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Global health inequity: scientific challenges remain but can be solved

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Review Series Introduction

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Global health inequity: scientific challenges remain but can be solved

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Introduction

The dawn of the 21st century was heralded by one of the most important advances in biomedical research, the sequencing of the human genome. Fueled by this and many other advances in science and technology, the prospects for a long and healthy life have never been better for individuals living in the developed countries of the world. Indeed, today the average life expectancy for people living in the developed world borders on 80 years (1), as compared with fewer than 50 years at the beginning of the 20th century (2). This is, in part, because we can now truly contemplate an understanding of most of the human diseases commonly suffered by individuals in the developed world at the cellular and molecular levels. In the past 30 years, this understanding has translated to the development and registration by the pharmaceutical industry of 1,500 new medicines for the treatment of these diseases (3). Such medicines have virtually transformed the practice of medicine. For example, statins have greatly reduced the risk of dying from coronary artery disease, and proton pump inhibitors and antibiotics have eliminated peptic ulcers as a health threat.

In the face of all this good news, it is almost surreal to contemplate the plight of billions of people living in the developing world. Although overall life expectancy in developing countries has risen from approximately 40 years in 1950 to 65 years today (1), life expectancy in southern Africa has decreased in the past 15 years, from 62 years in the early 1990s to under 50 years today (1). In addition, although the chances that a child will survive to age 5 have nearly doubled since 1970 (4), approximately 9.7 million children under 5 years of age — including four million under 1 month of age — die each year, mostly from preventable or treatable diseases (5). Each year five million people die in the developing world from just three diseases — tuberculosis (TB) (6), HIV/AIDS (7), and malaria (8). In contrast to the 1,500 medicines for diseases commonly suffered by individuals in the developed world, only 21 new medicines have been developed by the pharmaceutical industry for health problems mainly encountered in the developing world (3). In a recent analysis of the mortality risk faced by the world in the event of an avian flu pandemic, it is estimated that there would be as many as 62 million deaths, with greater than 95% of those projected to be endured by the poorest nations of the world (9).

How have we allowed such a great inequity to exist between rich and poor nations of the world? The biomedical research community must assume some ownership for redressing this disparity, for, after all, we hold the tools that led to the advances in quality of life in the developed world. Bill Gates proposed in his 2007 commencement address for Harvard University that "humanity's greatest advances are not in its discoveries but in how those discoveries are applied to reduce inequity." It is in this spirit that this Review Series on global health is presented.

Diseases of the developing world

In this Review Series are descriptions of the state of the science of the health conditions that account for the greatest loss of disability-adjusted life years in the developing world. As highlighted in the articles by Cohen et al., Young et al., and Greenwood et al. (10–12), substantial scientific challenges still exist in creating effective diagnostics, drugs, vaccines, and other prevention tools for the diseases of HIV/AIDS, TB, and malaria, respectively. Of the approximately five million deaths caused by these three diseases each year, 99% are in the developing world. Scientific gaps range from a lack of basic understanding of the biology of the pathogen (e.g., the latent infection established by the TB-causing pathogen) to the variation in pathology (e.g., benign versus deadly forms of malaria) to the response of the host immune system to the pathogen (e.g., the nature of long-term non-progression to AIDS in certain individuals infected with HIV-1). This knowledge is key to the creation of better tools, such as biomarkers of protection and better animal models, to support the development of useful health interventions.

The Reviews by Petri Jr. et al. and Scott et al. (13, 14) highlight how little we know about the causes of the diarrhea and pneumonia that result in the death of approximately four million children each year. Currently the full range of pathogens that contribute to these conditions, as well as the extent to which they contribute, is unclear. The role of host genetics in susceptibility to and the underlying role of malnutrition, in particular micronutrient deficiencies, in these conditions is also unclear. Our knowledge limits the ability to develop the best affordable drugs and vaccines as well as the accurate diagnostics to inform their use.

As outlined by Stuart et al. and Hotez et al. (15, 16), in the case of the neglected diseases caused by kinetoplastids and helminths,

Nonstandard abbreviations used: TB, tuberculosis.

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respectively, even less attention has been paid to the fundamental science despite the enormous burden of infection. As noted by Hotez et al. (16), approximately one-third of the almost three billion people that live on less than $2 per day in developing regions of sub-Saharan Africa, Asia, and the Americas are infected with one or more helminths. Similarly, Stuart et al. (15) note that half a billion people, primarily in tropical and subtropical areas of the world, are at risk for diseases caused by kinetoplastids, and it is estimated that more than 20 million individuals are infected with these pathogens, resulting in extensive suffering and more than 100,000 deaths per year. Despite the associated burden of morbidity and mortality, the basic information on genomes has only relatively recently become available for the kinetoplastids and is largely uncharted, and it is only just emerging for the helminths. Full exploration of the genomes and the underlying molecular basis of pathology has yet to happen. In addition, there is a substantial gap in the understanding of the interplay between these pathogens and the immune system.

Underlying the burden of disease in the poorest populations of the world is the burden of malnutrition, as discussed by Prentice et al. (17). Malnutrition, in particular micronutrient deficiencies, claims a direct burden of morbidity and mortality, but perhaps contributes with greatest impact to the effects of infectious diseases in children under 5 years of age and to the lifelong irreversible stunting in children malnourished before the age of 2. Research is needed to understand the interplay among malnutrition, the state of the immune system, the pathobiology of the pathogen, and the microbiome of the host. Little is understood about the relationships between these complex systems. Focus on these relationships is most needed in the poorest populations of the world, where malnutrition and ongoing infections are chronic. Studies have demonstrated at the population level varying impacts, both positive and negative, of micronutrient supplementation in the context of infection. The biological and molecular basis of these outcomes has yet to be examined in detail.

In the final article in the Review Series, Aitken et al. (18) highlight that potentially 700,000 maternal deaths resulting from unintended pregnancies could be averted if effective contraceptives were broadly available to women in the developing world. The market incentives for creating new contraceptives for these populations is limited given the range of effective contraceptives that work for the developed world; these contraceptives are sometimes not available to the women in need in the developing world, but in many cases are not appropriate for the targeted population (e.g., adolescent girls) or in the context of the social or cultural setting (e.g., an increased need for covert female contraceptives). To create the range of needed contraceptives requires expanding our exploration of the biologic leads that already have been identified and searching for new leads (such as non-barrier, non-hormonal contraceptives) that can safely support the choices of select populations such as adolescent girls. The tools of high throughput biology and genome analysis are likely to play a key role in revealing needed new approaches.

Future directions

Reducing the health inequity to which many of the poorest people of the world are exposed depends on the skills and commitment of the few talented scientists who can tease apart the remaining unknowns of these critical health problems to find the path to effective and appropriate health solutions. We hope that scientists will study the articles in this Review Series and find opportunities to apply their knowledge and expertise to the challenges that these problems present to the billions of poor people in the world so that they too may benefit from it.

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