiological Society of London and other institutions since the nineteenth century, geographical pathology provided a framework for an epidemiology of non-infectious diseases (Mendelsohn 1998). Finally, geographical pathologists linked environmental influences to specific changes in tissue structures, making the environment observable within the body. In the 2000s, epigenetics posed the question of "how environments come into the body and modulate the genome" (Landecker and Panofsky 2013, p. 349). In the postgenomic moment, epigenetics measures the environment on the molecular level of modifications of the deoxyribonucleic acid (DNA). The subfield of exposomics, which "seeks to assess 'the whole environment we have inside our bodies,'" emerges as the latest manifestation of a scientific research tradition that geographical pathology shaped (Shostak and Moinester 2015, p. 195).

Geographical pathologists studied liver cancer in the 1950s and 1960s to understand the role of the environment in carcinogenesis by comparing the occurrence between Europe and Africa, where doctors had observed high liver cancer rates since the 1920s (Higginson 1963). This comparison was key to explaining the etiology of liver cancer. Cancer has never been thought to be a problem exclusive to the developed world, at least not in twentieth-century cancer epidemiology. Specific configurations of knowledge—not the lack of knowledge—shaped which interventions researchers and public health officials could conceive. While geographical pathology made cancer in the tropics visible to biomedical scientists, the methods and framework legitimized deferring cancer treatment programs to an ever-distant future. Most geographical pathologists were removed from the daily needs of cancer care, focusing instead on the collection and analysis

of tissue samples. The European and North American sponsors of international cancer programs chose not to support treatment because these countries were building their own national cancer programs at that time. The global disparities of cancer care have thus been rooted not in a lack of knowledge but broader political, economic, and social inequities (Rouse 2009; Wailoo 2014). This conjuncture of international relations and epistemic limitations forestalled cancer programs that might have prevented the emergent cancer epidemic in Africa (Livingston 2012).

Tropical medicine for the world: geographical pathology and the global environment

When Max Askanazy moved from Königsberg at the shores of the Baltic Sea to become a professor of pathology at the University of Geneva in 1905, he was struck by the different diseases he observed in his new practice. Askanazy envisaged a collaborative endeavor to systematically uncover unknown etiologies through the comparison of these different disease "panorama." Together with Freiburg-based pathologist Ludwig Aschoff, Askanazy proposed founding the ISGP at the annual meeting of the German Pathological Society in 1927 (Schmorl 1927). The new society was established and quickly grew in membership.[1] The field was based on the idea of a global environment, pathological diagnostic methods, and an international network of researchers.

Geographical pathologists used the concept of *Umwelt* (environment) in the study of disease etiology. "The internal and external disease factors have to be considered, not only racial or constitutional pathology, to which questions of heredity and endocrine interactions belong," Askanazy expounded, "but also all influences of the environment: from climate, altitude […], light, nutrition, mechanical insults, special parasitisms, influence of poisons and effects of industrial harms whose consequences can hardly be assessed today" (Askanazy 1928, p. 59). *Umwelt*, added to the German lexicon around 1800, had recently become imbued with an ecology meaning (Harrington 1996). Geographical pathology was the theory of "the influence of the environment on the spread and nature of the diseases through the comparative study of the spread and the nature of disease under consideration of racial and constitutional anomalies (*Eigentümlichkeiten)* of the populations in different countries" (Adelheim 1929, p. 217). Askanazy's colleague Roman Adelheim distinguished between two types of environment: the natural environment "that surrounds us" and the artificial environment that "we create ourselves." Both types were already studied by separate medical specialties. "In the most extreme and perceptible form, we see [the influences of the environment on the human organism] in tropical medicine, which requires its own study in specific institutes," Adelheim wrote, while social hygiene, a hybrid of medicine and social policy, dealt with the artificial environment (Adelheim 1929, p. 218).

[1] These countries included Germany, the United States, Cuba, Colombia, Argentina, England, Austria, Belgium, Canada, Chile, Denmark, Spain, Estonia, France, Greece, the Netherlands, the Dutch Indies, Hungary, Italy, Japan, Latvia, Lithuania, Mexico, Norway, Poland, Portugal, Romania, Russia, Sweden, Switzerland, Czechoslovakia, Turkey, Yugoslavia, South Africa, Brazil, and Finland.

Geographical pathology straddled this separation. For Askanazy, tropical medicine had retained forms of geographical medicine but was limited to fulfilling practical tasks in European efforts of colonization. He sought to expand the thorough study of environmental health influences beyond tropical to temperate climates. "The tropics," historian David Arnold has argued, "existed only in mental juxtaposition to something else—the perceived normality of the temperate lands. Tropicality was the experience of northern whites moving into an alien world—alien in climate, vegetation, people, and disease" (1996, p. 143). For Askanazy, there was no such essential difference in the impacts of tropical and temperate environments on health; the environment exerted its influence around the globe. In tropical medicine, questions of environmental influence were receding at that time. Bacteriology with its focus on germs as causative agents of disease had gained traction across medicine and public health since the late nineteenth century. Practitioners of tropical medicine concentrated on developing sanitary programs to change people's unhygienic, germ-spreading behaviors (Anderson 2006). In Germany, bacteriology displaced pathology from its central role in medicine due to pathology's inability to determine disease causes (Prüll 1998).[2] However, bacteriology was not without its critics—Askanzy and the geographical pathologists among them—who argued that the pathogen alone was not a sufficient cause for disease and that the study of other influences remained necessary. There were a number of different subfields—and researchers moving between them—that focused on the role of environment, race, and *Volk* (peoples) on health. These factors were poles in a spectrum of explanation of disease patterns. Adelheim wrote "it is obvious that the biology of races and people [*Völker*] plays a great role here, but we are only beginning to understand gradually that the natural environment in its manifold forms and effects plays an unexpectedly large role" (Adelheim 1929, p. 218).

Social and racial hygienists, eugenicists, and other groups in Germany were dedicated to maintaining a healthy body politic through programs for racial purity and protection from noxious industrial and civilizational influences (Prüll 1998; Proctor 1999; Weindling 2000). These groups, including the geographical pathologists, had no single, stable definition of race or *Volk*. Askanazy did not dismiss racial factors but noted the difficulty of studying these factors, because there were hardly any "pure races." Moreover, the focus on race would often obscure more complex environmental, nutritional, and hormonal etiologies of cancer and other diseases.

The etiology of cancer was controversial in the nineteenth and early twentieth centuries. Some scientists assumed that cancer was a 'disease of civilization' that would not afflict black people in Africa or the United States (Wailoo 2011). British and German authorities asked their medical officers to investigate the occurrence of tumors among people in the African colonies. The German officers' reports indicated that most cancers found in Europe also existed in Africa, and researchers argued over possible cultural, racial, civilizational, and age-related explanations for

[2] Bacteriology itself was not a uniform field, and some bacteriologists responded to this criticism by studying the environmental effects on bacterial virulence (Mendelsohn 1996).

divergent rates. For example, Walther Fischer, professor of pathology in Rostock, pondered if the observation of higher cancer rates among black Africans who had been in contact with the "white civilization" was merely an artifact of better and more rigorous examinations by trained physicians. Fischer and his colleagues found it impossible to answer these questions conclusively, because comprehensive studies were lacking (Fischer 1927). In Europe in the 1920s, the League of Nations initiated cancer studies that did not identify clear racial and hereditary factors (Borowy 2009; Gaudillière and Löwy 2016). In 1922, Harvey Pirie at the South African Institute for Medical Research was "struck by the comparatively large number of [liver cancer] cases met with amongst African natives, either in the course of performing autopsies, or, more often, in the examination of specimens sent for report to the South African Institute for Medical Research" (1922). Liver cancer was found to be exceedingly rare in Europe. Pirie speculated that these high numbers in Africa might be associated with schistosomiasis and cirrhosis, while others attributed these numbers to syphilis or nutrition.

Explaining etiologies as complex as cancer required a collaborative effort that the ISGP sought to facilitate. The ISGP with members from more than thirty countries must have been a remarkable success for the German Pathological Society. International scientific societies had banned German scientists after World War I and only slowly readmitted them in the mid-1920s (Fox 2016). Askanazy kick-started the program by posing four questions to the chairs of the national committees of the ISGP (Askanazy 1928, pp. 57–59): do any diseases occur more frequently in your region? Do diseases occur rarely or not all? Does the disease have a natural history specific to your region? Can you already describe specific conditions (causes) that explain the local specificities? These questions were to be answered through a collaborative research program that depended on pathological anatomy for the diagnosis "by working with the microscope, culture, and animal experiment and by determining the initial stages of the disease" (Askanazy 1930b, p. 380). Moreover, Askanzy believed that statistics "with its use of probability calculus will have the greatest importance for the development of *Völkerpathologie*" (Askanazy 1930a, p. 1102). A. Bradford Hill, whose later collaborator Richard Doll would become a central figure in postwar cancer epidemiology and geographical pathology, developed such medical statistics in the United Kingdom at this time (Brandt 2007, Chap. 5).

The first meeting of the ISGP in October 1931 in Geneva focused on liver cirrhosis, which had been of interest to pathologists for a while. Eighty participants from nineteen countries attended the conference. Rodolphe de Josselin de Jong, professor of pathology at Utrecht University, analyzed the 69 documents that he had received from 20 European countries and elsewhere (de Josselin de Jong 1931). Geographic areas ranged from the city of Mannheim to the whole country of Japan, and the classifications of cirrhosis types differed. Comparing frequency, subtypes, and demographics, the pathologists discussed the relation of specific forms of liver cirrhosis to nutrition and exposures to noxious substances. The environment became inscribed in the physical structure of the liver. The researchers also considered the relation between liver cirrhosis and cancer. Only a small percentage of cirrhotic patients in Europe developed liver cancer, but 21 percent of cirrhotic patients in the

Dutch East Indies (present-day Indonesia) did so. On the nearby Malayan archipelago, cancer of the liver had the highest rate among all organ cancers. The reason for these divergences was completely unclear to the researchers. After the conference, Henry E. Sigerist, a member of the ISGP and one of the founding figures of the history of medicine in the United States, published a note in the first issue of the *Bulletin for the History of Medicine*. He argued for the relevance of the history of medicine to geographical pathology, considering that "cultural conditions have definite repercussion on the diseases of the time" (Sigerist 1933). However, his call remained unanswered. The ISGP met again in 1934 to discuss the etiology of arteriosclerosis and in 1937 to discuss anemia. The next meeting in 1940 in Rome was canceled because of the outbreak of World War II.

Salvage epidemiology: cancer, environment, and development

After the war, the community of geographical pathologists reconstituted itself and expanded beyond the ISGP. Max Askanazy and Roman Adelheim died and de Josselin de Jong retired. Others continued, such as the Swiss pathologist Frédéric Roulet, and new researchers, including Danish pathologist Johannes Clemmesen, British physiologist Richard Doll, and US pathologist Harold L. Stewart, joined the field. Newly founded international organizations, including UNESCO and the World Health Organization (WHO), as well as the International Union Against Cancer (UICC, *Union Internationale Contre Cancer*) supported the field. The US National Cancer Institute (NCI) established a Unit on Geographic Pathology of Cancer led by Stewart. Cancer became a pressing concern in North America and Europe in the postwar decade, and geographical pathology promised answers to urgent questions about cancer causation and prevention.

The geographical pathologists met at a series of conferences, sponsored by these organizations, to develop a methodology for the study of cancer and other non-infectious disease in the 1950s. An eight-day-long "Symposium on Geographical Pathology and Demography of Cancer" was held in Oxford in 1950, the ISGP dedicated its fifth conference in 1954 to cancer, and a conference on "Methods in Geographical Pathology" was convened in Paris in 1957. Further, meetings on specific forms of cancer were organized, such as a "Symposium on Cancer of the Liver among African Negroes" in Kampala in 1956.

The geographical pathologists considered the term epidemiology not suitable to describe the mode of occurrence of cancer, and the existing epidemiological methods inapt for the study of non-infectious diseases (Clemmesen 1951, p. 7). The idea that there was an 'epidemic' of cancer would have made little sense to the researchers. While physicians began noting an increase in non-infectious diseases in the interwar years, it had been hard to determine the tiny differences in low incidence rates in different parts of the world, where these diseases were endemic.[3] Geographical pathology, "defined as the comparative study of the incidence of

[3] George Weisz (2014) provides an account of the history of the related but different category of chronic diseases that emerged in the United States in the 1930s.

disease and the distribution of physiological traits in people belonging to different communities throughout the world and the correlation of these data with features of the social and geographical environments," sought to reveal and explain these almost indiscernible disease patterns (Doll 1959, p. 11).

To some, geographical pathology held the key to understanding a "vast experiment of nature [which] by-passes the unquestionable moral blocks to human experimentation" (Stewart 1951, p. 148). This experiment, which had created unique disease patterns in different communities was, however, in jeopardy. "Changes in the physical and cultural structure of society are taking place at a faster rate than ever before, and industrialization and the ease of communication are establishing a common pattern of life in areas which, until recently, provided a striking contrast in living conditions and ways of life," Doll warned. "Many of the contrasts which might throw light on the etiology of diseases are disappearing and any delay in initiating research may result in the loss of valuable opportunities" (1959, p. 54). Geographical pathological studies were needed to exploit the unique disease distribution, and these studies were needed now.

Doll's call to action reflected another reconceptualization of the environment in the mid-twentieth century. Grounded in the vision of development, some researchers considered that Africa, its people, and environment would soon undergo modernization and industrialization, eradicating any differences in environmental health influences (Cooper 2005; Packard 1997). This vision re-emphasized a distinction between the tropics and temperate regions; a distinction grounded in a framework of temporal difference. In this view, Africa was a "living laboratory" for research on the universal causes of non-infectious disease. The environment was temporally distinctive to discern the factors producing unique disease patterns. Other researchers working on the ground in Africa found these homogenizing visions of Africa hard to reconcile with their heterogeneous observations (Tilley 2011). For many cancer researchers, however, it was a present with a future but without a past (Wolf 1982).

Liver, cervix, and lung cancer were considered especially suitable for geographical pathological investigation, because the rates of these cancers differed significantly across populations (Kennaway 1951). While lung and cervix cancers could be studied in Europe, liver cancer became the paradigmatic case for geographical pathologists' studies in the 1950s because of its heterogeneous distribution between Europe and Africa. Charles Berman of the Consolidated Main Reef Mine Hospital in South Africa confirmed Pirie's earlier conjecture that liver cancer was among the most common forms of cancers of "African natives," occurring at much higher frequency than in Europeans or Americans (Berman 1951). Berman and his South African colleagues relied on broad racial classifications that defined their study populations as black Africans (Oettlé 1956a; Oettlé and Higginson 1956b).Together with researchers from the United States, the South Africans argued that environmental factors played a vital role in the etiology of liver cancer because high rates had been found in "the indigenous races of the Orient" and black Africans but not in black people in the United States, who were thought to be closely related to black people in Africa (Berman 1955; Kennaway 1944). Their comparison was based on studies that their US collaborator Paul E. Steiner had conducted at the Los Angeles County Hospital in the 1940s (Steiner 1954).

Historian Keith Wailoo has argued that "Steiner's choice of racial categories thus reflected a paradox, for while he rejected the older notion of black cancer immunity, he embraced other outdated practices of racial classification." (2011, p. 98). These outdated categories travelled well, enabling scientific collaboration across the United States, apartheid South Africa, and the late British Empire.

The scientists described these environmental factors in terms of climate, geography, and, increasingly, molecular relations. Molecularization—the perspective of the body and, in this case, the environment on the molecular scale—encompassed much of the life sciences and biomedicine in the twentieth century (de Chadarevian and Kamminga 1998; Rose 2007). However, molecularization was not a disruptive paradigm shift but a slow process in which studies on the molecular and other scales complemented each other. For example, the study of chemical carcinogenesis arguably molecularized in the 1920s, when laboratory studies identified specific molecules in coal tar that caused cancer in mice (Armon 2012). However, the researchers studied the health effects of these molecules on the level of tissue structure changes. Moreover, geographical pathologists described the environment in terms of geography and agriculture. They also expressed environmental influences in terms of molecules. A study in the 1950s stated that "as far as the South African native is concerned, we suspect that the high incidence of liver disease, disturbance in the metabolism at least of the bile, vitamin A, and the sterol hormones and to a lesser extent of the thyroid are most deeply implicated in the production of carcinoma of the liver," while climate might affect the utilization of food (Gillman et al. 1950). Some researchers speculated that "if some specific carcinogen is involved in Africans, it appears to be one that is fairly specific to the liver cells. Such a postulated carcinogen must be one that arises or can be encountered in African life and which can explain the curious geographic distribution of carcinoma of the liver" (Davies 1955, p. 1643).

Cancer treatment, the researchers contended, was not a concern, because the disease played no larger role in Africa's current health problems: Africans were generally younger than the ages at which cancer was frequent. The researchers warned that people would get older with improving health conditions in the future, and, thus, cancer prevention was still warranted (Clemmesen 1956; Sivaramakrishnan 2018). Health programs of colonial rulers, international organizations, and postcolonial African governments focused on primary care, malnutrition, and infectious diseases. However, this neglect of cancer treatment did not go unchallenged. Jack Davies, a pathologist in Uganda, objected that "cancer of the liver in Uganda, as elsewhere in Africa, is a common and important human disease causing much suffering and misery" and care should not be postponed into the indefinite future (1955, p. 1637).

Molecularized environments: practices of studying liver cancer in Kenya

In contrast to the neglect of cancer care in Africa, European and North American states created national programs for the development of cancer treatments in the 1940s and 1950s (Keating and Cambrosio 2012). When French intellectuals urged France's President Charles de Gaulle to propose the foundation of an international

organization for cancer research, funded by 0.5 per cent of the defense budgets of the developed countries, in 1963, the negotiations produced the much more modestly funded International Agency for Research on Cancer (IARC), which focused on geographical pathology and cancer epidemiology. The Soviet Union soon joined the WHO, France, Germany, Italy, the United Kingdom, and the United States in funding the IARC (Wild and Saracci 2015). The British and other initial critics were swayed by limiting the IARC's scientific program to geographical pathology, which was considered to be an international endeavor already. The new international agency would thus not encroach on the nation states and their newly established cancer treatment programs. The scientific advisors to the IARC recommended that the IARC become the hub for liver cancer research around the globe. John Higginson, who had been an active member of the geographical pathology community, was appointed to be the first director of the IARC.

The geographical pathologists had wondered since the mid-1950s about the existence of specific liver carcinogens in the environment of populations with high rates of liver cancer. Such a substance was identified in a place far away from southern Africa in 1960, when hundreds of thousands of turkeys died unexpectedly on British farms.[4] Researchers discovered the mold-produced molecule aflatoxin that killed not only the birds but also caused liver cancer in rats and other laboratory animals. Aflatoxin presented a possible answer to the riddle of liver cancer. The IARC accorded the highest priority to investigating the link between liver cancer and aflatoxin, establishing a Regional Research Center in Nairobi, Kenya, in 1967.

In many parts of Africa, medical research had been part of colonial states' practices of ruling and managing colonized populations (Comaroff and Comaroff 1997; Vaughan 1991). Africans were, however, not just docile subjects but creatively subverted and adopted medical practices and interventions, challenging the "nervous" colonial state (Hunt 2016). With decolonization in the 1960s, postcolonial African states continued funding medical research, mostly on infectious diseases (Ombongi 2011). Many of these research efforts dwindled, when international lenders imposed structural adjustment programs on Africa states in the 1980s and 1990s. International and non-governmental organizations provided research funding that lent them the appearance and functions of states but with none of the responsibilities. The research center that the IARC established in Nairobi was a forerunner of such "para-state" organizations that built on the edifice of the state, while being beholden to international donors (Geissler 2015).

Cancer research itself was not new to East Africa. Uganda had become a center for cancer research and treatment in the 1950s (Mika 2017). Denis Burkitt studied the eponymous lymphoma and other cancers through what he called "cancer safaris." Reminiscent of the lonely colonial medical officer, he moved between medical stations to record cancer incidence and create cancer maps (Clarke 2014). In Kenya, British researchers formed the Kenyan Cancer Council in the late 1950s in response to their Ugandan colleagues' inquiries. Charles Allan Linsell, a pathologist of the colonial Medical Research Laboratory in Nairobi, established a

[4] For a overview review of the history of aflatoxin and other mycotoxins, see Pitt and Miller (2017).

cancer registry to obtain much-needed systematic observations of cancer patterns (Linsell and Martyn 1962). After Kenya's independence in 1963, Linsell remained in Kenya as a staff member of the WHO, which had run nutrition surveys for several years. The WHO approached the Kenyan government to set up the IARC Regional Centre in Nairobi. The Kenyan government agreed to the proposal, and Linsell became the director of the new center in the fall 1966.

The geographical pathological study of liver cancer and aflatoxin was conducted in Murang'a County, where the agrarian Kikuyu people lived. The Kikuyu had been subjects of a series of British and WHO nutrition studies since the 1920s. Linsell and his colleague F. G. Peers hired two local research assistants, Samuel Mwangi and Peter Mbugwa, one of whom was an ex-schoolmaster. They were based in Fort Hall (present-day Murang'a) with a Land Rover and collected food samples directly from the plates of local people in the county. Market sampling was considered unrepresentative, because the researchers observed that women, who usually prepared the food, removed visibly moldy ingredients. The collectors depended on the hierarchies of the Kikuyu and on state infrastructure to obtain their samples. They relied on local chiefs to help them approach randomly selected tax-payers to be the center of a sampling cluster. They explained the purpose of the study and bought a sample of the daily main meal from the cluster center and seven close-by houses that cooked the meals separately (Peers and Linsell 1973). These samples were shipped in coolers to Nairobi and analyzed at the IARC laboratory for aflatoxin. Moreover, Linsell established a cancer registry in Murang'a county. The cancer incidences were compared to the national cancer registry in Nairobi (International Agency for the Research on Cancer 1968; Linsell 1967). Linsell and Peers divided Murang'a county by altitude into three different areas and determined the distribution of liver cancer and aflatoxin exposure in each area. Comparing the three areas, they found a weak correlation. The population in an area with increased liver cancer rates was also subject to increased aflatoxin exposure. However, this correlation was so weak that a few unrecorded cases would have rendered the result not statistically significant.

Linsell and Peers assumed that the high rates of liver cancer were the result of the lives that the Kikuyu had been living for a long time and of the food that they consumed locally. However, hundreds of thousands Kikuyu had been subject to brutal resettlement in detention camps and to confinement in villages by the British in response to the Mau Mau rebellion—the Emergency—in the 1950s (Elkins 2005). The case of the Kikuyu in Murang'a county was so stark that even the IARC researchers could not escape the recent history:

> As regards food sampling in the pilot area of Murang'a, this is possible but might prove more expensive than I thought, as many of the more remote areas of the district are now occupied by Africans previously accommodated in the consolidated villages. Following the Emergency and land consolidation, Africans in this area were accommodated in villages specially constructed by Government with services such as water supply and medical care. There has been, since Independence, a return to the more traditional way of life and they have left these villages for their own farms. Although this may make our work

> more difficult I think the isolation of individual farms may ensure a more meaningful study.[5]

For these reasons, Linsell viewed the Kikuyu's lives as "sufficiently static" to be studied. The annual reports of the colonial medical department repeatedly discussed how the life and dietary conditions in the camps impacted the health of the Kikuyu population (Kenya Medical Department 1956). This way of measuring the environment assumed a stable relation of the people and their environment, making visible seasonal changes but no short-term or long-term changes of diet and agricultural practices. When the British colonial rulers appropriated land for the cultivation of tea, coffee, and other cash crops in the first half of the twentieth century, they promoted corn, because this crop could nourish a larger population from smaller plots of farmed land (MacKenzie 1999). Corn was highly susceptible to aflatoxin and other pests. The cancer researchers cast the Kikuyu as a people bound in their traditional lives. Since these lives did not change, observations over a long period of time were unnecessary. This flattening of the temporality was one of the problems of geographical pathology that would soon emerge.

The Kikuyu had their own knowledge systems about health and agricultural practices. A number of anthropologists studied the community, among them Louis Leakey, who would later become a famous paleontologist, in the 1930s. Leakey described that the Kikuyu refer to some diseases as *kũrũara ini*, which he translates as "to be ill as to the liver." The Kikuyu considered this set of diseases to be often incurable and eventually deadly (Leakey 1977, pp. 928–929). It is impossible to know whether a contemporary biomedical doctor would have diagnosed *kũrũara ini* as liver cancer or anything related to the biomedical conception of the liver.

Epilogue: biomarkers, viruses, and the emergence of "placeless" cancer epidemiology

The Murang'a study became a key reference point for geographical pathology inquiries into cancer. Peers and Linsell followed up with a similar study in Swaziland, also finding a correlation between aflatoxin ingestion and liver cancer (Peers et al. 1976). Other studies in Uganda and Thailand in the early 1970s corroborated this correlation (Alpert et al. 1971; Shank et al. 1972). Yet these studies also signaled a shift away from the framework that geographical pathology had provided. Scientists begun to employ a blood test for alpha-fetoprotein to diagnose liver cancer. Alpha-fetoprotein was what would eventually be called a biomarker, an indicator of disease on the molecular level. Biomarkers came to replace pathological tissue analyses.

Aflatoxin, however, did not remain the only answer to the question of liver cancer causation. In the early 1970s, scientists hypothesized that the recently discovered hepatitis B virus could cause liver cancer (Koshiol et al. 2018). A series of Sino-US collaborative epidemiological studies sought to confirm this hypothesis

[5] C. A. Linsell to G. T. O'Conor, 21 June 1967, Research Centre—Nairobi, R 4/2 Nair, First Generation of Files, 1967 – 1984, Archives of the International Agency for Research on Cancer, Lyon.

(Jiang 2018). The researchers conducted a so-called cohort study that monitored the biomarkers for hepatitis virus infection and liver cancer over time. By bracketing the question of temporal development, geographical pathology had foreclosed the question of how individual exposures produced disease over time. This limitation pushed researchers to develop biomarkers for aflatoxin exposure in the late 1980s and 1990s. Subsequent studies found that aflatoxin and hepatitis virus infections synergistically caused liver cancer (Kensler et al. 2011). The virus research programs, which the US government heavily supported, thus exerted an influence on the study of chemical carcinogenesis, pushing the field toward specific modes of molecularization (Gaudillière 1998; Scheffler 2014). These biomarker studies allowed researchers to overcome what had already been seen as limit of geographical pathology in 1959, namely that the "final proof of cause and effect is not obtained from this type of study considered alone."[6]

However, the focus on biomarkers moved epidemiologists away from studying the relations of populations and environments. One of the crucial studies on hepatitis virus infections and liver cancer in Taiwan in 1981 made no effort "to study aflatoxins because there is no way to measure previous aflatoxin exposure; and because the Chinese diet is so complex, food sampling for aflatoxins is a formidable task" (Beasley et al. 1981, p. 1132). Instead, epidemiologists focused on populations and the indicators that were measurable within the body. Sociologist Sara Shostak argues that the trend went even further to individualize exposure and prevention in the United States, undermining environmental epidemiology's "traditional orientation to informing population-based interventions to protect public health" (Shostak 2013, p. 135). The IARC disbanded its Nairobi Center in the early 1970s, after dismissing proposals for establishing a permanent program to screen for environmental carcinogens.

It was not only the introduction of biomarkers that signaled the demise of geographical pathology. The concept itself had already started to lose its cohesiveness and power to corral researchers into working under its framework in the early 1960s. At an meeting in 1966, the IARC's Scientific Council discussed that "geographical pathology […] should not be regarded as a discipline per se, but rather as an approach to problems of pathogenesis which emphasize the collection and comparison of biological parameters in populations under differing environments to permit identification of etiological mechanisms."[7] In the copy of this document in the WHO Archives, a reader parenthesized "geographical pathology" and wrote epidemiology next to it.

Today, historians and sociologists once again see an opening for critical social science in the burgeoning field of epigenetics to study "how social inequality and other factors contribute to health and illness and can help focus social policy to achieve societal improvements" (Müller et al. 2017, p. 1681). Yet it remains to be seen if social scientists today are more successful than Henry Sigerist in convincing

[6] Kreberg, L., et al. "Working Paper on a Proposed International Cancer Research Programme for WHO," 1 March 1959, p. 15, WHO Library, Geneva: MHO/AD/19.59.

[7] "General Comments on the Future Developments of Epidemiological and Environmental Biology with Special Reference to a Multi-Disciplinary Approach," IARC Scientific Council, 4-5 April 1966, SC/1/5, p. 1, WHO Archives, Geneva: N70/370/2.

biomedical researchers of the relevance of their contributions. At the same time, geography and other fields have continued to study the relation between health, social forces, and place throughout the late twentieth century (Valenčius 2000; Guthman and Mansfield 2013). The question may thus be not only about finding new epistemic openings but also about urging international organizations to take questions of environmental health seriously.

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