

# **ASPECTS OF COMPLICATIONS ARISING FROM NEGELCTED TROPICAL CO-INFECTIONS AND THEIR SOCIAL AND ECONOMIC IMPLICATIONS IN SUB SAHARAN AFRICA**

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# Background

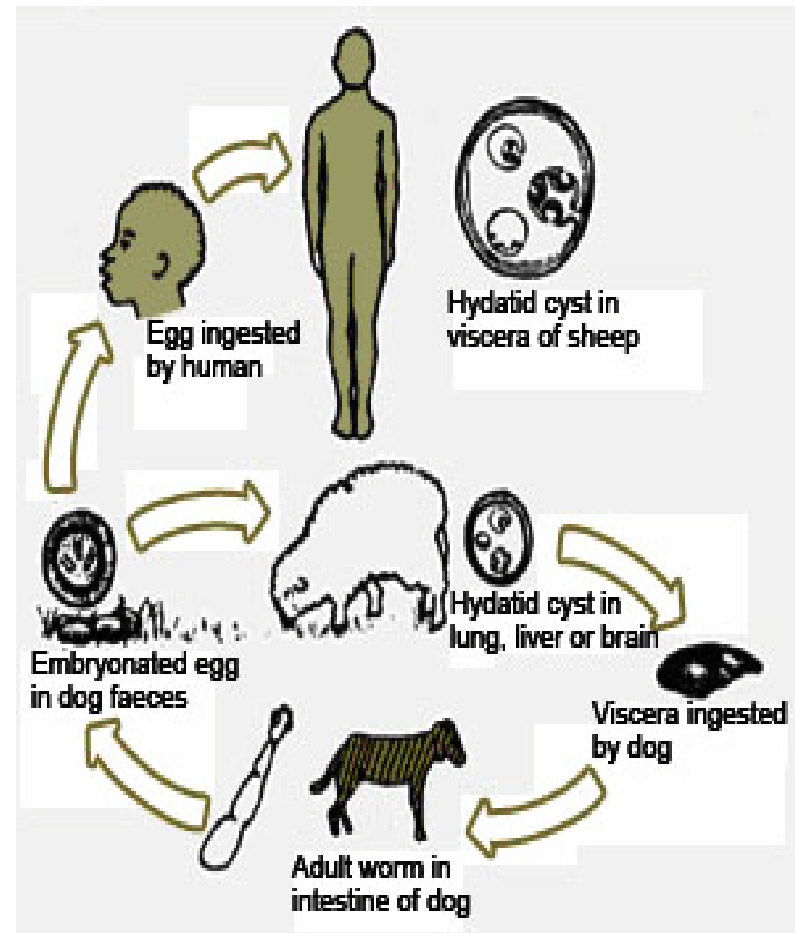
- There are several reports describing coexistence between two or more pathogens.
- In some cases, it is still unclear whether
  - the connection represents a true independent association, or
  - it merely reflects the independent correlation of each of these pathogens with underlying hematologic malignancy.

# Background Ctd

- For some infections, cell-mediated immunity plays a large defensive role
- for some immunocompromised patients, there are relapses after an apparent cure, and
- occasionally appear remote from the original infection.
- In other cases, treatment for the primary infection fails, leading to metastatic spread of the disease or late relapse.

# Morbidity/Mortality

- Tropical diseases do not occur in isolation. In most countries of sub-Saharan Africa, and in many other tropical and subtropical countries, at least five to six tropical diseases occur in the same region
- The implication of this geographic overlap is that a considerable proportion of the population of sub-Saharan Africa is poly-parasitized with one or more diseases, particularly among the very poorest populations

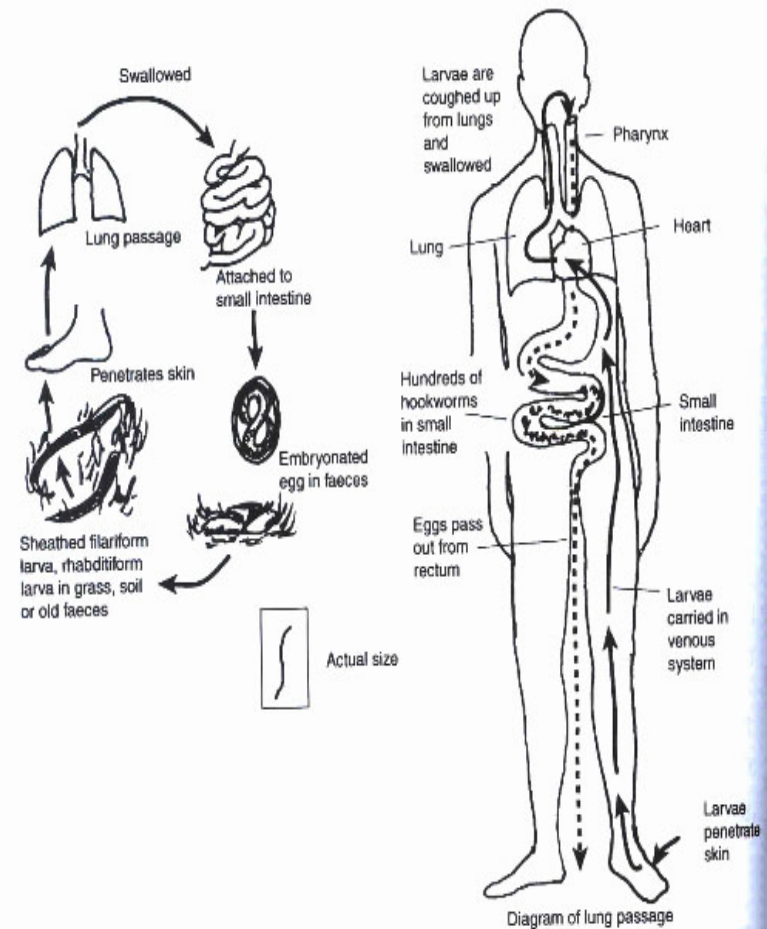


# Morbidity/Mortality ctd

- Hence Co-infections that lead to continuous morbidity
- Morbidity results into premature disability leading to loss of the years of life due to high mortality burden

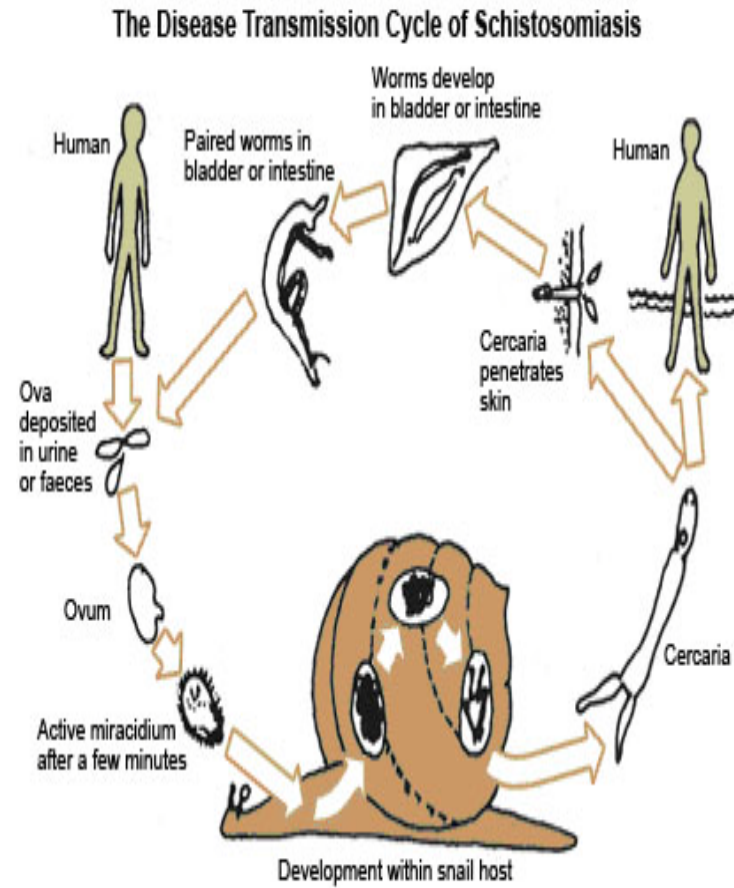
# Co-infections & HIV/AIDS, Malaria and Tuberculosis

In many parts of sub-Saharan Africa, the geographic overlap between HIV/AIDS, tuberculosis, and malaria is extensive. Indeed, Africa's catastrophic burden of disease resulting from HIV-associated tuberculosis and severe malaria in individuals with HIV is emerging as one of the first great human tragedies of the 21st century.



# Co-infections Vector-borne Protozoan diseases

- Adding to the complexity of Africa's big three (HIV/AIDS, tuberculosis, and malaria) is the geographic and epidemiologic overlay of tropical diseases such as **vector-borne protozoan infections**- leishmaniasis, human African trypanosomiasis, and Chagas disease; bacterial infections- trachoma, leprosy, and Buruli ulcer; and helminth infections- hookworm, ascariasis, trichuriasis, lymphatic filariasis, onchocerciasis, guinea worm (dracunculiasis), and schistosomiasis



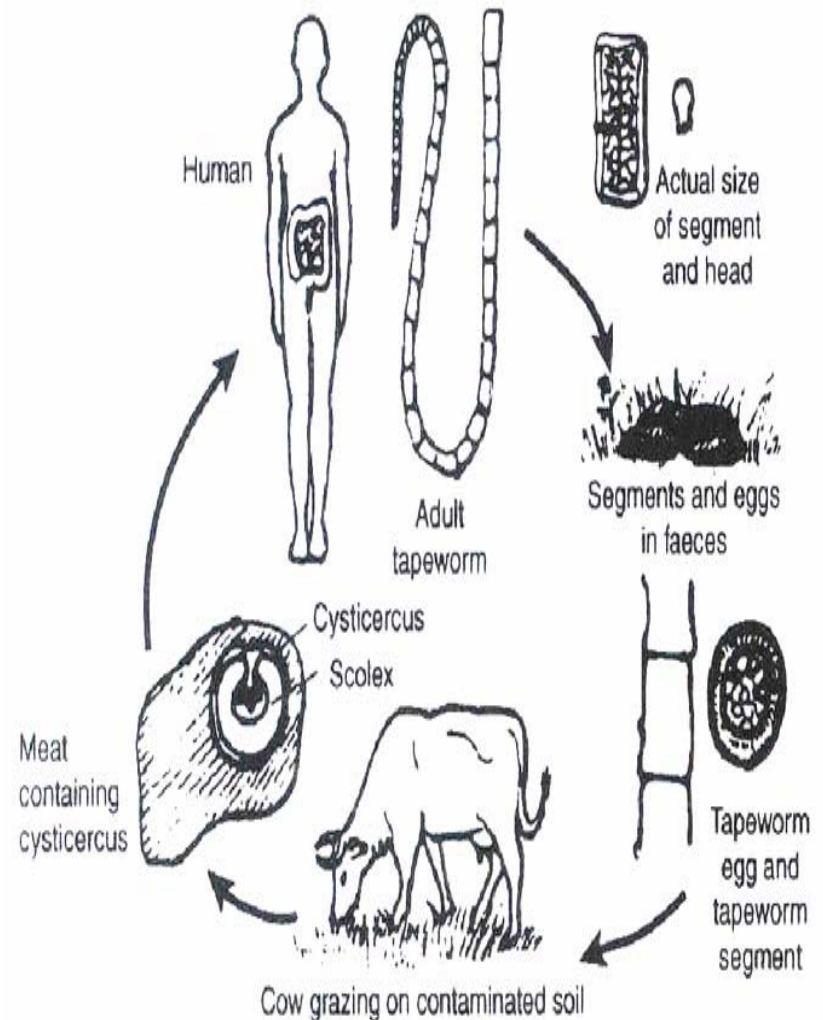
# Impact of Parasitic Co-infections

- Co-infection of a host by multiple parasite species (poly-parasitism) has important epidemiological and clinical implications.
- Unrelated co-infections are known to increase overall parasite virulence
- Such virulence stems from addition of more infections rather than to more aggressive growth by the individual infections.
- However, if, **by chance alone**, the co-infections are more related than expected, then the total reproductive output by all co-infections would be expected to be reduced - resulting in reduced virulence.



# Impact of Parasitic Co-infections ctd

- It has become increasingly clear that HIV/AIDS, tuberculosis, and malaria occur predominantly in populations who are poly-parasitized. Helminths are the most common parasites found in HIV-, tuberculosis-, and malaria-infected populations. Almost all of the major tropical diseases have been linked with HIV/AIDS, tuberculosis, and malaria.



# Social effects of tropical diseases

- Many of tropical diseases are **poverty-promoting** conditions.
- These diseases are **disfiguring** and **stigmatizing**, and have affected humans for millennia.
- However, because they affect the poorest of the poor, there are **few or no commercial markets for drugs and vaccines** against the neglected tropical diseases.



Elephantiasis caused by working in poor/unhygienic environment

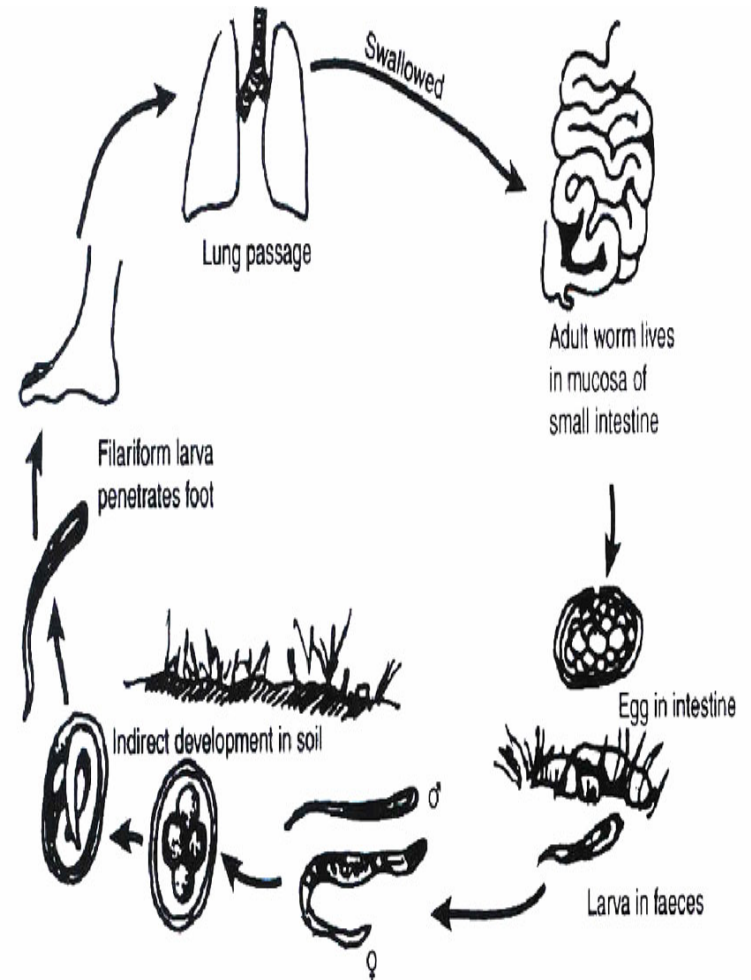
# Physical effects of tropical diseases

There is high endemicity in sub-Saharan Africa, where

- they **adversely affect childhood growth and physical fitness**,
- Such poly-parasitism has a **substantial impact on the physical health** of Africa's youth population,
- as well as on the **impairment of their intellectual and cognitive development**.
- Poly-parasitism also results in **anemia**,
- due to **intestinal blood loss**.
- In addition to host blood loss, anemia is caused through other mechanisms including **hypersplenism, red blood cell sequestration, autoimmune hemolysis**, and **chronic inflammation**.

# Disease burden

- The burden of disease resulting from neglected tropical diseases include
- high endemicity in rural and in impoverished urban areas of low-income countries,
  - ability to impair childhood growth, intellectual development, and education,
  - and ability to impair worker productivity.



# **Impact of tropical diseases on host susceptibility to HIV/AIDS, Tuberculosis, and Malaria**

- Co-infection with tropical diseases adversely affects the natural history and progression of HIV/AIDS, tuberculosis, and malaria.
- Several studies point to the increasing severity of clinical malaria that results from helminth co-infection. These studies include those from
  - Senegal showing enhanced risk or increased incidence of clinical malaria resulting from either Soil Transmitted Helminths (STH) or schistosome infections

# **Impact of tropical diseases on host susceptibility to HIV/AIDS, Tuberculosis, and Malaria ctd**

- Studies from:
  - Malawi show that women infected with hookworms were at 1.8 times higher risk of having malaria than uninfected women
  - Thailand show increased susceptibility to malaria in patients with STH infections.

# **Impact of tropical diseases on host susceptibility to HIV/AIDS, Tuberculosis, and Malaria ctd**

- Another body of evidence links helminth co-infections with increased susceptibility to HIV/AIDS or worsening progression of HIV disease
  - Gallagher et al. 2004 observed increased risk of mother-to-child HIV transmission in pregnant women with helminth co-infection.
- In addition to promoting susceptibility to HIV/AIDS, one major tropical disease in Africa, namely, visceral leishmaniasis, is an important opportunistic infection in individuals who are HIV-immunocompromised.

# Effects of co-infections on disease outcome

- Finally, there is some evidence that helminth infections adversely affect the outcome of pulmonary tuberculosis or the progression to active tuberculosis.
- Taken together, this evidence indicates that co-infection with one or more disease may profoundly affect the outcome of one or more of HIV/AIDS, tuberculosis, and malaria.
- Progression of disease from HIV/AIDS, tuberculosis, and malaria results from the co-morbidity associated with anemia from STH, and from the possible increase in susceptibility and worsening progression of disease that occurs with these infections.
- However, the latter concept is still not without controversy and requires additional scientific investigations.



# **Co-morbidity of tropical diseases with HIV/AIDS, Tuberculosis, and Malaria: Anemia**

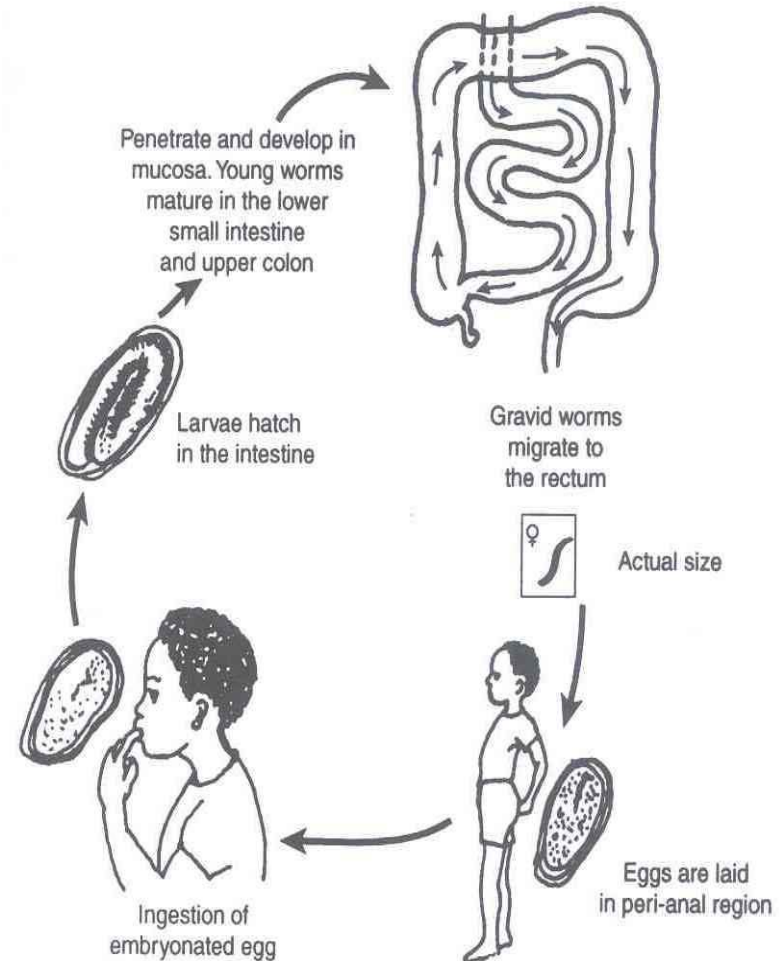
- We are still in the early stages of appreciating the full extent of the co-morbidity that occurs when tropical diseases are superimposed on HIV/AIDS, tuberculosis, and malaria. Anemia has been revealed as perhaps the most important of the leading co-morbid conditions.
- Children and pregnant women are particularly susceptible to anemia from hookworm and schistosomiasis.
- Each of HIV/AIDS, tuberculosis, and malaria also results in anemia, with malaria responsible for the greatest burden.

# Agriculture-related anemias

To make matters worse, many of these **same African populations** experience “**agriculture-related anemias**” to describe this “perfect storm” confronting African populations, this includes **changes in diet, population growth with limited sanitation and with the consequences of endemic Soil Transmitted Helminths (STH) infections, an environment prone to the emergence of vector-borne disease, and natural selection of variants that offer partial protection against malaria**—all of which resulted from the introduction of agriculture, Fleming 1994.

# High risk groups

- The severe anemia resulting from **helminth poly-parasitism and malaria** produces **several adverse health consequences** among three particularly important African subpopulations: **pregnant women, children, and individuals with HIV.**
- In pregnancy, anemia is a leading contributor to **maternal morbidity and mortality**, and is associated with **shock, risk of cardiac failure, decreased ability to work, and adverse perinatal outcomes.**
- Among individuals with **HIV**, anemia has been shown to be an independent risk factor for early death, with correction of anemia associated with reversal of increased risk.



# **A comprehensive pro-poor health policy**

- It is important to determine if there is a rationale for linking a pro-poor strategy for integrated disease control with ongoing programs that target HIV/AIDS, tuberculosis, and malaria.
- Recent evidence of the extensive geographic overlap between them and the tropical diseases, together with the deleterious interactions between both groups of infections, suggests significant, new opportunities to reduce the burden of disease in sub-Saharan Africa.

# **A comprehensive pro-poor health policy ctd**

- Success at integrating tropical disease control into the fight against HIV/AIDS, tuberculosis, and malaria partnership programs could dramatically reduce the number of life years lost from premature death and disability in Africa.
- The collateral benefits from including tropical disease control under the umbrella of the HIV/AIDS, tuberculosis, and malaria global partnerships are potentially huge.
- For example in Zimbabwe, treatment for schistosomiasis reduced the rate of HIV-1 viral replication and increased CD4 cell counts among individuals who were co-infected
- However this phenomenon was not observed in Ugandans who were co-infected.
- Therefore, it may be important to consider local and geographical differences when evaluating the impact of deworming on co-infections.

# Way forward

- New vaccines under development for HIV/AIDS, tuberculosis, and malaria also need to account for the influence of poly-parasitism on vaccine immunogenicity.
- Given the compelling logic and the very modest costs of embracing tropical disease control efforts, it is surprising that those aiming to control HIV/AIDS, tuberculosis, and malaria have largely ignored opportunities of the collateral benefits from reductions in anemia, worm burdens, and susceptibility to HIV/AIDS, tuberculosis, and malaria morbidity.

# Way forward

- Bilateral donors and the major HIV/AIDS, tuberculosis, and malaria partnerships should expand their portfolios to incorporate other neglected tropical disease control initiatives as a cost-effective means to reduce the morbidity and mortality of HIV/AIDS, tuberculosis, and malaria.
- Such interventions are inexpensive, effective, and fully compatible with the Millennium Development Goals.

# Way forward

- Co-infections raise the question of whether some drugs would alter the severity of diseases like malaria, and presents both challenges and opportunities for proposed “integrated control” programs that target multiple infections at once, Lu *et al* 2005.
- A resolution should be adopted urging communities to try by all means and reduce global disease burden and morbidity by fighting co-infections of all diseases not just HIV/AIDS, tuberculosis, and malaria.
- A comprehensive pro-poor strategy to integrate programs for the control or elimination of tropical diseases using existing drugs should be put forward.
- Such integration efforts are particularly relevant to sub-Saharan Africa because all diseases in Africa exhibit a high degree of geographic overlap.



# Way forward

- It is proposed that such integrated control or elimination could be achieved with available and affordable drugs as each of the drugs has overlapping specificity so that multiple pathogens would be concurrently targeted.
- It has been estimated that for US\$200 million annually, approximately 500 million Africans (US\$0.40 per patient) could be treated in a four-drug integrated pro-poor package.
- That package could reduce tens of millions of new infections while simultaneously addressing seven of the eight Millennium Development Goals (MDGs), including those related to poverty reduction, educational achievement, and child and maternal health.

# Way forward

- As scaling up integrated control moves forward, a number of research and monitoring questions will need to be addressed, including issues of **compliance, drug interactions, emerging drug resistance, and sustainability**.
- Moreover, proof of concept for the feasibility of integrated control will require attention to the specific populations (e.g., children versus adults) at risk for each of the diseases, and to the timing for administration of each of the drugs.
- Equally important will be undertaking an economic analysis of the rapid-impact package. The studies on the economic rates of return of large-scale and successful disease control and elimination programs have shown that these are of the order of 15%–30%.

# Way forward

- The World Bank and other agencies have recognized these programs as being among the most effective development investments in any sector, and it is hoped that an equal or greater rate of return could be achieved with a rapid-impact package targeting multiple tropical diseases.
- In the future, the concept of integration could be expanded beyond integrated chemotherapy-based morbidity control based largely on community-directed treatment to include access to clean water and improved sanitation; strengthening of surveillance, evaluation, and reporting systems; capacity building, deployment of new generation control tools; and education and communication strategies to address the root ecological and behavioral causes of the diseases.

In all we still have lots of epidemiological problems to research on in order to come up with (better) programs for improved health on the African Continent.