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Understanding HIV/AIDS in the African Context

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Understanding HIV/AIDS in the African Context

Abstract
This book of readings is intended for courses in Global Health. The editors asked Prof. Stillwaggon to contribute a chapter summarizing her years of work on the spread of HIV/AIDS in populations among whom bacterial, fungal, parasitic, and viral diseases are extremely common, particularly in sub-Saharan Africa. Her work has demonstrated that differences in behavior cannot explain differences in HIV rates between world regions.

Keywords
HIV/AIDS, Africa, STIs, poverty, context, heath care

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Comments
Foundations of Global Health: An Interdisciplinary Reader is a collection of highly readable articles with a significant amount of original text by the editors. Supplementary instructive materials include "conceptual tools" summaries, background information on authors and context, provocative section and article introductions, discussion questions, and suggestions for further reading and internet exploration. Like the field of global health itself, the readings focus on the public health challenges faced by low- and middle-income countries as well as the persistent problems of health disparities in high-income countries.

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EILEEN STILLWAGGON AND LARRY SAWERS

28 UNDERSTANDING HIV/AIDS IN THE AFRICAN CONTEXT

Note: This article should be read in conjunction with Reading 27.

Understanding HIV/AIDS in the African context is a complicated endeavor. This article provides a serious contrast to the previous reading, which emphasized the issue of concurrency in sexual relationships in southern Africa. In contrast, this article considers many broader interacting factors that provided conditions to make the HIV/AIDS epidemic spread in sub-Saharan Africa.

Epidemics do not occur simply because a pathogen crosses some geographical or biological barrier. Rather, the overall context must be conducive to an epidemic. This is one reason why epidemics are often associated with wars (see Reading 32).

Like other sexually transmitted infections (STIs), HIV/AIDS is only partially about sex. A variety of contextual factors including nutrition, hygienic conditions, and poverty that can constrain the behavior of individuals also affect disease transmission. Answering the question of why there is such a high rate of HIV/AIDS in sub-Saharan Africa requires an understanding and serious consideration of the contexts—both epidemiological and socio-economic. It is not sufficient to focus only on individual behavior. If we look only at individual behavior, we are likely to exaggerate the ability of people to make choices within particular social and economic contexts and also likely to underestimate the power of structural violence (see Reading 34).

This article first considers the disease burden and the ecology of poverty in populations with high rates of HIV. These factors make an individual more likely to become infected, because undernutrition and infectious diseases, such as other STIs, malaria, and schistosomiasis, lead to burdens on a person's immune system.

The health systems in many sub-Saharan African countries are so inadequate that the initial arrival of HIV/AIDS was barely recognized—quite unlike the United States. African health-care systems and epidemiological surveillance systems are overburdened and underfunded. Clinics often lack simple equipment like clean hypodermic needles. There are so many variables interwoven in the causation of the HIV/AIDS epidemic that it is probably impossible to measure them all in randomized controlled studies. It is certainly the case that the most basic epidemiological methods (like the 2×2 table) are inadequate for explaining the complex interaction of causes.

Science, including research on the causes of disease, is often polluted by the scientists' preexisting cultural assumptions and prejudices. This may be the case with assumptions about the sexual behavior of the other societies—in this case, the historical stereotype of Africans as hypersexualized may have led to an overemphasis on sexual explanations for the spread of HIV/AIDS.

This tendency to discover things that we already believe to be true is called confirmation bias. The only way to circumvent such bias is through repeated study and reanalysis. This article interrogates the concurrency hypothesis by critically examining the methods used by other researchers. Such arguments about methods sometimes seem unnecessarily trivial to students. In reality, however, looking at the methods that studies use is critical to understanding whether their findings are actually correct.

Remember that this article should be read in conjunction with the previous reading (Reading 27).

As you read this piece, consider the following questions:

- **The previous article concluded with two concrete recommendations for future HIV/AIDS prevention programs, but this article does not. In your opinion, what do you think that the authors would propose as solution(s) to the complexity of the epidemic?**

This article is original to this volume.

- **In your opinion, why has HIV/AIDS received more attention than "old" health challenges like undernutrition, malaria, schistosomiasis, or the neglected tropical diseases?**
- **Consider the difference that the authors propose between causes of cases and causes of incidence. Might this difference reflect the way that clinical doctors think, as opposed to people who practice public health?**
- **In your opinion, are there really "methodological handcuffs" that can hamper progress in health improvements? If so, what is the solution?**
- **Do you think that an incomplete consideration of a complex web of causation, as described here, can be considered "false facts?"**
- **The authors of this article are economists. Do you think that this makes a difference in their approaches to global health?**

CONTEXT

Eileen Stillwaggon is a professor of economics and Benjamin Franklin Professor of Arts and Sciences at Gettysburg College. Her primary interest has been on the relationship between health and economic development, described in her book, *Stunted Lives, Stagnant Economies: Poverty, Disease, and Underdevelopment* (New Brunswick, NJ: Rutgers University Press, 1998). Recognizing the problems with an individualized behavior approach to health interventions for HIV/AIDS, she wrote *AIDS and the Ecology of Poverty* (Oxford: Oxford University Press, 2006)—about the same time as the popular book discussed in Reading 27. She has also done research on economic development in Native American communities and in Latin America. Larry Sawers is a professor of economics at American University, Washington, DC. His major research interests are in the causes of economic underdevelopment, one of which is poor health, and economic development policy. He has been a Senior Fulbright Scholar in Tanzania, Ecuador, and Lithuania. His books include *The Other Argentina: The Interior and National Development* (Boulder, CO: Westview, 1996) and *Emerging Financial Markets in the Global Economy* (co-editor with Daniel Schydlowsky and David Nickerson; River Edge, NJ: World Scientific, 2000).

Large events are almost never like a meteor hitting the earth. They arise over time, from multiple, often interacting causes. Wars result from the combined effects of economic, political, and sometimes natural events. Famines reflect the inability to buy food due to income loss as well as supply factors, such as crop failures and logistical obstacles. Traditional epidemiology has always recognized that outbreaks of disease occur in a specific context of environmental, social, and economic conditions. For an individual, as for a population, "the epidemiology of an infectious disease reflects complex interactions between the infectious agent, the host, and the environment".[1]

We know a great deal about why epidemics spread. Random introductions of pathogens into human populations occur continually, but they rarely lead to epidemics or pandemics. Favorable conditions are necessary for a microbe to make a person sick or for the disease to spread throughout a population. Plague was introduced numerous times into Europe before 1348 without pandemic spread. But 30 years of falling per capita food consumption had weakened the population and provided the conditions needed for the Black Death.[2,3] For 100 years before 1991 there was no cholera outbreak in the Americas, although cholera *vibrio* was introduced into coastal waters throughout the region on countless occasions. The return of cholera to the hemisphere followed substantial deterioration in sanitary conditions throughout Latin America during the "lost decade" of the 1980s, a period of economic crisis, decreased government social expenditures, falling incomes, and increasing

inequality. From one squalid slum to another, cholera spread north and south from Peru across Latin America.[4]

Epidemiological, clinical, and laboratory evidence show that HIV infection is influenced by the same factors that promote transmission of other infectious diseases. People with nutritional deficiencies, with parasitic diseases, whose general health is poor, who have little access to health-care services, or who are otherwise economically disadvantaged have greater susceptibility to infectious diseases, whether they are transmitted sexually or by food, water, air, or other means. This essay examines the spread of HIV/AIDS in sub-Saharan Africa using this perspective, and shows how much writing about AIDS in Africa has neglected to take these factors into account.

The Health Environment of African AIDS

At the time the HIV epidemic was spreading in Africa, the real annual income of the average person in the United States was more than 60 times that of the average Tanzanian or Malawian.[5] Calorie intake per person in sub-Saharan Africa had not increased from 1970 to 2000 and was still only 70 percent of the consumption level of industrialized countries. Public and private spending on health services in Canada was 200 times what it was in Ethiopia.[5] Malnutrition and parasite infection contribute to greater susceptibility to any infectious disease, including those transmitted sexually. There are also certain diseases prevalent in Africa, but rare in the rest of the world, that sharply increase the probability of transmission of HIV.

When HIV emerged in the early 1980s, it was barely noticed in some African countries because of the routine enormity of suffering. Even today, HIV is far from the only threat to poor people in the region. When the HIV epidemic was already advanced in Malawi, a study of a plantation there reported three deaths per month from AIDS, certainly a terrible toll. But there were six non-AIDS deaths of adult workers per month, and 15 deaths per month of workers' dependents.[6] HIV flourishes where people are dying of other diseases. That is not mere coincidence.

Nutrition

From 1988 to 1998, when emerging or localized HIV epidemics developed into generalized epidemics in sub-Saharan Africa, 30 percent of the population of the region was malnourished.[7] Malnutrition increases vulnerability to infectious and parasitic diseases generally, increases HIV viral load and viral shedding, and undermines the integrity of the skin and mucosa, thereby increasing sexual and vertical transmission of HIV.[8–15] (For numerous additional sources on nutrition, see.)[16] Malnutrition alone cannot explain differences in HIV epidemics across the globe, but, given the well-understood connection between immune status and malnutrition, it surely played a role in accelerating the spread of HIV in sub-Saharan Africa.

Malaria

When generalized epidemics of HIV were developing in the region, there were nearly 200 million cases of malaria in Africa every year and nearly 1 million deaths.[17, 18] At the time, Uganda, Tanzania, and Mozambique had the highest incidence of malaria in the world, and Malawi, Zambia, and Zimbabwe were not far behind.[19] Then as now, more than 90 percent of acute infections and deaths from malaria were in sub-Saharan Africa.[17] Malaria increases HIV viral load up to ten times for as much as seven weeks after an episode of fever, and that can more than double heterosexual transmission.[20–22] An HIV-infected person could have elevated viral load for more than half of every year since people are repeatedly reinfected in highly endemic areas. Malaria also leads to anemia and impairs immune response, both of which make those with HIV more contagious.[23] Malaria is especially dangerous in areas of southern Africa where it occurs in seasonal epidemics (Botswana, Zimbabwe, Swaziland, South Africa, and Namibia), which are also the countries with the highest rates of HIV.[24]

Helminths

Infection with helminths, or parasitic worms, impairs immune response and increases HIV viral load, increasing transmission of HIV and accelerating progression to AIDS.[25–28] Because helminth infection is so prevalent in sub-Saharan Africa, even a small

additional risk of HIV transmission due to helminth infection could mean many additional HIV infections overall. A double-blind, controlled trial found that treating worm infections in HIV-infected persons results in a statistically significant improvement in immune system functioning.[29,30] That suggests that a simple, inexpensive (2 US cents) and effective deworming medication could allow HIV-infected people to be healthier while reducing the risk of infecting a partner, especially when antiretroviral treatment for HIV may be unavailable.

Schistosomiasis

Nearly 90 percent of cases of the parasitic disease, urogenital schistosomiasis, occur in sub-Saharan Africa, where it afflicts 120 million people.[31,32] Schistosomiasis is highly prevalent in almost every country in sub-Saharan Africa. Schistosome worms and their eggs colonize the reproductive tract in men and women, causing inflammation, viral shedding, and genital ulcers, all of which increase the transmission efficiency of HIV.[33–36] In endemic areas, from 33 to 75 percent of women have genital lesions and inflammation resulting from schistosome eggs.[37] The presence of eggs causes inflammation in the urogenital system and breaches in the integrity of the epithelial layer and the protective mucosal surface.[32,37,38] Women with genital ulcers of schistosomiasis have three to four times the risk of being infected with HIV as women in the same village without genital ulcers of schistosomiasis.[37–40]

Treatment with praziquantel is effective in killing the worms and stopping egg production and is safe even in pregnancy and during lactation. Lack of access to treatment can produce irreversible damage to the reproductive tract. Praziquantel costs US $0.30 per treatment, and even a single treatment in childhood can reduce adult disease by half. Fewer than 8 percent of people in need are treated although mass drug administration is feasible and inexpensive.[32,41]

Other Sexually Transmitted Infections

Sub-Saharan Africa has the highest burden of sexually transmitted infections (STIs) of all of the world's regions.[19,42] In 2004, the mean burden of STIs in sub-Saharan Africa [measured in disability-adjusted life years (DALYs) per 100 000] was nearly six times the mean burden outside the region, and all 47 sub-Saharan African countries for which there were data were among the world's 52 countries with the highest STI burden.[19] Poor access to health care services, antibiotics, and antivirals contributes to the persistence and spread of STIs in the region,[43] in spite of unexceptional or even conservative sexual behavior documented in empirical studies (see below).

Some STIs produce ulceration of the genitals that are open pathways for transmission of HIV. All sexually transmitted infections produce inflammation, increased HIV shedding, and increased viral load, all of which have been shown to increase the risk of HIV transmission. Numerous observational studies since the late 1980s demonstrate that STI coinfections make persons with HIV more contagious and make STI-infected persons more vulnerable to HIV acquisition.[27,43–48] STI diagnosis and treatment have been standard parts of the HIV prevention toolkit since the 1980s.

Non-Sexual Transmission

In addition to diseases that can increase HIV transmission rates during heterosexual and mother-to-child exposure, non-sexual modes of transmission could play an especially important role in sub-Saharan Africa and among other poor populations. There are numerous, common medical blood exposures (for example, injections with unsterilized syringes, blood transfusions, catheter and intravenous placements, and internal obstetrical examinations) and non-medical blood exposures (for example, barbering and hairdressing, tattooing, scarification, injections given by non-medical personnel, and intravenous recreational drug use) that can potentially transmit HIV.[49–51] Even if each one of those possible non-sexual routes of transmission produces only a small share of new infections, together they would play an important role in the epidemics of sub-Saharan Africa, where sterilization equipment in clinics could be lacking.

AIDS Policy in Africa

Since the argument above is well supported in mainstream epidemiology and in scientific research over the past four decades, why is it not reflected in AIDS

policy for sub-Saharan Africa? Why does funding for HIV prevention not cover prevention of co-factor infections, including malaria, urogenital schistosomiasis, and STIs?

There are several reasons for the departure of AIDS research from traditional epidemiology. Over the course of the twentieth century, the emphasis of medical research shifted from environmental and population-level factors to individual-level theories of disease causation,[16,52–54] and that change became evident in the evolution of AIDS discourse towards a focus on individual factors, in particular sexual behavior. We return to those methodological issues later in the essay. Here we examine the overwhelming emphasis on sexual behavior in HIV-prevention policy.

In the 1980s and 1990s, the enormity and speed of the AIDS pandemic were menacing. An incurable disease was spreading both in the West and in Africa, and ignorance of Africa served to allay Western fear by constructing AIDS as a disease of the social Other. Western stereotypes had long portrayed Africans as exotic and hypersexualized. Notions of racial difference pervaded the social science literature on AIDS in Africa and were especially explicit during the first 15 years of the epidemic. No one used the word race, but the notion entered into the discourse as "culture." Racial "science" in an earlier epoch and popular racial stereotypes that persist to the present day stress sexual differences between the races and portray sub-Saharan Africans as exotic, strange, and even disturbing.[55–57]

By the late 1980s, the presumption, promoted in scholarly and popular literature, that the extraordinary nature of heterosexual behavior in sub-Saharan Africa explained the high prevalence of HIV in the region became widely accepted among researchers and policy makers. Influential and frequently cited works were characterized by sweeping statements about pan-African sexuality, either without evidence or with only anecdotal evidence dating from the 1920s to the 1970s. Through suggestive language and innuendo, they conveyed the impression of Africans bent on self-destruction because of cultural factors that differentiated them from everyone else. (See among others.[58,59] For extensive discussion of racial innuendo in AIDS discourse, see).[16,60]

Racial stereotypes continue to pervade Western culture, casting their shadow over scholarship and public policy, even among persons who, on a conscious level, vigorously and sincerely oppose racial discrimination. The influence of notions of "race" in both the popular mind and in the imagery of science is insidious and difficult to counter because so much of racial stereotyping is in the "unstated assumptions and unthinking responses",[61] rather than in explicit postulates. That is aggravated by the tendency for both academic and journalistic writing about sub-Saharan Africa to consist of a "repertoire of amazing facts".[62] Writing about sub-Saharan Africans, popular and scholarly, almost always emphasizes how they are different from others, not their commonality with people everywhere.

Western researchers, editors of academic journals, bilateral donor agencies, and international organizations framed the spread of AIDS in sub-Saharan Africa in behavioral terms, neglecting the health environment in which the epidemic unfolded in the region. The power to define the causes of HIV in exclusively behavioral terms narrowed the research questions and policy responses. In spite of the lack of evidence, the theme in much AIDS scholarship and policy literature remains that "Africans are not like everyone else."

Inconsistencies in the Behavioral Paradigm

Serious researchers naturally sought data on sexual behavior to test the proposition that differences in sexual behavior could explain 50-fold differences in HIV prevalence between some African countries and the rest of the world. The UN Global Programme on AIDS, the Demographic and Health Surveys (DHS) funded by USAID, and numerous other researchers have produced a substantial body of survey research on sexual behavior in Africa and elsewhere. The surveys demonstrate that within every country there is considerable variation in sexual behavior—some people have many partners, for example, but most people have one, very few, or none—and prevalence of HIV across the globe and within sub-Saharan Africa does not correlate with patterns of risky behaviors. Evidence from those surveys showed that in sub-Saharan Africa sexual behavior was more conservative than in Europe, the United States, Canada, and Latin America, whether measured by

average age of sexual debut, prevalence of pre- or extra-marital sex, average number of partners, visits to commercial sex workers, or average number of partners in one year or over a lifetime.[63,64] (For extensive documentation, see).[16,65]

In the 1990s, a second important finding further undermined the validity of the behavioral paradigm. Researchers found that HIV is not a particularly virulent pathogen and that per-act transmission rates are quite low between otherwise healthy adults in heterosexual contacts, though somewhat higher during the first few weeks after initial infection.[66–70] Thus, empirical evidence on both the behavior and the biology needed for a behavioral explanation was lacking. Nevertheless, AIDS had become associated in the popular imagination, including that of researchers, as an exceptional, African behavioral phenomenon. Because asking how Africans are different from everyone else seemed so reasonable to most people, a new variant, the concurrency hypothesis, became the conventional wisdom without credible empirical support.

Concurrency to the Rescue

In the early 1990s, a few researchers proposed that long-term overlapping partnerships—also called multiple concurrent partnerships, or concurrency—might explain the difference in HIV prevalence between Africa and the rest of the world.[71,72] A decade later, it was clear that other forms of heterosexual behavior could not account for the extraordinarily high HIV prevalence in the region, and concurrency emerged as the dominant explanation.[73–75] It was argued that concurrency—in contrast to one-time or short-term sexual encounters—could permit sufficiently frequent sexual exposures during the first few weeks of HIV infection, when transmission efficiency is highest, to provide the missing engine capable of driving the African HIV epidemics.

The promoters of this updated version of the behavioral paradigm asserted that long-term concurrent partnerships are unusually common in sub-Saharan Africa.[73–79] Furthermore, they asserted that concurrent partnerships spread HIV much more effectively than sequential multiple partnering.[75] If either assertion is incorrect, then the concurrency hypothesis fails. We argue that neither is correct.

Is Concurrency More Common in Sub-Saharan Africa?

In 2010, we reviewed more than three dozen studies that proponents of the concurrency hypothesis had presented as evidence of extraordinarily high concurrency prevalence in sub-Saharan Africa.[65] We found more than 100 errors in their reporting of the results of those surveys. Moreover, most of the surveys recruited (rather than randomly sampled) a small number of respondents, often in a single neighborhood or village, so the results could not be generalized to the larger population.[65] The few surveys that randomly sampled a large population used a measure of concurrency that has been judged unreliable by the UNAIDS Reference Group on Estimates, Modelling and Projections.[80] None of the studies provided credible evidence that concurrency was unusually high in sub-Saharan Africa.[65] In 2010, the DHS (Demographic and Health Surveys) began to measure concurrency using the questionnaire proposed by the UNAIDS Reference Group. There are now surveys from 31 countries in sub-Saharan Africa that interviewed a representative national sample of adults, all using the same definition of concurrency.[81,82] The average prevalence of concurrency (having overlapping sexual partnerships six months prior to the interview) was 8.3 percent for men and 1.0 percent for women, or 4.7 percent for all adults age 15 to 49. Concurrency prevalence in the United States and several European countries is in the same range as the numbers from sub-Saharan Africa, though perhaps higher for women and lower for men.[83–85]

Is Concurrency Especially Effective in Spreading HIV?

One cannot conduct trials with humans to test if concurrency is an especially effective mechanism for spreading HIV, so to explore the issue one must use mathematical modeling of sexual networks, specifically using a technique called individual-based stochastic simulation modeling. The modeling takes a number of factors into account, including the average length of each partnership, the likelihood of

forming a concurrent partnership, and the daily risk or probability of acquiring HIV (which in turn implicitly assumes the frequency of sexual contact in each partnership). For the modeling to generate useful results, these parameters must be based on reasonable estimates from survey research or clinical studies. Early modeling appeared to show that HIV spreads far more rapidly with concurrent partnering than with serial monogamy.[75] Those results were cited by the modelers themselves and many others to make the claim that concurrency explained exceptionally high rates of HIV in sub-Saharan Africa. That proposition soon became widely accepted.

The original model, however, depended on parameters that were simply implausible. The modelers assumed that every person, male or female, had sex with every partner every day, with up to four partners. Moreover, they assumed that each day, in each sexual partnership, there was a 5 percent chance of HIV transmission. That 5 percent transmission risk is nearly 100 times larger than the consensus risk estimate of experts on the subject. Eaton and colleagues[86] adapted the original model's code and assumed an evidence-based per-day transmission risk. They found that HIV either does not spread through sexual networks at all or spreads far more slowly than the original model found.

We built on Eaton's work by assigning realistic values for other model parameters. Based on survey research in sub-Saharan Africa, we assumed that partnerships there, like everywhere else, last for many years. We also assumed that secondary partnerships have shorter durations on average and lower frequency of sexual contact than primary (marital or cohabiting) partnerships. With all of those errors corrected, the restructured model cannot generate *any* HIV epidemic that does not move to extinction, that is, the epidemic collapses on itself. That remains so whatever level of concurrency one assumes, even levels far above those considered in the original model and far above levels reported in the DHS surveys in sub-Saharan Africa.[81,82,87]

In sum, when properly measured, levels of concurrency in sub-Saharan Africa are not unusually high and, when properly modeled, concurrency at even implausibly high levels cannot produce sustainable simulated HIV epidemics. Thus, the concurrency hypothesis, the last bulwark of the behavioral paradigm, is without empirical or theoretical validity. And yet, HIV-prevention policy is still rooted in a behavioral, rather than a biomedical model.

What Should Inform AIDS Policy?

We have discussed how Western stereotypes of a hypersexualized pan-African culture, rooted in a belief that Africans are not like other people, allowed behavioral explanations to dominate the search for causes of high rates of HIV in sub-Saharan Africa. There are, however, methodological obstacles that also have prevented epidemiologists and public health practitioners from using the biomedical evidence described earlier in this essay. The increasingly individual-level focus of medicine and public health was aggravated by the excessive reliance on experimental and statistical methods that intentionally omit from consideration the context in which individual illness or population-wide outbreaks occur.

AIDS discourse about Africa and HIV-prevention policy are derailed by confusion over what Rose calls "causes of cases and causes of incidence".[32] Individual risk factors that are associated only with one proximate cause (such as sex) do not fully explain why one individual becomes infected and another does not, nor do they explain why one population has higher incidence than another.

Poor nutrition, malaria, helminths and STIs make each sex act and each birth more risky in sub-Saharan Africa and accelerate epidemics of HIV in the region. By targeting only one proximate cause, sex, policy makers ignore the fundamentally different distribution of risk factors between sub-Saharan Africa and affluent, temperate-zone regions. The 'background noise' of an environment teeming with bacterial, viral, and parasitic cofactors is the appropriate object of study to understand causes of elevated HIV risk for individuals and higher incidence in sub-Saharan Africa.

Methodological Handcuffs

Any causal explanation must involve some simplification, but randomized controlled trials (RCTs) are designed to evaluate the effects of just one singular cause. RCTs are essential in the evaluation of

new drugs for which the effectiveness and harmful effects are unknown, but they are blunt instruments for understanding infections or other pathologies that arise from multiple interacting causes, or evaluating public health interventions.[88,89] Epidemics are complex systems; trials that attempt to change one part of that system may show unreliable results because of multiple causes and delayed effects.[90,91]

Trials of vitamin A supplementation for HIV-infected pregnant women reveal the difficulty of attempting to isolate one factor in a complex terrain. Observational studies indicated that women who were deficient in vitamin A were more likely to transmit HIV to their infants,[92] but most trials of vitamin A supplementation failed to demonstrate a statistically significant difference in newborn infection,[93] although one trial supported the hypothesis.[94] Erroneously, some concluded that it is pointless to provide supplements to pregnant, vitamin-A deficient, HIV-infected women, in spite of known benefits of supplementation for women's health. Trial design permits only the conclusion that an intervention is or is not a unique solution. The trial cannot evaluate partial solutions or contributing causes. It does not matter how precise the answers are in such trials; their results are inaccurate because they do not include all causes. They are what physicists have called "not even wrong," because they do not ask the right questions and thus omit relevant data.

The STI–HIV Treatment Trials: Where Context Is Everything

Another example of the attempt to understand HIV without understanding its context is the case of the STI-HIV treatment trials. In the 1990s, a randomized controlled trial showed that even modest efforts to improve the quality of diagnosis and care for STIs in Mwanza, Tanzania led to a nearly 40 percent lower HIV incidence in communities with those interventions than in communities without the interventions.[95] Nevertheless, nine subsequent trials in diverse locations in sub-Saharan Africa using a variety of interventions did not find a statistically significant difference in HIV incidence between two or more randomly selected groups. There were, however, methodological flaws in each of those trials that make it invalid to draw policy conclusions from them. (For citations to all trials, see.)[48]

RCTs require clinical equipoise, which means that the researchers really do not know if the intervention is beneficial, considering both its efficacy and its side effects. STIs are serious, sometimes devastating diseases. Medications to treat almost all STIs were shown in earlier trials to be effective and have few side effects. Observational data and the Mwanza trial indicated, moreover, that STI treatment could decrease HIV incidence. Consequently, ethical conduct in all the trials after Mwanza required that participants in both intervention and control groups in the study received STI treatments. There was thus little difference in exposure (the interventions being tested) between the intervention and control groups and so one could expect little difference in HIV incidence between the two groups. In statistical terms, the post-Mwanza trials were underpowered to detect a statistically significant difference in HIV incidence. Since it is impossible to construct ethical and meaningful RCTs to measure the impact of STI treatment on HIV transmission, it was inappropriate to throw out evidence from scores of observational studies that demonstrated the efficacy of STI treatments and the likelihood of reducing HIV incidence. STI treatment is a neglected intervention in HIV prevention and public health generally. (For examination of numerous other methodological problems with the 9 post-Mwanza trials, see.)[48]

Many policymakers also dismiss treatment of schistosomiasis as an HIV-prevention strategy, citing those same STI trials. There is no doubt that treating schistosomiasis would alleviate substantial urogenital morbidity and other health problems at low cost. What is contested is whether praziquantel should be a standard part of HIV prevention. The observed three- to four-fold increase in HIV acquisition in several studies[39,96] suggests substantial attributable risk and should be sufficient to warrant wide implementation of praziquantel treatment. Given the high prevalence of schistosomiasis, over 120 million infected in sub-Saharan Africa, even a small increase in risk of HIV transmission would generate very large numbers of new HIV infections.

When an intervention is beneficial in itself, is safe, inexpensive, and logistically simple to administer in resource-poor settings, it does not make sense to impose the same burden of proof as one would for an intervention that is untested, or risky, or expensive, or complicated, such as for new drugs in the research phase.[97–99]

Emerging Understanding of Emerging Infectious Diseases

The mucosa of the genital tract is not a mere mechanical barrier. It is more accurate to refer to the microbial community of the genital tract as the ecosystem in which sex takes place. Poor genital health constitutes a disruption of vaginal microbial communities.[91] STIs can cause lesions that later become infected with staphylococci and streptococci. Antibiotics for bacterial STIs are ineffective in treating those secondary infections. Treating schistosomiasis, or STIs, is clearly beneficial, as it begins the restoration of genital health. But each treatment taken in isolation might not register as statistically significant due to the presence of inflammation or lesions from other causes. Recovery of the environmental balance may well exceed the time frame of an RCT. The response to an inadequate statistical methodology should not be to reject a beneficial intervention.

The multiplicity of environmental risks could seem like an insurmountable barrier to HIV prevention. On the contrary, it presents a range of opportunities. Even small improvements in the health of 'sick populations' could have large population-wide effects on HIV spread.[52] In complex systems, small differences in initial conditions can result in large differences in outcomes. Moreover, multiple interactions provide multiple entry points to improve health and improve resistance to new threats.[90]

In order to implement integrated disease prevention and treatment, changes are also needed in the methods of health economic analysis. Just as health research has been limited by a silo approach, economic studies attempt to measure the costs and benefits of interventions in isolation. Treatment for schistosomiasis or STIs, for example, has spillover effects on vulnerability to other diseases, the benefits of which are not generally considered in an economic analysis of a single intervention. This is true for spending outside the health sector as well. One intervention—in sanitation, education, health, job creation—can have multiple beneficial effects that are mutually reinforcing.[100,101] Recognition of spillover benefits and financing interventions across multiple budgets would enable policymakers to have a greater impact in choosing interventions with high impact at lower cost. Solutions to global health problems are easier to identify and cheaper to implement with recognition of the interaction among pathogens, hosts, and the environment, which shapes the context of health and disease.

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