

## Treating HIV/AIDS Patients Until the End of Life

### To the Editor:

We read with interest Palella et al's analysis of mortality trends in the era of antiretroviral therapy (ART)<sup>1</sup> and recognize the importance of such data in considering the needs of those who die as a result of HIV infection. Although the authors conclude that routine screening is necessary to detect the nontraditionally HIV-related conditions that are becoming more prominent in the risk of death, they did not discuss what appropriate intervention is required for those approaching the end of life.

There is no doubt that the current effective management of HIV and AIDS with antiretroviral drugs has had an enormous impact on the quality of life of patients and their families, and on extending good quality of life significantly.

There is also increasing emphasis on comprehensive prevention strategies, a key element in control of the pandemic. The facts that HIV patients die and that patients may experience a host of distressing symptoms during the period of illness before death are still ignored by many clinicians and people living with HIV/AIDS, however. The hope that ART brought to clinicians, patients, and families alike has allowed society to fall back into the comfortable illusion that death does not occur.

Although ART is central to the management of HIV infection, we believe that this has led to less than optimal outcomes for patients and family members. Evidence demonstrates a high prevalence of pain and other distressing symptoms throughout the disease trajectory resulting from the underlying infection and ART.<sup>2</sup> Despite this, HIV-related pain is undertreated,<sup>3</sup> and physicians detect around just one third of HIV-infected patients' pain and symptoms during clinical encounters.<sup>4</sup> There has been a dearth of research activity in this field, despite evidence for the effectiveness of palliative care in managing pain and symptoms for people with HIV disease.<sup>5,6</sup>

Lack of understanding of the complexity and active nature of palliative

care may contribute to the fact that clinicians do not implement palliative care principles alongside disease-oriented treatment. We conducted a systematic review of the abstracts presented at the recent International AIDS Society Conference (Toronto, 2006) to determine the evidence on the relation of pain and symptoms to prevention, treatment, and care and to identify management strategies. Our search strategy included all poster and oral presentations from the database, using search criteria of "pain," "symptom," "terminal," "end of life," "hospice," and "palliative" (combined with the "or" connector).

Of the 4384 presented abstracts, 47 described primary data on pain or symptoms. Interestingly, the range of studies linked the experience of pain and symptoms to a range of prevention, treatment, and care domains. Pain and symptoms were found to have high prevalence and were associated with intolerable ART adverse effects, poor satisfaction with ART, low ART uptake, poor ART adherence, lower quality of life, sexual dysfunction, increased risk behaviors, and poorer ability to provide informal care, and neuropathic pain was found to have a similar prevalence among those who did and did not access ART.

Clearly, the range of data demonstrate the importance of assessing and treating pain and symptoms to those who seek to prevent HIV, maximize quality of life, and ensure maximum treatment outcomes. Neglecting pain and symptom control can reduce the ability to affect other areas of health care activity.

We were concerned to see a large number of presentations reporting high mortality in resource-poor settings (where ART availability is limited) and resource-rich countries (with emerging mortality attributable to malignancies and liver failure), none of which mentioned care for these dying patients. In the era of ART, we also have a duty to care for those who die as a result of HIV/AIDS.

We urge HIV clinical services to learn from the 31 presentations that detailed strategies to control pain and symptoms and to improve advanced and terminal care. Management strategies included palliative radiotherapy; cognitive behavioral therapy; symptom

self-management instruction; changes to therapeutic regimens; and the provision of multiprofessional care for physical, spiritual, and emotional pain management at the end of life. Physical management in palliative care includes treatment support of ART, aggressive management of opportunistic infections, and pain and symptom management.

The World Health Organization (WHO) describes palliative care as an essential component of any HIV care service because of the distressing pain and symptoms experienced from the point of infection to the end of life, and skills to manage these problems are essential.<sup>7</sup> It is important that HIV clinicians develop the knowledge and skills to deliver effective palliative care together with ART to ensure the best possible quality of life for our patients.

There is no dichotomy between pursuing provision of ART and palliative care. Patients require integrated pain and symptom control alongside ART.<sup>8</sup> In addition, we have a duty to provide care throughout the lifespan of the infected patient, which requires the ability to provide appropriate end of life care for the 3.1 million people who died of HIV/AIDS during 2005,<sup>9</sup> even in those countries with universal ART access. Effective palliative care enhances treatment adherence and quality of life. It also ensures control of distressing symptoms and dignity in death for those patients who die from AIDS-related causes.

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## Association of HIV Infection With Poor Genital Hygiene and Medical Treatment for Prior Serious Illness Suggests Iatrogenic Transmission

### To the Editor:

Meier and colleagues' recent report<sup>1</sup> reveals an association of HIV infection in Kenyan men with receipt of medical treatment for serious illness (adjusted odds ratio [OR] = 5.1) and poor genital hygiene (adjusted OR = 0.41 for an index derived from behaviors including frequency and extent of bathing and bathing after sex). The authors interpret the latter result as a consequence of better hygiene reducing the risk of conventional sexually transmitted infections, which, in turn, presumably reduces the risk of sexually acquired HIV. Surprisingly, the authors neither discuss the strong association of prevalent HIV infection with having been "ever treated for a serious illness" nor clarify this variable's content.

Although we heartily endorse the authors' support for good genital hygiene, we also note that their results are consistent with the burgeoning evidence<sup>2–9</sup> for a key role that iatrogenic transmission probably plays in the propagation of HIV in sub-Saharan Africa and other regions with similar epidemiologic characteristics. In sub-Saharan Africa, HIV infection has been more strongly associated with treatment for sexually transmitted infections than with untreated sexually transmitted infections.<sup>5</sup> Inadequate genital hygiene can readily lead to inflammation,<sup>10</sup> which can lead to seeking treatment in formal or informal medical settings. Injection treatment is frequently demanded by patients in Africa or is administered by providers who think their patients expect injections, even when not medically necessary or appropriate.<sup>11</sup> Medical injections have been consistently associated with HIV transmission in many regions with poor medical hygiene.<sup>3,5,9,12</sup>

With cross-sectional data, it can be difficult to infer whether health care-related blood exposures involve HIV transmission or whether HIV-associated illnesses occasion health care-related blood exposures. The available evidence indicates that most of the cross-sectional association between medical injections and HIV infection may be attributable to injections received before the onset of HIV-related symptoms or illnesses. With perhaps a single exception,<sup>13,14</sup> medical injections have been repeatedly associated with incident HIV infection in sub-Saharan Africa.<sup>5,12,15,16</sup> Also, in a large sample of Zambian women without symptoms or signs of HIV infection, medical injections was the strongest correlate of HIV infection and presumed sexual risk behaviors were only weakly, and often inversely, associated with HIV prevalence.<sup>3</sup> Furthermore, a history of tetanus immunization during pregnancy was related to prevalent HIV infection in a national probability sample of Kenyan women; sexual behaviors were uncorrelated with HIV infection.<sup>9</sup> The purely prophylactic nature of the tetanus injections largely eliminates the possibility that injections were sought as a result of illness (reverse causality).

Meier and colleagues' "unexpected" results highlight the need to assess the full range of exposures and use research

designs tailored to the investigation of infectious disease for elucidating routes of HIV transmission, especially in poor countries.<sup>17,18</sup>

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## Response to “Association of HIV Infection With Poor Genital Hygiene and Medical Treatment for Prior Serious Illness Suggests Iatrogenic Transmission”

### Reply:

Brody and colleagues provide a useful critique of our article<sup>1</sup> that questions whether causation can be attributed to the detected association between genital hygiene and HIV-1 status among Kenyan males participating in a study of bacterial vaginosis (BV) in their female partners. They point to a potential confounder, injection treatment for illness, which they argue could possibly explain the associations of “ever treated for serious illness” and the hygiene measure with HIV-1 seropositivity. Previous studies from our group have indeed implicated penicillin injections as risk factors for hepatitis B virus infection<sup>2</sup> and for human T-lymphotropic virus type 1 (HTLV-1) infection<sup>3</sup> but not for HIV infection in female sex workers in another developing country setting.<sup>3</sup>

With regard to the issue of causation, we had stated in our results that “the decreased odds of HIV-1 infection associated with large values of hygiene component 2 suggest an inverse association between good hygiene and prevalence of HIV-1.” In the discussion section, we further stressed our unwillingness to assert causation, citing the cross-sectional nature of our study as a limitation.

Considering injection for illness as a plausible confounder and source of HIV-1 acquisition, we can provide additional clarification about the variables presented. Twenty-one of 150 male participants had been previously treated for a “serious illness,” a self-described condition, which was further specified by respondents: 8 had had tuberculosis (TB); 2 each had had road accidents and ulcers; and 1 each had had allergies, asthma, arthritis, chronic bronchitis, diabetes, hypertension, phimosis, pneumonia, and typhoid. In Nairobi, injection treatment is often used for some but not all of these conditions. It is plausible that some of the association of treatment for a serious illness could be attributable to iatrogenic transmission. The chronologic relation of HIV-1 infection and these illnesses (as with hygiene practices) is not known; however, it is quite likely that the most common of the serious illnesses reported—TB—and perhaps certain others simply reflect complications of HIV infection.

We may not be able to measure accurately whether hygiene, per se, is confounded by injection treatment of genital inflammation or sexually transmitted diseases (STDs). Neither the self-reported measure “number of times treated for an STD” nor “number of times diagnosed for an STD” was significantly associated with HIV-1 status in our cross-sectional study, however, whereas hygiene was. Several other groups have examined the evidence for iatrogenic transmission of HIV through injections in developing countries and have concluded that any role of injections is relatively small compared with the role of sexual transmission.<sup>4–6</sup>

We agree with Schmidt et al that “though there is a clear need to eliminate all unsafe infections, epidemiologic evidence indicates that sexual transmission continues to be by far the major mode of spread” in sub-Saharan Africa.<sup>5</sup>

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## The Need for Partner Consent Is a Main Reason for Opting Out of Routine HIV Testing for Prevention of Mother-to-Child Transmission in a Rural Ugandan Hospital

Across Africa in 2005, <10% of an estimated 13.5 million HIV-infected women accessed HIV counseling and testing (HCT) and <10% of pregnant

women received antiretroviral (ARV) prophylaxis for the prevention of mother-to-child transmission of HIV (PMTCT).<sup>1,2</sup> Studies on the acceptance of HIV testing in PMTCT settings have found that low HIV risk perception and stigma were often associated with not testing.<sup>3-6</sup> Most of these studies were conducted in settings offering traditional (opt-in) rather than universal (opt-out) HCT, however. The introduction of routine opt-out HCT at antenatal care (ANC) clinics using rapid tests with same-day results has been shown to greatly increase the uptake of PMTCT services.<sup>7-9</sup> Although the proportion of women opting out of routine HCT is relatively low, in Africa, each percentage point of women not testing represents nearly 1.5 million women,\* of whom an average of 7% (>100,000 women) can be expected to be infected with HIV.<sup>1,10,11</sup> Thus, as routine HCT becomes the standard entry point to PMTCT programs, understanding the reasons why some women decline the service is increasingly important.

**METHODS**

Tororo District Hospital (TDH) is a 200-bed government referral hospital servicing a catchment population of approximately 1 million people in eastern Uganda. In August 2004, TDH introduced opt-out HCT in the ANC clinic, whereby PMTCT education and HIV testing were provided routinely for all pregnant women unless they declined testing. In December 2004, a similar routine opt-out HCT service was established in the maternity ward for women presenting with undocumented HIV status.

Between October 2004 and June 2005, a sequential sample of 137 pregnant or postdelivery women who declined HCT in the ANC clinic or the maternity ward were asked to answer a short questionnaire about their main reason for opting out. Women provided

consent for participation after being assured of anonymity of the information collected. Those who declined to participate were not asked any further questions. Participants were interviewed in their own language by a trained midwife counselor. Respondents' age, parity, occupation, marital status, educational level, household size, and head of household status were recorded in addition to their main reason for declining to test. Questions related to opting out of testing were asked in an open-ended fashion, and the answers were coded.

All variables with a *P* value <0.05 in bivariate analyses were included in the multivariate model, and only those that remained significant using a backward elimination method were kept in the final model. Logistic regression was used to identify significant associations between reporting the need for partner consent as a reason for opting out and sociodemographic characteristics.

**RESULTS**

Between October 2004 and June 2005, 6.4% (218 of 3392) of pregnant women without a recent documented HIV test opted out of HCT in the ANC clinic, and 7% (25 of 354) of women in the maternity ward without a recent documented HIV test opted out. Five (3.6%) of 137 women declined to respond to the questionnaire. The 132 women interviewed for this evaluation represented 54% (132 of 243) of all women opting out of HCT during that period.

As shown in Table 1, 69% of women interviewed were ≤25 years of age (range: 15–42 years), 90% were married or cohabiting with a partner, 20% had no formal education, 51% had received some primary education, 84% were homemakers or peasants, 59% were nulliparous or primiparous, and 87% had their spouse or partner as the head of the household. There was no difference in age or parity distribution among these women and those who received HCT: the median and mean ages were 23 and 23.6 years (SD = 5.95), respectively, for women who opted out as compared to 23 and 24.5 years (SD = 5.89), respectively, for women who opted in. Median parity was 1 in both groups.

The main reason given for not accepting HCT was the need for

**TABLE 1.** Characteristics of Pregnant Women Opting Out of HIV Testing at Tororo District Hospital, Uganda (N = 132)

Characteristics	No.	
	Women	Percent
Age (y)	n = 128	
15–20	47	36.7%
21–25	42	32.8%
26–30	25	19.5%
31–35	8	6.3%
36–40	5	3.9%
41–45	1	0.8%
Marital status	n = 131	
Married/cohabiting	118	90.1%
Single	13	9.9%
Education	n = 127	
None	26	20.5%
Partial primary	27	21.3%
Complete primary	37	29.1%
Secondary	31	24.4%
Postsecondary	6	4.7%
Occupation	n = 130	
Homemaker	84	64.6%
Peasant	25	19.2%
Teacher	7	5.4%
Trade	7	5.4%
Other	7	5.4%
Parity	n = 107	
0	42	39.3%
1	21	19.6%
2–3	28	26.2%
4+	16	15.0%
Household size	n = 112	
2–4	50	44.6%
5–7	38	33.9%
8–12	20	17.9%
13–27	4	3.6%
Head of household	n = 127	
Self	8	6.3%
Husband/partner	111	87.4%
Relative	8	6.3%
Reasons for opting out	n = 131	
Already tested	14	10.7%
Needs partner consent	67	51.1%
Fears test result or disclosure	19	14.5%
Needs more time to decide	12	9.2%
Fears needle stick	5	3.8%
“Does not like it”	3	2.3%
Does not have the time	2	1.5%
Feels sick	2	1.5%
Fears reaction of relative(s)	1	0.8%
Others	6	4.6%

a partner's consent or presence before testing, accounting for 51% (67 of 131) of all women interviewed (see Table 1). Other reasons included fearing the test result (knowing one's status) or disclosure of the test result to one's partner (15%), needing more time to make a decision (9%), and having reportedly been recently tested (11%). Responses did not differ significantly among women interviewed in the ANC or maternity

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the Centers for Disease Prevention and Control.

\*Based on an estimated 2006 African population of 900 million, 55% of whom are women, 30% of whom are of reproductive age and sexually active.

ward. In bivariate analysis, invoking the need for one's partner's consent was associated with being married (odds ratio [OR] = 15.0, 95% confidence interval [CI]: 1.89 to 119.1), having one's spouse or partner as head of the household (OR = 5.39, 95% CI: 1.45 to 20.0), a household size <5 persons (OR = 2.29, 95% CI: 1.06 to 4.95), having had none or a partial primary education (OR = 2.29, 95% CI: 1.11 to 4.74), and age (OR = 0.93, 95% CI: 0.87 to 0.99). In multivariate analysis, only age (fitted as a continuous variable) and marital status remained significantly associated with women reporting partner consent as a primary reason for opting out (age: OR = 0.90, 95% CI: 0.84 to 0.96; marital status: OR = 23.1, 95% CI: 2.72 to 194.7).

## DISCUSSION

During the 9 months after the introduction of routine opt-out HCT in this hospital, <7% of pregnant women opted out of the service. The age distribution of these women did not differ from those who opted to get tested. Among women who opted out, younger married women were more likely to report the need for their partner's assent to get tested. A similar finding was made among women attending an ANC clinic in Brazil.<sup>12</sup> This is in contrast to the low HIV risk perception and stigma previously found to be associated with opting out of VCT programs.<sup>3-6</sup> A possible explanation might be that the community surrounding TDH has benefited from a sustained home- and facility-based HIV prevention, care, and treatment intervention since 2001,<sup>13</sup> and thus has high awareness and less stigma about HIV/AIDS.

Most women opting out were married and 25 years of age or younger. Thus, others factors not explicitly explored in this study could have better differentiated these women from those who opted in, such as domestic violence, which may be implicit to the need for partner consent or to the fear of disclosure. This is not supported by most studies about HCT and disclosure in sub-Saharan Africa, however.<sup>14</sup> In any case, our results indicate that partner involvement and disclosure may influence the uptake of and adherence to HIV care and

prevention interventions. This may be particularly relevant for young women who have limited access to education and whose partners control reproductive choices and resource allocations within the family, as is the case in many parts of sub-Saharan Africa.<sup>10,11,14,15</sup> In such contexts, it may be important to offer younger married ANC clients enhanced counseling support to empower them to convince their partner to get tested and counseled together with them. Counselors can also assist couple members to disclose their serostatus to each other.<sup>14</sup> At TDH, attempts to increase male attendance at the ANC clinic have been largely unsuccessful, and male attendance has remained at less than 5%.<sup>9</sup> However, we found that many more men accompany their partners to the maternity ward, and accept being tested around the time of labor and delivery.<sup>9</sup> Moreover, as in many health centers in Uganda, in TDH, VCT and PMTCT clinics operate in parallel, with widely divergent male attendance rates. Another strategy involving men that we are thus pursuing is to ask men systematically attending the VCT clinic if they have a pregnant wife or partner attending the ANC clinic, and if so, to offer them posttest counseling together.

Given the high prevalence of HIV serodiscordance among couples in Uganda and Africa and the prevention and care benefits of disclosure,<sup>16-20</sup> pregnant women need to be empowered to appreciate the importance of PMTCT for themselves and their family, to learn their HIV serostatus as early as possible in their pregnancy, and to involve their male partners actively in PMTCT.

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