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Enhancing research integration to improve One Health actions: learning lessons from neglected tropical diseases experiences

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INTRODUCTION: NEGLECTED TROPICAL DISEASES

Neglected tropical diseases (NTDs) represent a group of 20 diseases affecting more than one billion people in 150 countries, mostly in Africa, Asia and the Americas. They are considered as 'markers of stigma and poverty',[1] due to their debilitating consequences, also frequently impacting mental health, and because they mainly affect poor, vulnerable and marginalised people. NTDs cause heavy socioeconomic losses at the level of individuals, families, communities and countries. Despite a massive impact that amounts to billions of dollars per year, only 0.6% of the global healthcare funding is allocated to these diseases,[1] disregarding the negative impact of the COVID-19 pandemic that is still difficult to quantify.

Nevertheless, in the last decade, the consideration of NTDs in global health has evolved and gained momentum. This was heralded by the adoption of the WHO road map for NTDs in 2011, the London Declaration of 2012, the launching of the 2030 Sustainable Development Goals that specifically refer to NTDs, and recently the new 2021–2030 WHO road map on NTDs. These initiatives aimed at drawing stakeholders' attention to diseases that often remain apart from the main health programme streams: 'leave no one behind'. In the francophone world, the Organisation Internationale de la Francophonie wrote a specific resolution on NTDs at the Erevan summit of 2018, and the 'francophone network on NTDs' has just reiterated its strong support to the new WHO 2030 road map for NTDs.[2] In this road map, specific objectives, including scientific research targets, were set for each NTD according to their epidemiological situation: control, elimination as a public health problem, elimination of transmission and/or eradication (box 1).

By definition, NTDs have rarely been prioritised in the research and control actions' agendas in endemic countries. Traditional vertical intervention schemes have initially been used with success for some NTDs, as for example, the prevention or therapy of geohelminthiases through mass drug administration using cheap, stable and safe oral drugs. However, the intrinsic complexity of pathogens' life cycles and the limited resources allocated to NTDs have fostered alternative strategies to the classical vertical approaches. Hence, multidisciplinary research approaches at the fundamental, translational and applied levels progressively bloomed in the field of NTDs by necessity, to improve scientific knowledge at the service of control interventions. We believe that lessons from NTDs may

SUMMARY BOX

- ⇒ Most neglected tropical diseases (NTDs) are intrinsically embedded within the One Health approach: NTD researchers have already been dealing with multidisciplinary and intersectoral work for decades simply because it is essential for understanding and controlling the usually complex transmission of the pathogens causing NTDs.
- ⇒ This long experience has already enrooted the idea of the horizontal integration of research, control, elimination and eradication strategies.
- ⇒ The ongoing epidemiological transitions of most NTDs urges pursuing and amplifying the development of co-constructed multidisciplinary and intersectoral research initiatives for improving control/elimination/eradication processes.
- ⇒ Lessons from NTDs may also be useful for other diseases targeted by ongoing One Health initiatives.

Box 1 Definitions

⇒ **Control**: The control objective aims at reaching a local reduction of the disease prevalence to an acceptable level—this usually requires continuous interventions to maintain this reduction. *Significant efforts in both cognitive and applied research are usually required in parallel for reaching the next elimination step.*

⇒ **Elimination as a public health problem** (ephp), through a 'validation' process: The ephp targets the overall achievement of given measurable goals. When achieved, the process can be validated by WHO, yet an action is still needed to maintain the goal and/or to advance towards elimination of transmission. *Translational research is highly beneficial to this step.*

⇒ **Elimination of transmission** (eot), which requires 'verification': The eot aims at reducing the incidence of an NTD to zero in well-defined areas, with minimal risk of re-introduction. The process is verified by WHO and further actions may be necessary to prevent re-emergence of the disease. *Maintaining a minimum level of applied research is also necessary here.*

⇒ **Eradication**, which needs 'certification': Ultimately, the eradication goal should lead to the permanent reduction to zero transmission of a given pathogen, without risk of re-introduction. This process requires WHO certification.

be useful for other diseases targeted by ongoing One Health initiatives.

IMPACT OF MULTIDISCIPLINARY FUNDAMENTAL RESEARCH ON NTD CONTROL

Combining traditional medical surveillance strategies with scientific research programmes in social science and anthropology, ecology, vector and reservoir host biology, parasite biology and host-pathogen interactions has improved our knowledge and evidenced new challenges. Some of these challenges originate from the discovery of new key fundamental aspects of pathogens' maintenance and/or transmission. For, instance, it has been recently demonstrated that the emergence of animal reservoirs of *Dracunculus medinensis*, particularly in fish-consuming domestic dogs (93% of all Guinea worms detected worldwide in 2020 were in dogs in Chad), has become the major impediment to eradication of this human disease.[3 4] For human African trypanosomiasis, the importance of latent infections in seropositive asymptomatic individuals,[5] the identification of domestic pigs as reservoirs of *Trypanosoma brucei gambiense*[6] and the probable role of skin-dwelling trypanosomes in transmission maintenance[7 8] are active research areas that may be crucial for reaching the elimination goal.[9] Actually, the lack of fundamental scientific knowledge about the natural reservoirs and even the transmission of *Mycobacterium ulcerans*, that still remain elusive in most endemic areas,[10] is also pointing to the crucial need for more fundamental knowledge on NTDs.

IMPACT OF MULTIDISCIPLINARY TRANSLATIONAL RESEARCH

Improving the sustainability of interventions by considering the multiple ecological, biological, and socioanthropological determinants of NTDs and by mobilising multiple actors (communities, leaders, health centres, local authorities, health authorities, etc) in a multidisciplinary way (ie, anthropological studies before sensitisation, environmental studies prior to selecting a vector control strategy, etc) was seen to be key when means were scarce. For example, *Triatoma infestans* (the main vector of *Trypanosoma cruzi* causing Chagas disease) has been efficiently eliminated from large areas of South America through multinational and vertically organised insecticide spraying campaigns.[11] However, these campaigns were not implemented in areas where secondary vectors (often sylvatic) are involved in human dwelling infestation. In these contexts, alternative or additional strategies developed in Southern Mexico and Central America, based on an eco-bio-social approach and participatory research, have shown promising outcomes.[12] The successful results obtained against lymphatic filariases[13 14] and human African trypanosomiasis[15 16] were also due, at least in part, to the use of multiple strategies, based on the integration of research outputs for improving medical surveillance and vector control (with insecticide-treated bed nets and insecticide impregnated screens, respectively) with an important component of participatory research.

NEW CHALLENGES TO SUSTAIN PROGRESS AND ACHIEVE ELIMINATION OF NTDS

The ongoing epidemiological transitions of most NTDs urges pursuing and amplifying the development of co-constructed multidisciplinary and intersectoral One Health initiatives for improving early integration of applied and cognitive research approaches to the NTDs control/elimination/eradication processes.

In this context, some new challenges will emerge from the absence or inefficient translation of scientific data and knowledge into public health recommendations and interventions. For example, dog-transmitted rabies control strategies are the very resources demanding to ensure annual mass revaccination of more than 70% of a country's canine population to maintain sufficient immunity to stop virus transmission. Hence, the results obtained are fragile and can be annihilated by prematurely stopping the vaccination effort.[17 18] Canine vaccination strategies would certainly benefit from developing potent rabies vaccine inducing lifelong immunity in dogs that would shorten and lighten the burden of the mass dog vaccination campaigns, and stepping up oral vaccination schemes[19] as well as better understanding human-dog relationships.[20] At a broader scale, scientists still have to improve tools (diagnostic tests, treatments, vector control tools, etc) and strategies (mathematical modelling, vector control plans, etc) according to the evolution of the epidemiological context and consider cultural, economic, geographical, ecological, climatic and veterinary aspects from a One Health perspective.

Some other new challenges would appear from a decline in interest towards risk of infection when local

communities are not sufficiently sensitised (eg, reluctance of the populations towards chemoprophylaxis), and/or when the authorities are no longer fully committed, especially when the threat significantly declines or disappears (such as in human African trypanosomiasis and onchocerciasis). Improving this would especially require local communities to be permanently sensitised on the risk of transmission and/or that of re-emergence[21] after having implemented socioecological and anthropological studies to better include the communities in the choices of the strategies and for the development of fine-tuned health education and promotion.

CONCLUSION: LESSONS FROM NTDS FOR OTHER ONE HEALTH INITIATIVES

If the concept of a One Health approach is gaining considerable attraction, NTD researchers and workers have already been dealing with multidisciplinary and intersectoral work for decades simply because it is essential for controlling the usually complex transmission of the pathogens causing NTDs.[2] We believe that multidisciplinary One Health approaches have already paved the way towards an integration of sustained research activities serving the control, elimination and eradication processes of NTDs. Lessons from the past, whether negative or positive, and present research programmes on NTDs, especially those that aim at understanding the entire pathogen transmission cycles and at optimising sustainable control interventions, may also light the way for other diseases.[22]

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