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DOI: 10.1056/NEJMc1615253

THE AUTHORS REPLY: Gerhard raises an important question. Iron overload and advanced liver disease have been associated with *V. vulnificus* infection, specifically with septicemia,[1] and experimental models support enhanced vibrio replication in iron-rich environments.[2] Isolated cases of hemochromatosis diagnosis after *V. vulnificus* wound infection have been reported.[3] However, we are aware of no epidemiologic studies of *V. vulnificus* wound infection and iron overload. Given the recognized association of *V. vulnificus* infection with liver disease, which is often coincident with iron overload, we agree that it is prudent for patients with liver disease or iron overload to take precautions with shellfish exposure. In the absence of other indicators of hemochromatosis, the usefulness of screening patients with *V. vulnificus* infection for this diagnosis remains uncertain.

In our patient, iron studies revealed a depressed serum iron level of 16 μg per deciliter (normal range, 40 to 159) and a calculated transferrin saturation of 7% (normal range, 25 to 45). These findings were consistent with hypoferremia induced by acute inflammation,[4] and the values subsequently normalized.

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Since publication of their article, the authors report no further potential conflict of interest.

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DOI: 10.1056/NEJMc1615253

Multidrug-Resistant HIV-1 Infection despite Preexposure Prophylaxis

TO THE EDITOR: Preexposure prophylaxis with emtricitabine (FTC)–tenofovir disoproxil fumarate (TDF) has been shown to be efficacious in preventing human immunodeficiency virus type 1 (HIV-1) infection in men who have sex with men and in whom adherence to treatment is high, as measured by levels of tenofovir diphosphate (TFV-DP) in dried blood spots.[1] We describe a case of HIV-1 infection despite FTC-TDF–based preexposure prophylaxis.[2]

A 43-year-old man in Toronto who reported having sex with men began to receive oral daily FTC-TDF in April 2013 and had seven nonreactive fourth-generation HIV screening tests over the next 21 months. Pharmacy dispensation records provided support for his report of "perfect" adherence to preexposure prophylaxis over 24 months.

On day 0, the initial result of a combination assay to detect antibodies to HIV types 1 and 2 was antigen/antibody-reactive, p24 antigen–reactive, and negative on Western blot testing. This test was followed by screen-positive, p24 antigen–negative, Western blot–negative results 7 days later. Since the level of p24 antigen peaks 3 to 4 weeks after infection and becomes nonreactive at 5 to 6 weeks, this change provided support for the clinical suspicion of HIV acquisition during the patient's reported receptive anal sex with multiple partners without the use of condoms 2 to 6 weeks before day 0.[3] In addition, the infection date estimated by means of viral deep-sequencing analysis (BEAST software, version v1.8.3) was within the exposure period. Details are provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

Liquid chromatographic–tandem mass spectrometric analysis of a plasma sample obtained on day 0 revealed a tenofovir concentration of 152 ng per milliliter; this finding was consistent with recent administration of the drug. Dried blood spots were obtained on day 24 to assess long-term adherence, at which time the expected TFV-DP concentration (±SD) would have been 722±217 fmol or more per dried blood–spot punch had the patient not been receiving FTC-TDF before learning of his infection status on day 4. Steady-state TFV-DP concentrations after 8 weeks of daily FTC-TDF administration are usually 1560±468 fmol per punch.[4] The observed TFV-DP concentration, 2297 fmol per punch, was consistent with long-term adherence.

Genotypic and phenotypic testing of a plasma

Table 1. Results of Genotypic and Phenotypic Drug-Resistance Testing of the Patient's Plasma Sample on Day 7.*

Drug Class and Drug	Drug Resistance on Genotypic Testing	Relative Drug Susceptibility on Phenotypic Testing
Nucleoside or nucleotide reverse-transcriptase inhibitors		
Abacavir	Intermediate	Susceptible (3.9 × IC_{50})
Lamivudine	High	Resistant (more than maximum IC_{50})
Emtricitabine	High	Resistant (more than maximum IC_{50})
Tenofovir	Low	Sensitive (0.6 × IC_{50})
Nonnucleoside reverse-transcriptase inhibitors		
Efavirenz	Intermediate	Sensitive (0.56 × IC_{50})
Etravirine	Intermediate	Sensitive (0.19 × IC_{50})
Nevirapine	High	Resistant (19 × IC_{50})
Rilpivirine	Intermediate	Sensitive (0.53 × IC_{50})
Protease inhibitors: all agents	Susceptible	Susceptible
Integrase strand-transfer inhibitors		
Raltegravir	Intermediate	Reduced response (9.6 × IC_{50})
Elvitegravir	High	Resistant (>100 × IC_{50})
Dolutegravir	Low	Reduced response (2.7 × IC_{50})

* Genotypic results are from standard consensus sequencing and independent Illumina MiSeq "deep" sequencing on human immunodeficiency virus type 1 (HIV-1) protease, reverse-transcriptase, integrase, glycoprotein 41, and V3 regions, with interpretations from the Stanford University HIV Drug Resistance database. Phenotypic drug-resistance testing was performed with the use of the PhenoSense (Monogram Biosciences) assay for the HIV-1 protease and reverse-transcriptase regions and an in-house recombinant phenotype assay (British Columbia Centre for Excellence in HIV/AIDS) for integrase. Mutations included the following: nucleoside or nucleotide reverse-transcriptase inhibitors: 41L, 67G, 69D, 70R, 184V, and 215E; nonnucleoside reverse-transcriptase inhibitors: 181C; protease inhibitors: 10I; and integrase strand-transfer inhibitors: 51Y and 92Q. IC_{50} denotes 50% inhibitory concentration.

sample obtained on day 7 revealed multidrug resistance (Table 1). The M184V mutation, which compromises FTC activity, in addition to several thymidine analogue mutations, revertant substitutions, or both, which slightly decrease TDF susceptibility, probably explain this failure of preexposure prophylaxis. The multiple thymidine analogue mutations detected are unlikely to have been selected in the short duration of drug exposure; this suggests that resistance was transmitted rather than acquired after drug exposure.[5]

Although data from Toronto are not available, in British Columbia, the proportion of patients with a plasma sample containing circulating virus that was resistant to FTC, TDF, or both was 1.7%, 0.004%, and 0.001%, respectively, in 2014–2015. Continued surveillance of mutations that may affect the efficacy of preexposure prophylaxis is needed.

Incident HIV is possible despite adherence to preexposure prophylaxis when persons are exposed to FTC-resistant virus, TDF-resistant virus, or both. We recommend that patients be counseled regarding the use of preexposure prophylaxis as part of a combination approach to HIV prevention.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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DOI: 10.1056/NEJMc1611639