Gender Agenda

We know AIDS in women is different. Now research must tell us how.

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It's no secret that women experience HIV quite differently from how men do. For one, we die faster. When it comes to particular symptoms or drug side effects, there are complex gender differences—more than just the obvious gynecological complications. While women's reduced access to state-of-the-art care contributes to our worse health, differences in physiology and biology also play an important role. Researchers have recognized this disparity with other diseases, but with AIDS, it's been an uphill struggle. And that, in turn, has greatly limited the basic and clinical research that women with HIV need when making life-and-death treatment decisions. To this day, there is no coordinated effort to conduct such research.

Since the start of AIDS, federal agencies have blocked the inclusion of women in meaningful studies, largely because of institutionalized sexism. Researcher Norma Muurahainen, MD, an expert on metabolic function in AIDS, gives this example of the underlying attitudes: "Studying women requires doing pelvic exams, but many male doctors don't know how—or don't want—to do that. One wasting trial of women required measuring clitoral size, which made some male doctors uncomfortable."

Activists have forced new initiatives in women's AIDS research, but there's a long way to go. In 1993, after much community pressure and public humiliation, the CDC reluctantly expanded the AIDS case definition to include some of the conditions specific to women. After that, the number of reports of women with AIDS mounted, but only small trials of women have ever been funded. Six years after its launch, the federal "Women's Interagency HIV Study" (WIHS), which tracks disease patterns, remains underfunded and has offered no guidance to providers who treat women.

And WIHS, like much research, is overly focused on our reproductive organs, such as searching for HIV reservoirs in the vagina. What about other viral hideouts—such as lymph nodes and the brain? Likewise, most federally funded studies of women have focused on pregnancy and HIV transmission. Yet most women with HIV in this country are not pregnant, and CDC statistics show that women are much more likely to be infected by others than to be a source of infection.

Another problem is the severe underenrollment of women in HIV clinical trials. This hinders the

collection of meaningful data about possible gender differences in drug function. I was a coplaintiff in an ACT UP lawsuit that forced the FDA in 1993 to lift its ban on trial participation by women of "child-bearing potential"—but requirements remain to use two forms of birth control. Women now make up 32 percent of the new cases of HIV in this country, yet they make up only 17 percent of participants in federally funded AIDS clinical studies—twice the level of a decade ago, but not enough. Studies by drug companies, perhaps more attuned to changes in their market, have done only slightly better.

In recent years, research on a range of diseases has increasingly demonstrated that clinical trials made up mostly of men do not yield the data that women need. Studies show that women taking certain medications can experience differences in blood levels, toxicities and side effects, compared with men. There are several likely reasons: First, women appear to metabolize drugs differently than men do, particularly during the menstrual cycle. Second, women generally have smaller bodies, which means that the standard dosage can trigger different effects based on gender. But in the field of AIDS, we still have only hints about dosage differences, clues about metabolic differences and suggestions of what viral load levels mean for HIV progression in women.

Women with HIV would benefit tremendously from expanded scientific research that looks at gender differences in the following areas:

Viral load, CD4 count and disease progression
Last year, a Johns Hopkins University study found that among current or former injection drug users, women's viral loads on average were half those of men with similar CD4 counts. No other factor—race, treatment history or use of street drugs—could explain the difference. This was the third recent study to find such a disparity. Researchers concluded that officially recommended viral load counts that determine when to begin antiretroviral therapy should be reduced for women. But the studies to fine-tune that have not begun.

Opportunistic infections, cancers and symptoms
Rates of these conditions vary considerably by gender. Women have more frequent infections of Candida, herpes and certain types of cytomegalovirus than men have. How much of this is biologically based and how much is due to treatment access or psychosocial factors is unknown. And the way these conditions manifest can also vary. For example, a recent study by Italian researchers showed that Kaposi's sarcoma in the lungs is more aggressive in women because of biological differences.

Drug metabolism, dosages and resistance
A 1995 Dutch study found that AZT was released in women's bloodstreams 42 percent more slowly than in men's. The following year, Judith Currier, MD, reported that some women in a federal study (ACTG 175) of AZT and ddI decreased their dosages to avoid side effects, yet they reaped the same benefits as their male counterparts taking the full dosage. The most striking result was in a 1997 study of delavirdine (Rescriptor)—women made up 19 percent of participants—which found that levels of the drug in the bloodstream were 1.8 times higher in

women than in men, although the effectiveness appeared to be identical. With enough research, scientists should be able to determine the correct drug dosage to use to suppress HIV in women.

Side effects, toxicity and interactions

Several studies have found different side-effect patterns by gender. For example, women taking ritonavir (Norvir) experienced more nausea, vomiting, depression and fatigue than men did. And recent studies of antiretroviral-related lipodystrophy have shown that women are more likely to have central fat accumulation, whereas men tend to have higher levels of fat and lower levels of HDL, a blood lipid that can prevent cardiovascular disease. This has led researchers like Julian Falutz, MD, to call for more investigation of the role that women's hormonal activity may play in these differences.

All of this evidence demonstrates the need not only to include adequate numbers of women in clinical trials but to commission specialized all-women studies. Still, women with HIV are left wondering: How long does it take for a drug to clear my body? Why am I intolerant of some therapies? What side effects am I likely to experience? Could my doctor be giving me the wrong dosage? These uncertainties cause many women to postpone or stop therapy—which can significantly impair their survival. At a time when treatment adherence is as valuable as the drugs themselves, doctors expect women to stick to their prescribed regimens based on the clinical trial experiences of only a few. The push for adherence is often so intense that some women suffer harsh side effects in silence.

As the number of HIV infections increases among women, so does the urgency of developing an effective strategy to conduct basic and clinical research. Let's make this October's National Conference on Women and HIV in Los Angeles the launch of a new campaign to implement a research agenda to save women's lives.
