not only to strengthen health systems but to recruit and train physicians and nurses to underserved regions where they, in turn, can help to train and then work with community health workers in supervising care for patients with AIDS and many other diseases within their communities. Such training should be undertaken even where physicians are abundant, since close community-based supervision represents the highest standard of care for chronic disease, whether in developing or developed countries. The United States has much to learn from Rwanda.

Fifth, the barriers to adequate health care and patient adherence that are raised by extreme poverty can be removed only with the deployment of "wrap-around services": food supplements for the hungry, help with transportation to clinics, child care, and housing. Extreme poverty makes it difficult for many patients to comply with therapy for chronic diseases, whether communicable or not. Indeed, poverty in its many dimensions is far and away the greatest barrier to the scale-up of treatment and prevention programs. In many rural regions of Africa, hunger is the major coexisting condition in patients with AIDS or TB, and those consumptive diseases cannot be treated effectively without adequate caloric intake.

Finally, there is a need for a renewed basic-science commitment to the discovery and development of vaccines; more reliable, less expensive diagnostic tools; and new classes of therapeutic agents. This need applies not only to the three leading infectious killers—against none of which is there an effective vaccine—but also to most other neglected diseases of poverty.

MALARIA

Chapter 248 reviews the etiology, pathogenesis, and clinical treatment of malaria, the world's third-ranking infectious killer. Malaria's human cost is enormous, with the highest toll among children—especially African children—living in poverty. In 2010, there were ~219 million cases of malaria, and the disease is thought to have killed 660,000 people; 86% of these deaths (~568,000) occurred among children <5 years old. The poor disproportionately experience the burden of malaria: more than 80% of estimated malaria deaths occur in just 14 countries, and mortality rates are highest in sub-Saharan Africa. The Democratic Republic of the Congo and Nigeria account for more than 40% of total estimated malaria deaths globally.

Microeconomic analyses focusing on direct and indirect costs estimate that malaria may consume >10% of a household's annual income. A study in rural Kenya shows that mean direct-cost burdens vary between the wet and dry seasons (7.1% and 5.9% of total household expenditure, respectively) and that this proportion is >10% in the poorest households in both seasons. A Ghanaian study that categorized the population by income group highlighted the regressive nature of this cost: responding to malaria consumed only 1% of a wealthy family's income but 34% of a poor household's income.

Macroeconomic analyses estimate that malaria may reduce the per capita gross national product of a disease-endemic country by 50% relative to that of a non-malaria-endemic country. The causes of this drag include impaired cognitive development of children, decreased schooling, decreased savings, decreased foreign investment, and restriction of worker mobility. In light of this enormous cost, it is little wonder that an important review by the economists Sachs and Malaney concludes that "where malaria prospers most, human societies have prospered least."

Rolling Back Malaria In part because of differences in vector distribution and climate, resource-rich countries offer few blueprints for malaria control and treatment that are applicable in tropical (and resource-poor) settings. In 2001, African heads of state endorsed the WHO Roll Back Malaria (RBM) campaign, which prescribes strategies appropriate for sub-Saharan African countries. In 2008, the RBM partnership launched the Global Malaria Action Plan (GMAP). This strategy *integrates prevention and care* and calls for an avoidance of single-dose regimens and an awareness of existing drug resistance. The GMAP recommends a number of key tools to reduce malaria-related morbidity and mortality rates: the use of insecticide-treated bed nets (ITNs), indoor residual spraying, and artemisinin-based combination therapy (ACT) as well as intermittent preventive treatment during pregnancy, prompt diagnosis, and other vector control measures such as larviciding and environmental management.

INSECTICIDE-TREATED BED NETS ITNs are an efficacious and cost-effective public health intervention. A meta-analysis of controlled trials in seven sub-Saharan African countries indicates that parasitemia prevalence is reduced by 24% among children <5 years of age who sleep under ITNs compared with that among those who do not. Even untreated nets reduce malaria incidence by one-quarter. On an individual level, the utility of ITNs extends beyond protection from malaria. Several studies suggest that ITNs reduce all-cause mortality among children under age 5 to a greater degree than can be attributed to the reduction in malarial disease alone. Morbidity (specifically that due to anemia), which predisposes children to diarrheal and respiratory illnesses and pregnant women to the delivery of low-birth-weight infants, also is reduced in populations using ITNs. In some areas, ITNs offer a supplemental benefit by preventing transmission of lymphatic filariasis, cutaneous leishmaniasis, Chagas' disease, and tick-borne relapsing fever. At the community level, investigators suggest that the use of an ITN in just one household may reduce the number of mosquito bites in households up to a hundred meters away by reducing mosquito density. The cost of ITNs per DALY saved—estimated at $29—makes ITNs a good-value public health investment.

The WHO recommends that all individuals living in malaria-endemic areas sleep under protective ITNs. About 140 million long-lasting ITNs were distributed in high-burden African countries in 2006–2008, and rates of household ownership of ITNs in high-burden countries increased to 31%. Although the RBM partnership has seen modest success, the WHO's 2009 World Malaria Report states that the percentage of children <5 years of age using an ITN (24%) remains well below the World Health Assembly's target of 80%. Limited success in scaling up ITN coverage reflects the inadequately acknowledged economic barriers that prevent the destitute sick from gaining access to critical preventive technologies and the challenges faced in designing and implementing effective delivery platforms for these products. In other words, this is a *delivery* failure rather than a lack of knowledge of how best to reduce malaria deaths.

INDOOR RESIDUAL SPRAYING Indoor residual spraying is one of the most common interventions for preventing the transmission of malaria in endemic areas. Vector control using insecticides approved by the WHO, including DDT, can effectively reduce or even interrupt malaria transmission. However, studies have indicated that spraying is effective in controlling malaria transmission only if most (~80%) of the structures in the targeted community are treated. Moreover, since a successful program depends on well-trained spraying teams as well as on effective monitoring and planning, indoor residual spraying is difficult to employ and is often reliant on health systems with a strong infrastructure. Regardless of the limitations of indoor residual spraying, the WHO recommends its use in combination with ITNs. Neither intervention alone is sufficient to prevent transmission of malaria entirely.

ARTEMISININ-BASED COMBINATION THERAPY The emergence and spread of chloroquine resistance have increased the need for antimalarial combination therapy. To limit the spread of resistance, the WHO now recommends that only ACT (as opposed to artemisinin monotherapy) be used for uncomplicated falciparum malaria. Like that of other antimalarial interventions, the use of ACT has increased in the last few years, but coverage rates remain very low in several countries in sub-Saharan Africa. The RBM partnership has invested significantly in measures to enhance access to ACT by facilitating its delivery through the public health sector and developing innovative funding mechanisms (e.g., the Affordable Medicines Facility—malaria) that reduce its cost significantly so that ineffective monotherapies can be eliminated from the market.

In the last several years, resistance to antimalarial medicines and insecticides has become an even larger problem than in the past. In 2009, confirmation of artemisinin resistance was reported. Although the WHO has called for an end to the use of artemisinin monotherapy, the