milliliter. The median total 25OHD concentration was 15.8 (IQR: 9.2–26.6) ng/mL; 60.0% of patients had vitamin D deficiency (<20 ng/mL); and 28.8% had severe vitamin D deficiency (<10 ng/mL). The median $25OHD_2$ concentration was 1.1 (<0.7 to 1.9) ng/mL, and the median $25OHD_3$ concentration was 14.2 (7.7–25.3) ng/mL. The median percentage of total 25OHD that was $25OHD_2$ was 8.5 (4.5–16.0) percent. Consistent with our earlier observations,[8] we noted associations between total 25OHD and ethnicity, season of sampling, and estimated glomerular filtration rate. By contrast, $25OHD_2$ levels were unaffected by age, gender, ethnicity, body mass index, CD4 cell count, season of sampling, or estimated glomerular filtration rate.

Our data confirm the earlier reported high prevalence of vitamin D deficiency and severe vitamin D deficiency in our HIV-positive patients.[8] None of the women in our cohort had $25OHD_2$ >4 ng/mL compared with 7% of those studied by Adeyemi et al.[1] This may relate to differences in food fortification practice, for example, milk in the United States is typically fortified with up to 400 IU per quart (385 IU/L) of either vitamin D_2 or D_3, whereas no vitamin D is added to milk in Britain. The minimal contribution of $25OHD_2$ to total 25OHD levels in our study suggests that previous studies using methods which may have underestimated the contribution of $25OHD_2$ to total 25OHD concentrations are unlikely to have significantly overestimated the prevalence of vitamin D deficiency. For HIV-positive patients in the United Kingdom, sunlight exposure and ingestion of vitamin D_3 are the predominant sources of vitamin D.

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Investigators Involvement in the Care of HIV-Infected Individuals: The Experience in Recent Clinical Trials

To the Editors:

Highly active antiretroviral therapy (HAART) has become the standard for treating HIV infection.[1] The introduction of HAART resulted in an appreciable decline in morbidity and mortality due to HIV infection.[2] An improvement in the life expectancy among subjects with HIV infection receiving HAART has been reported from low-income countries, such as Uganda.[3]

In the December 2010 issue of the Kennedy Institute of Ethics Journal, Wendler and Abdoler[4] raise the issue of investigators' intentions in conducting clinical research and if this would eventually benefit research subjects. The authors conclude that "investigator intentions per se are not relevant to the ethics of clinical research".

Over the last 30 years, research on HIV/AIDS has been constellated of many successes and failures, and there remain with many challenges particularly in prevention and treatment. As Dieffenbach and Fauci[5] have recently pointed out, the critical elements in controlling and ultimately ending the HIV/AIDS pandemic are (1) seek, test, and treat HIV-infected persons; (2) cure at least a proportion of existing HIV infections; and (3) prevent new infections with comprehensive combination prevention programs. Recent experiences in developed and undeveloped countries have been reinforced by recent demonstrations of HIV treatment as prevention in the HIV Prevention Trials Network (HPTN) 052 trial, which shed more light in the field of preventing the spread of HIV/AIDS.[6] In the article of Cohen et al,[7] among the 1763 couples with a discordant HIV serological status enrolled in 9 countries who were randomized to receive an early or a delayed therapy, a total of 39 HIV-1 transmission events were observed and 28 of 39 were genetically linked. Of these 28 linked transmissions, 27 occurred in the delayed-therapy group and only 1 in the early-therapy group, giving a 96% reduction in the rate of transmission. All 27 transmissions in the delayed-therapy group occurred when the HIV-infected partner was not receiving antiretroviral therapy. As the investigators underline, none of these results could have been obtained without a strong and enthusiastic involvement of all physicians and nurses who contributed to the trial, which was conducted between 2007 and 2010.

Recently, other clinical trials have been performed in settings where

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the sexual transmission of HIV is very prevalent, such as the Centre for the AIDS Program of Research in South Africa (CAPRISA)[8] and the Pre-Exposure Prophylaxis Initiative (iPrEx)[9] trials. The intention-to-treat evaluation of such trials did not reach the critical 50% efficacy, nevertheless even small reductions in transmitting HIV infection could be regarded as an important breakthrough considering the deadly toll of HIV. Because the 2 mentioned studies were placebo controlled, their optimistic findings posed renewed ethical questions about placebo-controlled trials to halt sexual transmission of HIV.[10]

In HIV prevention trials, a pivotal effort is to involve subjects and their communities and physicians and nurses in the active participation in the experimental study from beginning to end. As the Declaration of Helsinki states, all potentially enrolled subjects must be adequately informed on all aspects related to the study and on the risks and benefits derived from the study treatments and procedures.[11] After this point, no research is justified without aiming to benefit the single subject who is enrolled in the trial. The Convention of Oviedo (article 2) stresses the supremacy of the human being over any therapeutic intervention.[12] HIV-infected individuals are deeply affected by the disease, both physically and psychologically, and, as care providers, we must always respect the self-determination of a patient seeing a physician who is proposing any clinical trial. The understanding and the assent of the subject to participate in the clinical experiment is the responsibility of the physician, and this responsibility is ethically reinforced by the patient's informed consent. HIV patient care involves a good amount of abilities and emotional participation starting from zidovudine monotherapy trials back in the 80s to the newest randomized clinical trials in 2010–2011. Being an infectious disease physician, the act of enrolling a patient in a clinical trial is already an act of responsibility that you take because you first and foremost seek the good of that particular person. When you inform, get the consent, and enroll your patient in a clinical trial, you make a long-term ethical evaluation.

In principle, the statement by Hans Jonas could be agreed upon, especially when he asserts that each technology is an exercise of the human power, is a "modus operandi"; all human beings are subjected to a moral exam.[13] An ethical evaluation has to be performed when we decide to design and conduct any research activity: In this case, it is more appropriate to talk about an ethical evaluation, which embraces a scientific examination given to any research project.

Considering all the critical aspects within HIV research, both in prevention trials and in specific pharmaceutical trials, we must take into consideration all the ethical issues in protecting human subjects involved in our clinical studies. Most importantly, we should constantly be involved, as recent trials have indicated, in maintaining and updating the patient–physician relationship to the highest standard.

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