The Challenge of Developing Therapeutics for Emerging Infections

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The global impact of SARS-Cov-2 infections reminds us of the need to continually address the importance of emerging infections from both a public health and a management perspective. The current public health injunctions of social distancing, facial masks, hand washing and decreased population density dates back to the influenza pandemic of 1918. Then, as now, the implementation of these recommendations has been fraught with failure of adoption by many segments of our society. In the absence of the implementation of such recommendations, vaccines and therapeutics become of the utmost importance. Ideally, prevention of disease by active vaccination is the optimal approach; yet, it will likely be early 2021 before the United States Food and Drug Administration licenses any candidates that are currently in clinical trials, if benefit is proven in controlled studies. Thus, therapeutics become a 'stop-gap' approach, albeit a necessary approach, until vaccines become available.

The development of therapeutics for emerging infections poses a unique challenge for the pharmaceutical industry. In the absence of financial incentives, there has been a uniform lack of enthusiasm and commitment to developing drugs for emerging infections. Only with the impact of COVID-19 disease being fully appreciated has there been an effort to push forward new medications as well as examine the potential of 'repurposed drugs.' Nevertheless, one medication has demonstrated activity as an antiviral of clinical benefit – namely remdesivir.

Remdesivir was originally developed as a potential therapy for respiratory syncytial virus infections, a common cause of lower respiratory tract infection in young children. In vitro screens performed against numerous other viruses, including Ebola, Marburg, and SARS, all indicated potential antiviral activity. With the outbreak of Ebola in West Africa, this medication was provided to the US government for controlled studies; however, efficacy was not proven.

Fast forward to 2020, through studies funded by the NIH, remdesivir was shown to be active in cell culture and animal models against SARS-Cov-2. With such data, the sponsoring pharmaceutical company pushed the medication forward into controlled clinical trials wherein limited efficacy was established. Further treatment advances are under evaluation.

The success of the remdesivir story illustrates several important lessons. First, the rapid advance of the drug into humans represented a 'public-private partnership,' involving academic institutions, the government and the NIH. No one group of this triad could have done it alone. Second, controlled clinical trials sponsored by the NIH were mandatory, as illustrated by the hydroxychloroquine debacle. Third, pandemic infections will surely recur. As medical scientists, we must be attuned to potential for another influenza pandemic. Similarly, with climate change, mosquito vectors will be redistributed in North America to cause dengue, chikungunya, and a

variety of encephalitis, among others. Certainly, investment in the technology of improved vaccines and therapies is of the utmost of importance.