

CROSSROADS: WHERE MEDICINE AND THE HUMANITIES MEET

Post-Exposure Anti-Retroviral Chemoprophylaxis for the Human Immunodeficiency Virus: Rights, Duties, and Liabilities

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Growing medical belief supports the hypothesis that human immunodeficiency virus (HIV) infection may be aborted through post-exposure anti-retroviral chemoprophylaxis (1). When initiated immediately after exposure (less than 1-72 hours), anti-retroviral drug therapy is thought to 'inhibit local HIV replication and allow the patient's immune defenses to eradicate the virus inoculum' (1). Following recommendations by the US Centers for Disease Control and Prevention (CDC) in 1995 (2) and by Health Canada in 1997 (3), post-exposure prophylaxis (PEP) constitutes the current standard medical treatment for health care professionals exposed to HIV in the workplace. On October 23-24, 1998, the Canadian Joint Federal/Provincial/Territorial Advisory Committee on AIDS held its first conference to consider the issue of PEP for non-occupational exposure. The title of the conference *HIV Post-Exposure Prophylaxis in the Non-Occupational Setting: Decision-Making in the Face of Uncertainty* alludes to the many ambiguities surrounding PEP. Despite the growing body of evidence in favor of the treatment, many lingering doubts remain over its efficacy, and the practicality of administering anti-retroviral drugs to patients where the certainty of infection from the exposure cannot be verified.

Naturally, such fears engender multiple ethical and legal concerns over whether PEP should be offered to individuals exposed to HIV in the non-occupational setting, and what consequences might arise from not

offering this therapy. This article explores the emerging rights, duties, and liabilities surrounding post-exposure anti-retroviral chemoprophylactic intervention for exposure to HIV. We begin with an overview of the medical basis for PEP, focusing on the unique ethical, economic, and legal issues raised by the treatment. A series of brief hypothetical cases follow, to illustrate and contextualize these concerns.

MEDICAL RATIONALE

Post-exposure anti-retroviral chemoprophylaxis for accidental exposure to HIV was first practiced in the occupational health care setting following percutaneous exposure to infected blood products. Early treatment to abate HIV infection following such incidents consisted of AZT (Zidovudine) monotherapy, and was employed as early as 1988 (4,5). Word of the treatment quickly spread among health care workers, prompting the CDC to issue a position statement in 1990 (6). Although preliminary research conducted in the animal research setting had substantiated the validity of the PEP model (7,8), the CDC could not recommend for or against the treatment, owing to the lack of human studies on its efficacy.

The practice nevertheless continued and by 1995 a retrospective study had documented a 79% reduction in seroconversion risk among health care workers who had pursued a course of anti-retroviral chemoprophylaxis with AZT monotherapy, following occupational exposure (9). Around this same time it was also shown that administration of AZT to pregnant HIV-positive women during pregnancy (orally), delivery (intravenously) and to the newborn, for six weeks after birth, can reduce the risk of transmission by approximately 67% (10,11). Although AZT is the only

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drug that has been found to reduce the risk of HIV infection in retrospective studies of occupationally exposed health care workers, combination therapy is believed to be even more effective for prophylaxis (12). Despite the inherent limitations of the research (non-prospective and non-double blind trial) it is on this basis that PEP has been advanced (13).

In 1995, the CDC reversed its statement and issued a recommendation in favor of PEP following occupational exposure to HIV (2). Surprisingly, no recommendations were made for *non*-occupational exposure. The situation was further complicated by the growing number of authors voicing support for providing PEP treatment in the non-occupational setting. In September of 1998, the U.S. Public Health Service finally issued a statement based on the latest CDC information. Owing to a lack of data supporting the use of PEP for non-occupational exposure, the Public Health Service was “[u]nable to recommend for or against this treatment” (14).

In Canada, medical authorities have been slower in reacting to PEP. Health Canada’s Laboratory Centre for Disease Control did not issue a statement in favor of PEP for occupational exposure until March 1997 (3). The issue of non-occupational exposure is still being worked out. While some provincial governments have drafted model protocols for handling patients who are exposed to HIV outside the occupational health care setting, there remains no consistent approach. The decision whether a patient will receive post-exposure prophylactic therapy for non-occupational exposure to HIV ultimately rests with physicians who must balance a complex array of medical, ethical, and legal concerns.

ETHICAL ISSUES

Perhaps the most obvious ethical issue surrounding PEP is the ostensible double-standard towards treatment. Medical officials in Canada and the United States have already approved the therapy for occupational exposure, but remain reluctant to advise treatment for non-occupational exposure. This reluctance invites serious questions about the degree to which medical professionals can ethically justify, withholding from patients, a treatment that they would not hesitate to prescribe for themselves.

Some have tried to account for the disparity by pointing out the complexity of anti-retroviral drug therapy regimens. A typical PEP treatment regimen begins with an emergency “starter kit” of anti-retroviral drugs found in hospital emergency departments. Treatment is ideally started as soon as possible, and continues for four weeks. Unfortunately, not everyone who initiates the therapy, pursues the treatment regimen to the end of the four week period (15). Many patients

stop taking the drugs because they are unable to tolerate the heavy side-effects, or because they rationalize that their chances of actually becoming infected from their exposure is so low. Given the high rate of virus production and the error-prone nature of HIV replication, the appreciable dropout rate of patients receiving PEP therapy raises the prospect of viral mutation resulting in the creation of treatment-resistant strains.

The threat of drug-resistance brought about by therapeutic non-compliance has given rise to suggestions that treatment be denied to patients who are unlikely to complete the drug regimen (16). While this prospect may seem harsh, consider the predicament of a patient who becomes infected with a treatment-resistant strain of HIV, which evolved as a result of therapeutic non-compliance by others. One of the most troubling aspects of PEP therapy attrition is the presence of occupationally exposed health care workers among the ranks of those who prematurely discontinue therapy. The CDC found that 31% of health care workers who initiate treatment do not complete the full four-week regimen (15). One might expect that health care professionals, who have thus far been privileged in terms of access to PEP therapy, would be more sensitive to the risk of developing treatment-resistant HIV strains through non-compliance.

ECONOMIC ISSUES

Another factor that complicates the decision to offer treatment is the uncertainty of infection. The per-episode risk of HIV infection from unprotected receptive vaginal sex has been estimated at between 5 and 15 in 10,000 (1). For intravenous drug-use exposure, the per-episode risk of acquiring HIV from using a contaminated hypodermic needle has been estimated at 6.7 in 1000 (2). The highest-risk sexual activity, unprotected receptive anal intercourse with an infected partner, carries a 8 to 32 in 1000 risk of seroconversion (1). Ironically, although percutaneous occupational needlestick exposure carries a comparatively low seroconversion risk (3 in 1000), this type of exposure is most likely to result in PEP treatment (3). These numbers should be interpreted with caution since they do not reflect many variables, notably the HIV RNA level in the blood to which a patient is exposed to. A recently infected or advanced late-stage HIV seropositive person is believed to be more infectious than someone whose illness has tapered off to the set point level (3). Other factors that can aggravate seroconversion risks include the amount of body fluids exchanged and the concentration of HIV RNA within the sample (eg., a teardrop vs. a pint of transfused blood) (3).

Since the results of HIV tests will usually only be available after the initial treatment window has closed, treatment must be initiated immediately, before it is known whether the patient has been infected by that particular exposure. Given the unlikeliness of infection from any one particular exposure, the cost of PEP treatment might outweigh its benefits. PEP is very expensive when one considers drug costs, the cost of publicizing treatment availability, and the cost of maintaining “starter kits” in emergency rooms and health clinics. A 1998 Ontario study estimated the cost of PEP combination drug therapy to be \$1,150 for a single four week regimen (13). Treatment costs must be carefully balanced against the adverse side-effects of the drugs as well as the potential long-term medical costs of caring for a patient with full-blown AIDS.

LEGAL ISSUES

In the traditional medical treatment model, the legal obligations of physicians are dictated by the accepted “standard of care”. When novel therapies like PEP emerge, physicians are faced with tough choices. Does PEP constitute: (i) research; (ii) non-validated practice; or (iii) standard practice (13)? The answer will dictate the standard of care and consequent legal obligation to the patient. Based on current clinical practice, and the paucity of controlled case studies, some authors have argued against classifying PEP as standard medical practice since standard practice usually necessitates “a ‘professional consensus’ as to the therapeutic merits of the treatment” (13). Moreover, no studies have yet attempted to validate the use of PEP for non-occupational exposure. PEP may therefore be classified as non-validated practice. Unfortunately, while physicians are obligated to provide treatment that has been validated, there are no well-established legal frameworks for dealing with non-validated therapy (13). Further complicating the issue, is the fact that PEP does not lend itself to controlled case study, and there exists the distinct possibility that no “professional consensus” will ever emerge (13).

Although physicians may not be under a strict legal obligation to provide PEP therapy, the changing nature of medical liability casts some doubt on the ability of physicians to absolve themselves from liability for not providing PEP on the grounds that it does not constitute standard medical practice. The term “medical malpractice” is sometimes used to refer to wrongdoings which fall under the common law tort of negligence. A patient pursuing a claim in negligence against a physician who denied him/her access to PEP therapy would have to establish: (i) the existence of a patient-physician relationship; (ii) that a reasonably prudent physician would not fail to offer PEP for treating

possible exposure to HIV; (iii) that the patient contracted HIV from the exposure for which the physician was consulted; and (iv) that the patient would not have seroconverted if the physician had prescribed PEP drug therapy (13).

Liability standards can change over time, and so while in the past it might have been unimaginable to expect a doctor to offer non-validated treatments to patients, we are arguably moving towards a scenario where such efforts are to be expected. Examples of this phenomenon can be found in several high profile disputes involving novel breast cancer treatments. For instance, in *Fox v. Health Net*, a California woman’s insurance company refused to pay for her autologous bone marrow transplantation treatment on the grounds that this treatment did not constitute standard medical practice (17). Notwithstanding the fact that this treatment was considered “experimental and investigational” at the time it had been requested, a jury awarded the woman \$89 million in damages on the basis of the emotional distress that she and her family had experienced when the novel therapy had been denied.

In practical terms, physicians ought to imagine trying to justify their decision not to offer PEP to a patient, while on the witness stand in a courtroom. In this setting, how amenable will a court be to a doctor who unabashedly acknowledges his/her own inclination to pursue PEP therapy in the event of accidental occupational exposure to HIV, while attempting to justify the denial of similar treatment to a patient, on the grounds that the efficacy of PEP therapy has yet to be verified for non-occupational exposure?

HYPOTHETICAL CASE STUDIES

Hypothetical Case Number 1

A 30 year-old homosexual male presents himself for treatment in the emergency department the morning after engaging in unprotected receptive anal intercourse. The patient had taken the street drug Ecstasy (methylenedioxymethamphetamine) and other stimulants which affected his judgment. The patient demands drug therapy because it was provided by a hospital emergency room when the same situation occurred six months prior.

Judgmental attitudes towards patient behavior appear in the medical literature in terms of questioning treatment for those who engaged in activities which made them more susceptible to HIV infection, and also in terms of therapeutic compliance with drug therapy. For example, the American Medical Association only recommends

anti-retroviral drug treatment for patients who are “committed to the complex, long-term therapy” (16). Although physicians might be able to deny treatment that will not be effective, one author astutely advises doctors “should not turn away patients who repeatedly put themselves at risk for HIV infection”, noting that such patients are in greatest need of counseling and help (1).

In some circumstances, particularly where, as in the case of HIV disease, members of an identifiable class (homosexual men and injection drug users) are disproportionately affected, patients could argue that a denial of treatment constitutes *de facto* or *de jure* discrimination. In *Brown v. British Columbia (Minister of Health)*, the provincial Ministry of Health was sued by a group of HIV patients who were denied funding for Zidovudine therapy (18). Claiming discrimination under section 15 of the *Canadian Charter of Rights and Freedoms*, the patients argued that HIV disease disproportionately affected homosexual and bisexual males (19). The patients also claimed that in refusing to cover the cost of treatment, the British Columbia government was violating the security of their persons which is guaranteed by section 7 of the *Charter*. Both claims were rejected on the grounds that: (i) no direct discrimination could be found, and (ii) the deprivation was economic in nature, since patients were free to make alternate funding arrangements to pay for the drugs. Section 7 does not contemplate economic deprivation (20).

Brown might nevertheless be distinguished from a case involving PEP treatment denial because patients seeking therapy for exposure to HIV are constrained by time. Denying PEP drug therapy during the narrow window of treatment can irreversibly prejudice a patient. Since treatment must be initiated immediately, a patient like the one in our hypothetical case, might successfully sue a physician who denies him PEP therapy, for negligence.

Recourse might also be available, through human rights legislation, against the hospital and provincial or territorial health ministry. This may be particularly true where discriminatory protocols have been drafted beforehand, to systemically exclude certain classes of patients (e.g., injection drug users) from receiving treatment. Since provincial health care plans are not obligated to fund prescription drugs, hospitals might escape liability by providing patients with an emergency starter kit of PEP drugs, and a prescription to cover the remaining treatment regimen.

Hypothetical Case Number 2

A surgeon operating on an HIV seropositive patient pricks himself with a needle containing blood drawn

from the patient. The doctor immediately begins anti-retroviral drug therapy as per hospital policy. Half-way through the four week treatment regimen, the doctor finds the medication’s side-effects too strenuous, and decides to stop taking the pills, rationalizing that since no HIV antibodies have turned up in subsequent blood tests, he was likely not infected by the exposure.

Since PEP is advised for occupational exposure by both the CDC and Health Canada, there remains little question that it constitutes the standard of care for treating occupationally exposed health care workers. More complicated is the issue of non-compliance which could lead to the development of treatment-resistant strains of HIV. Although it is unlikely that sanctions could be imposed on someone who failed to complete a course of HIV anti-retroviral chemoprophylaxis, should such a person be precluded from receiving the treatment again?

Hypothetical Case Number 3

A 21 year-old female student is brought to the emergency department by police after being sexually assaulted by a stranger. The attending physician prescribes emergency contraception (morning-after pill) but does not offer post-exposure prophylaxis for HIV.

This hypothetical scenario draws out the legal issue of informed consent and its relationship to the range of treatment options offered to a patient. Although consent is most frequently discussed in terms of disclosing to a patient the potential risks of a given treatment, the doctrine of informed consent intimates that all reasonable medical treatment options, and their relative merits, have been revealed to the patient.

The leading Canadian case on informed consent is *Reibl v. Hughes* where the Supreme Court of Canada held that physicians must disclose to patients all material risks which might affect their decision to receive treatment (21). A higher standard was established for disclosure with respect to research in *Halushka v. University of Saskatchewan*, where the Saskatchewan Court of Appeal held that physicians providing such treatment must reveal all risks including those which are remote (22). Unfortunately, there are few cases on the disclosure standards for non-validated practice, particularly the degree to which physicians must inform patients about the existence of novel therapies (13).

One of the strongest legal arguments in favor of providing PEP therapy for sexual assault victims is the inclusion of sexual assault as a category contemplated

by some hospital and government PEP protocols. The notion of what constitutes the standards of care is ever-changing, and even though there remains disagreement among scientists as to the benefits of PEP for non-occupational exposure, it is increasingly becoming the accepted standard of care for treating such patients. If one interprets the duty to informed consent found in *Reibl* to include an obligation to fully disclose the existence of therapies which have not been validated, but might still benefit the patient, physicians might be compelled to inform sexual assault victims of the risks of HIV infection and the possible therapeutic benefits of PEP.

Hypothetical Case Number 4

A 25 year-old intravenous heroin user presents himself for treatment after inadvertently sharing a needle with someone whom he knows to be HIV seropositive. The patient had previously been meticulous about not sharing needles, and expresses a willingness to properly follow the anti-retroviral drug regime.

This example once again raises the possibility of discrimination against patients who engage in "risky behavior." The delicate legal issue of patient compliance must be weighed against the prospect that an injection drug user's addiction might be categorized as a disability. Physicians often find themselves trying to compel addicted patients to accept medical treatment, yet in this example the patient has clearly indicated a desire to pursue PEP therapy. Lingering doubts might remain as to whether or not the patient will actually complete the treatment, however, this should not discourage physicians from prescribing PEP treatment. As long as the physician has some reason to believe that the patient will follow the treatment regimen, and that the therapy could be effective, one could argue that there remains an obligation to treat the patient (1).

CONCLUSION

Post-exposure anti-retroviral chemoprophylaxis has already been established as the standard course of treatment for occupational exposure to HIV. As word of the treatment spreads, it is quickly emerging as the standard therapy for non-occupational exposure as well. Although there remain some unanswered medical questions about the effectiveness of PEP, and while some might consider it to constitute non-validated medical practice, physicians need to be aware of the changing nature of medical liability. Liability standards can change over time, and so while in the past it might have been unimaginable to expect a doctor to offer last-

chance unproven treatments to patients, we are fast moving towards a scenario were such efforts are expected. Physicians and health care providers should consider making PEP available to any patient who might stand to benefit from the treatment.

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