Emerging Infectious Diseases and New Pandemics: Dancing with a Ghost! Lessons in inter- and transdisciplinary research in French Guiana, South America

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Perspective

Emerging infectious diseases and new pandemics: dancing with a ghost! Lessons in inter- and transdisciplinary research in French Guiana, South America

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ABSTRACT

In light of current international public health challenges, calls for inter- and transdisciplinary research are increasing, particularly in response to complex and intersecting issues. Although widely used under the One Health flag, it is still unclear how inter- and transdisciplinary science should be applied to infectious disease research, public health, and the different stakeholders. Here, we present and discuss our common scientific and biomedical experience in French Guiana, South America to conduct and enrich research in vector-borne and zoonotic infectious diseases, with the aim to translate findings to public health and political stakeholders. We highlight the successful progressive dissolution of disciplinary boundaries that go beyond One Health positive-driven assumptions and argue that specific local conditions, as well as strong support from research and medical institutions, have facilitated an emulsion toward inter- and transdisciplinary science. This argument is intended to improve responses to public health concerns in French Guiana and other countries and regions of the world.

1. Introduction

French Guiana (FG), the only outermost European Union (EU) region in South America (SA), is famous for the book and movie "Papillon" by Henri Charrière that retraces Charrière and one colleague's adventures during the French penal convict. Located at 53°W and 4°N, FG is between northern Amazonia and Atlantic Ocean (see [1] for geographic location). Covered by 97% Amazonian equatorial forest, FG enjoys an exceptional biodiversity. Covering 83,846 km^2 and constituting one of the least fragmented forest domains in the world, FG is bordered by Suriname to the west and Brazil to the east and south. With a 2020 population of 285,133 concentrated along the Atlantic Ocean and Surinamese border, there has been strong economic growth supported by the European rocket launching stations and construction sector. The relative geographic isolation from but cultural connection to the EU mainland, combined with its rich, tropical biodiversity and increasing population density, make FG an ideal area to study emerging infectious disease (EID) patterns and processes.

This EU territory is also known for having developed a substantial and long-term biomedical literacy in tropical medicine begin-

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ning in the early colonial period of physicians and naturalists, *e.g.*, J. B. Leblond and J. F. Artur in the XVIIIrd century [1]. The mobilization of research and medical institutions has strengthened research on EIDs for more than 25 years [2], with exemplary epidemiological surveillance systems.

The COVID-19 pandemic has highlighted the need for an integrative understanding of the origins of human infections using the One Health approach. We support the importance of this approach in infectious disease medicine. However, the One Health concept often remains academic, with narrow perspectives that do not address questions that would allow understanding complex interactions among the environment, animals, and human health [3,4]. Of the approximate 75% of human infections of animal origin, One Health ignores that before occupying an animal host, most pathogens have an environmental and, often, plant root origin. Here, we discuss considerations for strengthening and expanding the One Health approach using the collective and interdisciplinary study of EIDs in FG as an example for other regions facing rapid environmental changes.

2. A context to facilitate interdisciplinary research

Researchers positioned at the interface of domains in FG, *e.g.*, epidemiologists, clinicians, and ecologists, have played pivotal roles in promoting interdisciplinarity [2]. Teams working on cutaneous leishmaniasis (CL), Buruli ulcer (BU), and toxoplasmosis have expanded a number of candidate animal species as natural reservoirs for these human pathogens, contributing to debates on biodiversity-disease relationships. Better consideration of the environment has raised awareness of regional climatic dynamics on diseases (*i.e.*, El Niño Southern Oscillation and global climate change affecting diseases, such as CL, malaria, dengue, and BU), making FG one of the world's most documented regions for understanding climate-disease interactions [2]. However, this approach in FG has demonstrated that climate change currently explains only 4-12% of the disease incidence [2], leaving other considerations of environmental, demographic, and socioeconomical aspects open for study. For instance, forest loss and natural habitat modifications are more important than climate in transmission of Chagas, BU, and hantavirus pathogens [2]. One example is the description of a novel tick-borne disease agent in 2022, *Candidatus* Anaplasma sparouinii, from an undocumented miner in a remote forest area of FG [5]. Methods classically involved in ecoevolutionary investigations, *e.g.*, 16S recombinant DNA sequencing and multilocus typing and phylogenetics, facilitated the discovery of this novel bacterium, genetically related to *Anaplasma* species, infecting sloths. Recent surveys in FG also reported the presence of novel tick-borne pathogens of yet undetermined zoonotic potential [5]. Living in close proximity to forests has also favored the transmission of known diseases, such as malaria.

The relatively small geographic area of FG with strong institutional communication, commitments of international researchers in the field with staff residents on site, and the sharing of research approaches and methods have been the basis for this inter- and transdisciplinary emulsion (Table 1) in a way that can serve as an example for other areas of the world.

3. Scaling host-pathogen systems and their study

Understanding the scale of species distribution determinants has long been the focus of biogeography and macroecology and a tenant of disease ecology for predicting host-pathogen dynamics to anthropogenic environmental disturbances [2,7]. Applied to disease [8], macroscale environmental conditions determine the possible suitable envelopes for host-pathogen systems, but the effects of biotic interactions are expected to be averaged out at larger scales, a concept known as the Eltonian noise hypothesis [8].

Field studies in FG on human CL support that ecological interactions and local resources determine host-pathogen system distribution at fine spatial scales, whereas coarse-scale abiotic factors (*e.g.*, temperature and precipitation) operate at broader scales, with local scale interactions lost within the background noise. CL risk areas occur where deforestation is evident, a factor triggering epidemic foci, with less influence exerted by bioclimatic factors at this scale [8]. Applying this to the Amazonian region, we also highlight the importance of considering local biotic conditions (*e.g.*, mammal richness), social activities (*e.g.*, human impact), and epidemiological factors (*e.g.*, vaccination coverage) for accurate spatial predictions of yellow fever risk [9].

Considering scale in disease dynamics, we can expect reasonable success in macroscale modeling of host-pathogen system shifts with global change. However, it will be challenging to address smaller scales for mechanisms that determine local host-pathogen distribution dynamics, and how they relate to macroscale processes and distributions [10]. Such efforts will require massive, high resolution, and real-time local data that will correct sampling bias, data gaps, and representativeness [10]. A hierarchical view of niche relations and consideration of the Eltonian noise hypothesis that includes anthropogenic, political, and sociocultural dimensions will help reconcile scale-dependent effects on predicting the disease system distribution patterns.

4. Microfoci of disease emergence from widely distributed microbes

The long history of tropical medicine in FG has shaped efficient disease surveillance and early detection of EID events important to understanding patterns of outbreaks. As for Brazilian Amazonia, all major disease outbreaks in FG during the last few decades were caused by introduced pathogens, *e.g.*, dengue, Zika, chikungunya viruses. By contrast, most of the latest indigenous EID hotspots have occurred at small spatial scales, without widespread dispersal.

For instance, despite a potential for significant emergences, only one recent outbreak of Oropouche virus has been reported, and it was short-lived and spatially constrained. The incidence of Mayaro fever is currently unknown, and hantavirus infections are rare and patchily distributed but never clustered [11]. The incidence of human rabies virus in bat saliva is below one in 3000 (*unpub.*). Similarly, Amazonian toxoplasmosis occurs in small and very localized foci, and CL, a forest and forest-edge disease, occurs in small foci, with high incidence or with more widespread diffusion and low incidence in anthropized coastal areas, depending on parasite species. Chagas disease occurs sporadically, and distribution depends on the vector and host ecological requirements. Leptospirosis, which causes major epidemics elsewhere in association with hurricanes or floods, has frequent but isolated cases in FG. BU, widely distributed in tropical regions, has a low incidence rate, with most cases occurring along the coastline adjacent to marshy ecosystems.

At first glance, Amazonia ecosystems appear as homogeneous landscapes, but this image obscures enormous ecological complexity, highly diverse but cryptic species communities, wide ranges of ecological niches for wildlife and microbes, and circumstances for unique evolutionary relationships. Nonexclusive hypotheses may explain the diverse array of zoonotic and vector-borne disease life cycles observed in SA. For instance, Amazonian forest species have smaller ranges than those of other forested regions. Although the spread of nonindigenous pathogens mainly relies on opportunistic, synanthropic, or even introduced species, indigenous microbes may rely on more specialized hosts with lower dispersal poten-

Table 1
Factors and contexts that stimulated inter- and transdisciplinary research in French Guiana.

Main factors and context features	Implication and interest for transdisciplinary research and biomedicine
Research is place-based	It facilitates and promotes exchanges and actions toward transdisciplinarity
Research is long-term intensive	It favors long-term studies, cohort analysis, integrative studies, allowing to take into account the temporality of phenomena, and test hypotheses
Scientific research, biomedical institutions and public health authorities share similar topics and ambitions, with spatial proximity	Researchers, biomedical actors, public health authorities, regional government and local communities and ethnic groups work together for better health and well-being of populations
Research is merging multiple knowledge streams and value systems	The presence of different disciplines and skills, the local context of institutions and organizations, stimulate collaboration and biomedical actions
Research applied to complex problems	Specific contexts promote addressing complex research and biomedical questions, e.g., climate change and health, biodiversity-disease relationships
Research shows well-developed leadership skills, equipment and other facilities	Many scientists and medical doctors are top-leading authorities in their respective fields, with important logistics, research stations and biomedical places located over the territory
Significant national, European and foreign funding endowment, European membership and citizenship	It favors long-term and transversal research and biomedical activities, and stimulates transboundary research and biomedical programs

Legend. Multidisciplinaryresearch is the cooperation of researchers from several different disciplines that have historically worked separately, with little cross-fertilization. Interdisciplinary research involves a much closer interaction, including transferring methods and knowledge among disciplines. Transdisciplinarity focuses on theoretical unity of knowledge, to transcend disciplinary boundaries and to involve nonacademic societal actors, and with a focus on specific, complex, societally relevant, real-world situations or problems [6]. This Table 1 is complementary to Table 1 in reference [2].

tial that constrains disease spread. Also, Amazonian mammals have much lower densities than other world ecosystems [12], likely reducing microbial circulation and potential zoonotic outbreaks.

In addition, despite recent and alarming trends, forest fragmentation in SA remains below that of other tropical areas, reducing the widespread transmission events of pathogens to humans. Biodiversity disturbance relationships often involve complex processes that depend on host-microbial interactions, including nonlinear and even antagonist effects [2]. Local forest modifications can destabilize fragile ecological conditions and contribute to the epidemic foci of exposed human populations. These attributes create conditions for producing a mosaic of host populations and ecological communities, along with microbial pathogens that encounter suites of environmental conditions that influence adaptation so that epidemic foci are not panmictic but highly diversified and patchy.

5. Human pathology and specific clinical outcomes in FG

Some ubiquitous infections may present an original marked pulmonary tropism in FG that can be considered coincidental [1]. However, consistently high temperatures and humidity, in addition to deforestation and habitat clearing activities, may favor human airborne inoculation of several environmental or zoonotic pathogens found in FG and elsewhere. This may be a transmission pathway inducing pulmonary symptoms before possibly evolving toward more complex life cycles, intrahost selection, and pathogenic effects in humans. One example is Q fever, a bacterial zoonosis caused by *Coxiella burnetii*, usually contracted by pathogen inhalation of genital secretion emissions by ruminants at calving [13]. Pulmonary involvement accounts for 8-34% of acute Q fever cases in France but greater than 80% in FG; in the FG capital of Cayenne, 24-38% of hospitalized cases for acute community-acquired pneumonia are caused by *C. burnetii* [14]. This particular tropism could be associated with the supposed higher virulence of the MST 117 clone, which is found only in FG and more virulent than European strains.

Leptospirosis is caused by the bacteria of the genus *Leptospira*, usually contracted through mucosal membranes or areas of skin trauma from soil or water contaminated with rodent urine. The usual symptoms are a “dengue-like” syndrome, with fever and diffuse pain, with moderate to more severe forms sometimes being fatal. If pulmonary symptoms are not rare in the old world, they seem particularly frequent in FG [15].

Amazonian toxoplasmosis is an acute interstitial lung disease by *Toxoplasma gondii* infection, observed in immunocompetent patients [16]. It is characterized by severe forms, with pulmonary involvement not yet described in other areas of the world. Atypical and more virulent strains of *T. gondii* are reported in FG, and transmission may occur through the ingestion of undercooked game meat or water contaminated with oocysts excreted by salvage felids.

Although old world hantaviruses cause hemorrhagic fevers with renal syndrome, new world hantaviruses are responsible for hantavirus pulmonary syndrome, associating a febrile hypoxemic respiratory attack with a high fatality rate. Between 2008 and 2022, 11 cases of hantavirus pulmonary syndrome occurred in FG, with four between March and September 2022, attributed to a virus secondarily named Maripa virus and related to Laguna Negra species reported in Amazonia. Hantavirus particles are transmitted by inhalation of dust contaminated with feces and urine of rodents [17].

6. Current health challenges toward health promotion

Initiated in FG for malaria mitigation and HIV care in remote areas and based on community inputs, health mediation and community initiatives have undergone major expansions since the COVID-19 pandemic. The management of COVID-19 successive waves in remote Amerindian villages required activities of local people. Local persons trained quickly as mediators assisted in combating skepticism by native people about disease severity and vaccine safety and efficacy. The deployment of the vaccination campaign, with the known mitigated success, required the strengthening of these new public health approaches to gain management efficiency and public consent [18].

Most infectious diseases in FG are treated with plants, and disciplines, such as ethnobotany and anthropology, can help identify future medicines, contributing to the growing interdisciplinarity science of the region. Potentially useful molecules may be identified in traditional remedies; thus, better integration of local knowledge in research is needed to improve medicinal plant biodiscovery while respecting the Nagoya protocol, genetic resources property, and associated traditional knowledges.

7. Health mitigation and control and the future of vector-borne and zoonotic diseases in the region

FG is in a phase of epidemiological transition, with a decrease in infectious disease burden. Premature deaths (age <65 years) between 2005 and 2015 were mostly related to traumatic causes (37%), followed by cardiocerebrovascular diseases (17%), then infectious diseases (14%, of which 60% related to HIV-AIDS) and perinatal diseases (12%) [19]. Zoonotic and vector-borne diseases disrupt this epidemiological transition.

Chronic diseases, in particular diabetes (9.3%), high blood pressure (17.9%), and obesity (18%), are likely to increase with lifestyle changes, including malnutrition, and act as risk factors for higher morbidity of other diseases. Diabetes does not seem to favor serious infections by arboviruses but could be an important factor for severe *P. falciparum* infections [20], which has now much lower prevalence than *P. vivax* in FG [19]. Diabetes and obesity are also risk factors for several recent emerging respiratory diseases, such as influenza A or COVID-19 severe forms. Health system improvement, with health indicators that are regularly increasing, will be more reactive for the management of new epidemics.

However, there are arguments that vector-borne and zoonotic diseases will increase in FG. Population impoverishment, with 50% living below the poverty line in 2017, leads to deteriorated living conditions and increased population density. The consequences are increased fecal peril, vector-borne diseases, and leptospirosis or hantavirus disease. Migratory movements and travel may lead to increases in novel pathogen importation and spread not currently present in FG, and the presence of competent vectors will facilitate new arboviral epidemics. The risk of zoonotic diseases linked to human encroachment of rainforests remains high, particularly with gold mining activities. This is similar to other heavily impoverished regions of the world.

8. Conclusion

With decades of political stability and significant national and European funding, most national French research and biomedical institutions work collaboratively in FG. The link with main France, as well as international collaborations on the Guiana shield, Amazonia, French Caribbean, and in SA, all provide strong scientific networks that facilitate access to good infrastructure and enhance researcher mobility. This situation results in high-quality scientific and medical activities in a remote tropical region of the world. Combining long-term experience in neotropical taxonomy and biodiversity with anthropological approaches, social sciences, and epidemiology has allowed precise measures of disease drivers and risk factors in vulnerable local human communities. The developments of recent research initiatives on biodiversity-disease relationships promoted inter- and transdisciplinarity and produced original, substantial, and internationally recognized scientific and biomedical contributions to the field of infectious disease.

In the Amazonian region and elsewhere, there will be future hotspots of newly emerging diseases. Although dancing with the ghost of many microbes sleeping in the primary forest, active scientific and biomedical research constitutes a form of exorcism to protect FG and surrounding populations against new emerging threats. Lessons learned from these interdisciplinary activities may serve as examples for other areas of the world facing increasing population densities at the interface of high biodiversity and habitat destruction.

Declarations of competing interest

The authors have no competing interests to declare.

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Ethical approval

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Author contributions

JFG and BdT conceptualized and wrote the first draft of the opinion view paper and specifically wrote sections 1-4 and 8. LE, MD, and MEB substantially and equally contributed to the work in producing specific sections of the manuscript (5-6, 7, and 2-4, respectively), and all authors contributed to the different sections and participated in the final version writing.

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