Targeting Pulmonary Vascular Disease To Improve Global Health

Pulmonary Vascular Disease: The Global Perspective

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Although there is widespread agreement on the need to address the glaring health-care disparities that exist in underserved countries in the world, there has not been an accepted approach to address these disparities that has proven to be successful. The international agenda has chosen to focus on maternal/fetal needs and infectious disease-based illnesses. However, cardiovascular diseases remain the leading cause of morbidity and mortality in the developing world. Since the adoption of the United Nations Millennium Development Goals in 2000, progress in raising the health-care standard in poorer countries has been slow. As an alternative approach, a global health-care strategy that targets cardiovascular disease may prove successful. The Pulmonary Vascular Research Institute has adopted a ground-up strategy by enlisting physicians from developing countries as partners in a virtual heart and lung institute. Realizing that pulmonary vascular disease is often a manifestation of advanced cardiovascular disease, we need to explore those illnesses that are prevalent in poorer countries where pulmonary hypertension is a resulting problem. Through education, capacity building, research, and clinical trials it should be possible to establish a successful paradigm that addresses the needs of patients and physicians while simultaneously expanding the knowledge and expertise about pulmonary vascular diseases worldwide. Eventually regional centers of excellence will be established worldwide that will serve the populace of both the developing and developed worlds combined. CHEST 2010; 137(6)(Suppl):1S–5S

Abbreviations: CVD = cardiovascular diseases; MDGs = Millennium Development Goals; PVD = pulmonary vascular disease

The current global perspective on health-care disparities

At the turn of the new millennium, leaders of the developed world joined together to acknowledge the wide disparities in the world related to poverty and established the Millennium Development Goals (MDGs). In adopting the Millennium Declaration in 2000, the international community pledged to “spare no effort to free our fellow men, women and children from the abject and dehumanizing conditions of extreme poverty.” The MDGs are eight international development goals that 189 United Nations member states and 23 international organizations agreed to achieve by the year 2015 (Table 1).

Only three of the goals are related to health care, and they focus on child mortality, maternal health, and infectious diseases. Halfway through the MDG timeline, few milestones have been met. For example, a child born in a developing country is still > 13
times more likely to die within the first 5 years of life than a child born in an industrialized country. Trends in reducing under-five mortality remain barely above zero.

Although the MDGs are noble in and of themselves, they do not adequately address the scope of healthcare disparities in the developing world, particularly those related to chronic, noncommunicable diseases of high burden. For these reasons, the medical and global health community needs to address a wider spectrum of medical conditions if tangible changes are to be realized in underserved populations around the world.

**The Prominence of Cardiovascular Diseases as a Cause of Worldwide Morbidity and Mortality**

A review of global health-care issues reveals that chronic diseases account for six of every 10 deaths, 80% of which occur in low- and middle-income countries. Cardiovascular disease (CVD) is the leading cause of death globally, with an estimated 17 million annual deaths, representing roughly 30% of deaths globally. In contrast, the infectious diseases included in the MDGs caused (in 2005) 2.8 million deaths from HIV/AIDS, 1.6 million from TB, and 0.8 million from malaria. Thus, CVD causes more than three times more deaths than these infectious diseases combined. It is, therefore, crucial that health inequity related to CVD be included and supported more prominently in the global development agenda. Despite the epidemiologic and economic data suggesting that CVD imposes large health and economic burdens in low- and middle-income countries, the annual budgets of large development agencies, including the World Health Organization, are allocated to chronic diseases. CVD deaths are spread evenly among the developed and developing world; this is not a disease specific to wealthy nations. But CVD death rates in middle-aged people are considerably higher in low- and middle-income countries than in wealthy countries. These burdens also have a reciprocal relationship with poverty, because poverty contributes to CVD, and CVD contributes to poverty.

**Table 1—The United Nations Millennium Development Goals**

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<th>Goal</th>
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<tr>
<td>Eradicate extreme poverty and hunger</td>
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<td>Achieve universal primary education</td>
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<tr>
<td>Promote gender equality and empower women</td>
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<tr>
<td>Reduce child mortality</td>
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<tr>
<td>Improve maternal health</td>
</tr>
<tr>
<td>Combat HIV/AIDS, malaria, and other diseases</td>
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<tr>
<td>Ensure environmental sustainability</td>
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<td>Develop global partnerships for development</td>
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Of the world’s population, 80% of all CVD deaths occur in countries with a per capita income in 2001 of <US $9,000 per year. Almost half of CVD deaths occur among people <70 years of age. As we take a closer look at the impact of CVD on underserved populations, it becomes obvious that remarkable gains could be realized by reducing the CVD burden. Whereas targeting infectious diseases has appeal as a more defined goal, with the expectation that as an infectious agent is eradicated the gains will be readily noticeable, targeting CVD requires patience, as the effects of treatments may not be felt for years to decades.

In 2000, CVD became the leading cause of death in the developing world, as it had been in the developed world since the mid-1900s. Yet the progress that has been made in reducing morbidity due to cardiovascular diseases in the West has not spread globally. Hypertension, for which there are abundant drug treatments, goes undetected because of a fundamental lack of education and basic health-care systems addressing preventive health screening. Coronary artery disease thrives in part because cigarettes are marketed to developing countries where pollution and poor nutrition are additive factors. Infectious diseases that cause CVD, such as schistosomiasis and Chagas disease, remain endemic in many areas of the world. And perhaps most regrettable is the wide prevalence of congenital heart disease.

**CVD in Children as a Cause of Worldwide Morbidity and Mortality**

There is a natural inclination for us to focus on health care for our children. They are the Nobel laureates of the future. Fortunately, there is increasing realization that the lack of facilities for sustainable pediatric cardiac services in the developing world results in a massive number of preventable deaths and suffering. It is estimated that 15 million children die or are disabled annually by potentially treatable or preventable cardiac diseases. Ignored for a long time, this issue is starting to be a cause of major concern to individuals, governments, and, most importantly, cardiovascular specialists who can appreciate the gravity of the problem and that the current situation is unacceptable. However, there remain several countries with populations between 15 and 70 million people without a single pediatric cardiac center.

The pediatric population constitutes a larger proportion of the community in developing countries, where it is common for >40% of the population to be <18 years old. Children in developing countries have a significantly higher incidence and prevalence of serious cardiac diseases, and congenital heart
disease commonly goes undetected and untreated.\textsuperscript{16} Rheumatic fever remains a significant risk in pediatric populations, producing acute and chronic valvular heart disease.\textsuperscript{17} Rheumatic heart disease, which is practically unheard of in the United States, remains a major cause of valvular heart disease in the developing world\textsuperscript{17-19} where it mostly affects children, especially where poverty is widespread. This would be equivalent to the third leading cause of death in the United States.\textsuperscript{20} In addition, many of these children develop more rapid deterioration in their clinical condition as a result of accelerated forms of secondary changes in the heart and other organs, such as PVD. Pulmonary hypertension, a consequence of serious cardiac disease in children, is devastating\textsuperscript{21} and is a major cause of mortality in cardiac disease overall. It has been estimated that 8% of those with congenital heart disease will develop pulmonary hypertension, as well as as many as 70% of those with rheumatic heart disease.\textsuperscript{22} It represents one of the most obvious unmet medical needs in the world.

### Confronting the Unrecognized Importance of PVD in the Developing World

When approaching the challenges of worldwide health problems, one would anticipate that a small change in a disease affecting a large number of people will have a greater impact than a large change that affects a small number of people. The two are not mutually exclusive. In addition, PVD is hardly an illness that affects a small number of people. Between congenital heart disease, rheumatic heart disease, and schistosomiasis, PVD may result in preventable mortality in more children than all other noncommunicable diseases combined (Table 2).\textsuperscript{23}

It is appreciated that PVD is a challenging, difficult disease to diagnose, and there are wide variations in the treatment approach even in the developed world.\textsuperscript{24} Consequently, physicians are very receptive to learning more about the proper diagnosis and treatment of PVD. Educational efforts to increase awareness about the worldwide epidemiology of PVD are essential. There is remarkably little recognition of the prevalence of PVD in people affected with schistosomiasis, rheumatic heart disease, or congenital heart disease by primary care physicians.\textsuperscript{25} This will require education at the primary care level for a physician or nurse to be able to recognize a person with PVD. The most common symptom, breathlessness, is too nonspecific to allow early detection.\textsuperscript{25} Making the diagnosis with existing technology, such as echocardiography, is too expensive and requires technical expertise and medical specialty expertise.\textsuperscript{26} One potential project might be to create a simple, inexpensive probe that can be placed on the chest at the time of a routine health visit to indicate with a yes/no response whether the patient might have elevated pulmonary artery pressure.

Regional centers of excellence in PVD need to be established in developing countries. Because PVD does not discriminate on the basis of wealth, centers can be established that will serve those who can afford health care and those who cannot. High-volume centers increase the level of expertise and, through economies of scale, reduce the costs of care.\textsuperscript{27} Recognized centers of excellence in PVD can offer opportunities for clinical training at their institutions to interested physicians from underserved areas. Additionally, symposia jointly sponsored by established academic groups along with local medical societies around the world will help increase the awareness and the understanding of the complexity of the issues.\textsuperscript{28} Journals that offer multilingual translations will also help engage physicians in the developing world. The establishment of comprehensive workshops that will incorporate lectures, interactive case presentation, and hands-on experiences with available technologies for physicians, nurses, and other health-care professionals are needed. Ultimately it would be desirable to create distance-learning modules which, when satisfactorily completed, would lead to certification that will harmonize the level of knowledge of physicians around the world.\textsuperscript{29}

Concomitantly with educational efforts focusing on the diagnosis and treatment of PVD, we need to educate governments, health ministries, and grass-root physician groups about the prevalence of the disease. The creation of a global database that can combine existing PVD databases from large centers to serve as a comparator for databases that will be created in the various underserved regions is critical. Knowledge about the impact of PVD on the health of local populations will be essential in order to make a case for governmental and nongovernmental organization support.\textsuperscript{30} There are also indirect benefits, such as helping improve locally relevant standards of care and creating an infrastructure building for clinical research. Screening algorithms will need to

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**Table 2—Causes of Pulmonary Vascular Diseases With a Large Potential Burden of Morbidity and Mortality in the Developing World**

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<tr>
<td>Congenital heart disease</td>
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<td>High-altitude pulmonary hypertension</td>
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<td>Schistosomiasis</td>
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<tr>
<td>HIV</td>
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<td>Sickle cell anemia</td>
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<td>Rheumatic heart disease</td>
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<tr>
<td>Hypertensive heart disease</td>
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<tr>
<td>Coronary heart disease</td>
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<tr>
<td>Chagas disease</td>
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<td>Lung disease related to smoking and pollution</td>
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be used in high-volume health clinics that encounter patients who are at increased risk, such as HIV or malaria clinics. To be successful, this will require the support of health ministries, local medical societies, and industry in a joint effort. There are no donors and no recipients here, only partners. Politics and profits must become secondary to humanitarian needs if we are to have a realistic hope of making progress.

The price of the existing medical therapies for pulmonary hypertension is so high that few patients in the developed countries can afford them. However, many generic, low-cost treatments hold great promise as potential treatments and are awaiting clinical trial development. Conducting clinical trials in developing countries has enormous appeal. It will help train physicians about an evidence-based approach to treating disease, while at the same time facilitating the local health systems as they try to accommodate the needs of affected patients. And it can lead to affordable therapies for underserved populations. It would not be surprising if discoveries made in the developing world at the same time. Finally, let us not overlook the inherent knowledge and skills of the physician scientists in these countries. Many have been trained in some of the most sophisticated research institutes in the world and are eager to explore the science of PVD at the molecular and translational levels. In collaboration with recognized academic institutions it should be possible to establish research laboratories in their medical centers where the cost of conducting scientific experiments is a small fraction of the costs borne in Europe and the United States. It would not be surprising if discoveries made in the developing world, where the conditions and patient populations are unique, provide important insights into CVD and PVD that also advance our understanding of the disease in the West.

We have outlined an ambitious agenda. However, given the obstacles that remain as barriers to success with traditional approaches, we are responding to the call for novel and creative solutions to narrow the gap in worldwide health-care disparities. Clearly, the future is now.

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