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Commentary

Developing and financing neglected disease vaccines in our new era of “blue marble health” and the anthropocene epoch

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A B S T R A C T

New findings of widespread neglected diseases among the poor living in wealthy group of 20 (G20) economies and the concept of “blue marble health” offer innovative mechanisms for financing urgently new vaccines, especially for vector-borne neglected tropical diseases (NTDs). This approach could complement or parallel a recently suggested global vaccine development fund for pandemic threats.

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1. Introduction: Tropical and infectious disease “Whack-a-Mole”

The “decade of global health” that was launched with the 2000 Millennium Development Goals (MDGs) ignited a series of overseas development assistance (ODA) initiatives for poverty-related diseases in Sub-Saharan African and other resource-poor nations [1]. Recent assessments through the Global Burden of Disease Study now show that ODA largely worked, especially through major health initiatives to address HIV/AIDS, tuberculosis, malaria, and NTDs (e.g., PEPFAR, The Global Fund, and the USAID NTD Program) and the vaccine-preventable killer diseases of childhood (e.g., GAVI), with significant reductions in the prevalence and incidence of these conditions [2–5]. For several of these diseases it is now even possible to consider elimination or even eradication strategies [6].

Countering some of these successes has been the recent and dramatic emergence of new infections, such as zoonotic diseases from bats (e.g., Ebola and Nipah virus infections and coronavirus [CoV] infections), rats (e.g., Lassa fever), birds and domestic animals (e.g., influenza strains with pandemic potential and Rift Valley fever); and key vector-borne NTDs transmitted by arthropods (e.g., leishmaniasis, Chagas disease, dengue fever, chikungunya, and Zika virus infection) and snails (e.g., schistosomiasis and food-borne trematodiases) [7]. Shown in Table 1 is the global health impact of some of these 21st century emerging and neglected diseases. They include large epidemics of Ebola virus infection, SARS and MERS CoV, and H1N1 influenza, which since 2009 have killed almost 300,000 people [8–11], and the 17 NTDs responsible for almost 150,000 deaths but also 25 million disability adjusted life years due to the chronic and disabling features of most of the NTDs [1–4].

Under this scenario, we are watching unfold a global version of “whack-a-mole”, referring to a type of futile arcade game. Thus, since 2000 we have experienced large reductions of some high disease burden infections through effective programs of ODA, only to see the emergence of a new group of diseases, mostly zoonotic infections with pandemic potential and vector-borne NTDs (Fig 1).

The rise since 2009 of serious zoonotic pandemic threats and vector-borne NTDs has become a critical global public health issue. It has also becoming apparent that these infections are adversely affecting economic development, together with a new stark reality that they may threaten global security.

2. The new drivers: anthropocene forces and blue marble health

The uptick of major zoonotic pandemic infections and vector-borne NTDs is not by coincidence. Major drivers include both critical environmental and social forces. Among the former they include climate change and deforestation, while the latter include urbanization and human migrations, which in some cases is linked to refugee populations fleeing conflict zones of the Middle East and East Africa [12]. Such forces might partly explain for example the recent occurrence of widespread Ebola in West Africa, cutaneous leishmaniasis in the Middle East, visceral leishmaniasis in East Africa, and chikungunya and Zika virus infections in the Americas.

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There is a lot of promising science and technology being pursued at Table 1 and highlighted above. They include new vaccines for CoVs, of leishmaniasis, Chagas disease, arbovirus infections, and snail-borne NTDs, including both major forms of leishmaniasis, Chagas disease, arbovirus infections, and snail-borne NTDs including African sleeping sickness, the poor living in Saudi Arabia, and Australia fostering neglected disease burdens in selected areas [1]. Still another critical factor is poverty. It was recently noted that of 20 (G20) wealthy economies, together with Nigeria whose economy exceeds the bottom three or four G20 countries [1]. Based on data from both the WHO or the Global Burden of Disease Study 2013, the G20 nations and Nigeria account for more than one-half of the disability-adjusted life years from the NTDs and most of the cases of diseases such as Chagas disease, dengue, helminth infections, leishmaniasis, leprosy, and even tuberculosis, among others [14]. Certainly the poor living in large middle-income countries such as Brazil, China, India, and Indonesia account for much of this NTD burden, but in addition there are pockets of intense poverty in the Southern United States, Europe, Saudi Arabia, and Australia fostering neglected disease burdens in selected areas [1]. Thus, with the exception of Ebola virus infection and a few other NTDs including African sleeping sickness, the poor living in G20 countries represent the next wave in neglected diseases highlighted above [1,7].

3. The need for vaccines

We urgently need new vaccines for many of the diseases in Table 1 and highlighted above. They include new vaccines for CoVs, Ebola and Nipah virus infections, Lassa fever, Rift Valley fever, and pandemic and zoonotic influenza viruses. But also critically needed are vaccines for the vector-borne NTDs, including both major forms of leishmaniasis, Chagas disease, arbovirus infections, and snail-borne NTDs, including African sleeping sickness, the poor living in G20 countries represent the next wave in neglected diseases highlighted above [1,7].

4. Financing new vaccines: blue marble health as an alternative to new global funds

Partly in response to the inability to have in hand Ebola and CoV vaccines, in 2015 Plotkin, Mahmoud, and Farrar proposed establishing a global vaccine development fund to pay for the expensive elements of downstream development including phase 3 pivotal clinical trials and industrial scale manufacture [16]. Such a fund they argue, beginning at the $2 billion level, would be essential to incentivize multinational pharmaceutical companies to embark on neglected and emerging vaccine development, while simultaneously ensuring a market for product sales [16]. The emphasis of such a fund would be to support emerging pandemic threats as well as some neglected disease pathogens [16]. Out of this proposal emerged a new initiative, known as the Coalition for Epidemic Preparedness Innovations (CEPI), an initiative linked to WHO that would focus on gaps in product development resulting from market failure. Clearly, there is need for economic and political innovation at a level that is commensurate with the scientific innovation needed to develop vaccines. Both CEPI and the Plotkin et al. proposal represent one approach to this problem, if it can overcome the multiple complexities associated with the launch and administration of a fund. Such complexities include the fact that the US Government is already the largest contributor to neglected disease R&D according to the G-FINDER Report, together with previous findings that it remains highly uncertain the US Government could tapped again for an additional research and development funds [17]. Also of concern are the governance and distribution mechanisms of a global vaccine development fund, including how the list of vaccines is prioritized, and whether the scientists and administrators from donor countries represent the next wave in neglected diseases high-lighted above [1,7].

Table 1

| Public health impact | Neglected tropical diseases in 2013 [2-4] | H1N1 2009–10 Influenza epidemic [8,9] | Ebola in West Africa West African 2014–15 [10] | SARS and MERS CoV in 2012–6 [11] |
|----------------------|-------------------------------------------|------------------------------------------|-----------------------------------------------|---------------------------------|
| Prevalent and incident cases | >2 billion | 24% of the population in 19 countries evaluated | 28,652 (total cases, suspected, probable, and confirmed) | 1841 |
| Deaths | 142,400 | 201,200 respiratory deaths | 11,325 | 652 |
| Disability-adjusted life years | 25.2 million disability-adjusted life years (DALYs) | 284,500 total deaths | 9.7 million years of life lost (YLLs) | Not determined |
| | | | | |

Fig. 1. 21st century infectious diseases “whack-a-mole”.

[7,12], while in Southern Europe vector-borne NTDs such as dengue, chikungunya, West Nile virus infections and even schistosomiasis have emerged [12,13]. Many of these external forces were recently ascribed to the ‘Anthropocene’, referring to the origins first geological epoch associated with human-driven activity [12].

While there is a lot of promising science and technology being pursued at the preclinical level for developing such vaccines, it is increasingly evident that our business model for bridging several “valleys of death” in product development, including the ones between discovery and phase 1 and then between phase 2 and phase 3, respectively, is broken. As a result we have almost no pipeline for the new 21st century pandemic and neglected disease threats.

A good example of our broken business model can be illustrated for Ebola virus infection, for which the basic scientific discoveries for developing new Ebola vaccines had been published by 2003, but then the technology languished for a decade [15]. Ultimately true vaccine product development ensued only after the US Government put up more than $100 million to incentivize multinational pharmaceutical companies to translate those efforts into vaccines for clinical testing [15]. By the time the vaccine clinical testing began in West Africa, Ebola had mostly disappeared but only after 11,000 people lost their lives [15]. A similar situation occurred for MERS CoV in which hundreds died in outbreaks on the Arabian Peninsula and South Korea due to the absence of a safe and effective vaccine.

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countries would be willing to cede control of funds to an international entity in Geneva or elsewhere. As an alternative or complement to a global vaccine fund, I proposed building on the concept of blue marble health, which recognizes that most of the world’s neglected and emerging infections actually occur among the poor living in G20 countries [1]. Specifically, national funds established in each of the G20 nations could support indigenous scientists and research institutes and incentivize them to partner with international industrial manufacturers and the half-dozen vaccine non-profit product development partnerships (PDPs), which are specifically focused on NTD and other neglected disease vaccines [1,6]. Currently the Japanese Government’s Global Health Innovation Technology (GHIT) Fund is one recent example of a national fund that simultaneously supports PDPs and Japanese academic, research, and industrial institutes. In this blue marble health model each national fund would similarly promote indigenous scientists and manufacturers, while simultaneously providing support for new neglected disease vaccines [1].

The possibility remains that parallel financial mechanisms – (1) a global vaccine development fund and (2) national funds in the blue marble health nations – could co-exist and work together (Fig. 2). The former would focus on emergency zoonotic pandemic threats such as Ebola, Nipah, MERS Cov, Lassa Fever influenza, and even some arbovirus infections such as Zika and West Nile Virus infections, while the latter would emphasize vaccines for chronic and debilitating vector-borne NTDs such as cutaneous and visceral leishmaniasis, Chagas disease, schistosomiasis, onchocerciasis, and food-borne trematodiasis, as well as some of the arbovirus infections. Both mechanisms are essential in order to prevent the unacceptable situation in which the sole development of vaccines is focused on preventing pandemic threats of concern to populations living in North America and Europe.

5. Concluding remarks

As we soon enter the third decade of the 21st century it is apparent that modern Anthropocene forces together with poverty are promoting the dramatic rise of zoonotic pandemic threats, as well as vector borne NTDs. The concept of blue marble health finds that many of these diseases are now occurring mostly among the poor living in G20 economies. Beyond the scientific innovation, we will require extensive reform on how we finance next generation vaccines that would serve as countermeasures for such health, economic, and global security threats [18]. Dual funding mechanisms that address both pandemic threats and vector-borne NTDs may help to address this critical gap.

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