

Priority Research themes in the fight Against the COVID-19 with particular reference to Cameroon *

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Abstract

The ongoing SARS CoV-2 pandemic also known as COVID-19 is a highly infectious and deadly disease that has disrupted socio- economic activities and killed over 500 000 people worldwide during the past six months since it first erupted in Wuhan China in December 2019. While intensive efforts are under way in the developed countries to find a vaccine and cure for the disease, Cameroon and other African countries should not fold their hands and wait , but join the search for new remedies including from cures from traditional herbs while rigorously applying barrier and social distancing measures that have proven effective in curbing the spread of the disease. Herein we enumerate a short list of research priorities that are feasible in our milieu and that could improve on diagnostics, treatment and prevention of the disease in the short and medium terms.

Key Words: SARS CoV-2, COVID-19, research, diagnostics, medicinal plants, traditional medicine, pandemic, Cameroon.

Resume

La pandémie en cours du SRAS CoV-2, également connue sous le nom de COVID-19, est une maladie hautement infectieuse et mortelle qui a perturbé les activités socio-économiques et tué plus de 500000 personnes dans le monde au cours des six derniers mois depuis son apparition à Wuhan en Chine en décembre 2019. Alors que des efforts intensifs sont en cours dans les pays développés pour trouver un vaccin et guérir la maladie, le Cameroun et les autres pays africains ne devraient pas croiser les mains et attendre, mais se joindre à la recherche de nouveaux remèdes, y compris à partir de remèdes à base d'herbes traditionnelles, tout en appliquant rigoureusement une barrière et des mesures de distanciation sociale qui se sont révélées efficaces pour enrayer la propagation de la maladie. Nous énumérons ici une courte liste de priorités de recherche réalisables dans notre milieu et susceptibles d'améliorer le diagnostic, le traitement et la prévention de la maladie à court et moyen termes. (Crédit : Google Translator.)

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INTRODUCTION

The Corona Virus Disease (COVID-19) has been making headline news since December 2019 when it first broke out in Wuhan, China. We witnessed with horror how it spread in Europe, then North America, particularly the USA, holding our breaths and wishing that this time around Africa would be spared. This hope was short lived as the African continent soon became affected with new infections and death counts now rapidly rising in many countries. Today the question is how to stop the spread of the disease, treat those who are infected and prevent future infections. These questions are classical in the sense that they apply to all epidemics. They are posed with increasing urgency because SARS CoV-2, the virus that causes COVID-19 is highly infectious, is at least 10 -20 times more lethal than the common cold, and does not respect socio-political and economical boundaries (WHO,2020). The World Health Organization (WHO) The African Academy of Sciences (AAS) have defined urgent research priorities to address the COVID19 pandemic. Recently, a group of researchers in a thought-provoking editorial entitled, *Shining the Light over Africa*, defined urgent actions to be taken against the pandemic (Rosenthal et al; 2020). In this brief report, I focus on those research topics which are relevant to the Cameroonian context and by extension to sub-Saharan Africa. For greater impact I have chosen a question and answer format to introduce the priorities. I then expand on the prerequisites for working with highly infectious pathogens like SARS CoV-2 especially in resource constrained countries like ours. I conclude with perspectives and future directions.

How do we stop the spread of COVID-19?

The answer to the first question is known. Isolate the infected persons from the rest of the population and institute barrier and distancing methods such as have been described by the

WHO and public health agencies around the globe. These strategies are time honored and have been shown to be effective in stopping the spread of recent epidemics and pandemics like Ebola in the DRC and in West Africa and the ongoing COVID-19 in countries like Singapore and South Korea, etc. However, we have witnessed how difficult it has been to implement effective quarantine measures through lockdowns and stay home injunctions without totally destroying the economy and normal social life.

The relevant question is how to adapt effective infection control strategies to our context so that life can continue more or less normally while seeking long-term solutions to address this pandemic. The Academy can provide leadership through its college of social sciences to provide guidance on effective communication and sensitization methods to effectively enforce the quarantine strategies.

How do we design clinical studies to evaluate therapies for COVID-19 adapted to our context?

The question of evaluating effective treatments for the disease is equally high on the agenda. There are currently limited treatment options for COVID-19. An NIH led randomized clinical trial recently showed that the antiviral drug Remdesivir provides modest benefit by reducing the time to recovery by 33% for patients with severe COVID-19 when compared to placebo. Although now available in the USA through an emergency use authorization (EUA) this drug has not been evaluated in the African context and is currently not available to our populations. Supportive care measures for patients with COVID-19 remains the mainstay of treatment for patients in Cameroon, but our healthcare systems have limited capacity to provide a high level of care such as mechanical ventilation and other critical care interventions. Therefore, innovations adapted to the African context are encouraged to provide supportive care

to those who are infected and require hospitalization. In this regard the invention of a cost-effective ventilator in Senegal should be encouraged.

More than 100 drugs are under various stages of clinical development in the developed world, particularly in China, USA and Europe, and it is hoped that once a treatment is found it will eventually get to Africa. This hope, however, should not discourage local efforts to find new treatments for the disease. Even when drugs are discovered in the more developed countries, it takes time and significant financial investment to make these interventions available to the African population. The case of anti-retroviral drugs for HIV reminds us of the precarity of depending entirely on externally sources of medication supply whilst neglecting local possibilities. The medicinal plants of Africa are a rich resource that have historically produced cures for many endemic diseases. The announcement by Bishop Kledar of Cameroon and the President of Madagascar of herbal treatments for COVID-19 are encouraging signs that African traditional medicine should not be neglected in the search for cures for COVID19.

However, two important conditions must be met by all drugs destined for human consumption: their **safety and efficacy must be demonstrated through ethically conducted research studies**. This last requirement has not been formalized in Cameroon, where traditional healers produce and distribute their preparations without licensing or registration. **The Academy can provide guidance on the testing of traditional medicine preparations for the treatment of fevers for possible activity against corona viruses**. It should be pointed out that plants are rich sources of anti-viral agents, some of them falling in the chemical categories

of essential oils that might be of generated in herbal steam- bath treatment of fevers.

Several projects can be initiated in the broad **category of drug development**. This is, however, a long and expensive process from discovery, pre- clinical studies, clinical trials, registration, manufacturing and distribution to pharmaco-vigilance. The process is well codified and regulated in countries around the world, but will be challenging to establish in the timeframe needed to address the pressing outbreak of COVID-19 in Cameroon.

For traditional medicine preparations the process may be simplified, without compromising safety and efficacy (WHO,2000). **This then gives an opening for the Academy to develop projects aimed at testing and validating traditional medicine preparations following the scientific method. The Academy may also develop projects aimed at validating antivirals isolated from plants, first in vitro, and subsequently in animal models thus following the classical pathway for drug development.** (Reichling et al; Forsch Komplementmed, 16(2):79-90;2009) There is currently a lot of concern on social media that Africans will be targeted as “guinea pigs” for drug and vaccine development. International collaboration is crucial in the fight against the COVID19 and African countries cannot *apriori* exclude themselves from participating in the research for solutions. What needs to be done is to ensure that the same ethical and safety standards are respected for research in evaluating new drugs and vaccines. For this to happen African countries need to build expertise in all aspects of drug development including the ability to verify on a case by case basis all medications and vaccines. We already have such a structure in many African countries including Cameroon, but these need to be strengthened. **The Academy can take the lead in strengthening through training**

and monitoring our drug and vaccine experimentation and registration platforms.

4. How can COVID19 be prevented?

Methods for disease prevention are many and varied depending upon the particular ailment, its causes, and means of transmission. For transmissible diseases and some forms of cancer **vaccines are a major and particularly effective means of prevention.** With regards to COVID-19 more than a 100 vaccine trials are ongoing, with the expectation that a vaccine could become available in 12-18 months. Vaccine development is similar to drug development in many aspects though even more rigorous than drug development in some respects. Though we can be cautiously optimistic in our hope for an effective vaccine, SARS-COV-2 is a virus that is newly introduced into the human species and our understanding of the pathogen and the disease need to improve before a vaccine can be developed. Of note MERS-CoV and SARS-CoV-1 are similar to SARS-CoV2 and have been around much longer and we still do not have effective vaccines for these.

Many of the vaccine candidates in clinical trials are based on the ‘golden bullet’ principle whereby the vaccine is designed to block a single target—a kind of heal of Achilles—thereby neutralizing the pathogen. Such univariate vaccines work best when the target does not mutate frequently, and where the function to be neutralized or blocked is not by-passed by other mechanisms. Without digressing into the theories of vaccination, let me say that we have challenged the golden bullet or univariate target approach at least in the case of *Plasmodium falciparum* malaria, where we have used a multivariate approach to develop a malaria vaccine candidate that works well in mice, but remains to be tested in humans (Titanji et al, 2017 & 2009; Dinga et al, 2018).

Vaccine development therefore offers another opportunity for the Academy to intervene with projects, including:

- **the investigation of acquired immunity to SARS-CoV-2 in our milieu;**
- **determining whether the antibodies developed are neutralizing and therefore protective;**
- **designing and testing multivariate vaccines, at least in vitro, before moving on to the other steps in vaccine development pipeline.**

What are the prerequisites for working with highly infectious agents like SARS CoV-2, the causative agent of COVID?

The corona virus is a very highly infectious pathogen. Specialized training and specialized laboratories are required to work with this virus. At least a Level-3 containment laboratory is required to work with the intact virus whereas growing the virus in cell culture requires Level-4 containment. To my knowledge the most sophisticated laboratories in Cameroon are Level-2 containment laboratories. The Biotechnology law of Cameroon makes mention of these levels of containment and special authorizations are required to create level-3 and Level-4 laboratories. **The Academy can provide advice and training in collaboration with the Ministry of Research and Innovation on the setting up, regulation, and functioning of Levels 3 & 4 Containment laboratories.** Appropriate infrastructure is required to carry out research safely on COVID-19 and other infectious pathogens. In the short term I recommend that the Biotechnology Center in Nkolbisson Yaoundé and the Biotechnology Unit at the University of Buea be strengthened with Level-3 laboratories since they have both the space and the expertise for work with infectious organisms.

6. Urgent themes of Research.

Considering what has been stated above I propose that the Academy includes the following eight themes among its priorities for fighting COVID-19.

6.1 Characterization of the virus (SARS CoV-2) the causative agent of COVID19. It is

important to isolate and sequence the genomes of the COVID 19 circulating in our milieu. This can be done within a national or international collaborative effort. Access to reliable genomic data is indispensable for development of diagnostics, therapeutics and vaccines.

6.2 Diagnostics. New rapid tests that can be performed in resource poor environments at affordable costs are needed.

6.3 New drugs: Our Focus should include working with plant derived medicines since plants have proven to be reliable source of new drugs.

6.4 Vaccines and vaccination: A better understanding of the immune responses to SARS CoV-2 in our milieu is necessary for both evaluation of new vaccines, and design of immunotherapies.

6.5 Epidemiology. An understanding of the spread of the disease, its transmission modes, and its disaggregated prevalence in the population important for rational control strategies.

6.6 Mathematical modeling tools should be developed/adapted to enable the follow up and prediction of disease trends in a bid to better deploy control measures.

6.7 Human behavior and response to the pandemic. Knowledge attitudes and Practices (KAP) studies should be undertaken in our communities about the COVID-19 its spread and management. This topic is being addressed by the College of Social Sciences to which the reader is referred.

6.8 Capacity building at the level of infrastructure and technical competence is indispensable for achieving themes 1-7 above.

7. Conclusions

It should be emphasized that even if new drugs and vaccines are approved within the time limit predicted, it will take time to reach end users in Africa. In the meantime, the infection control strategies have proven their efficacy in controlling the spread of infectious disease pathogens, and as such, should be rigorously applied.

- An earlier version of this review was submitted to the Cameroon Academy of Sciences Task Force of COVID-19 Statement.

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