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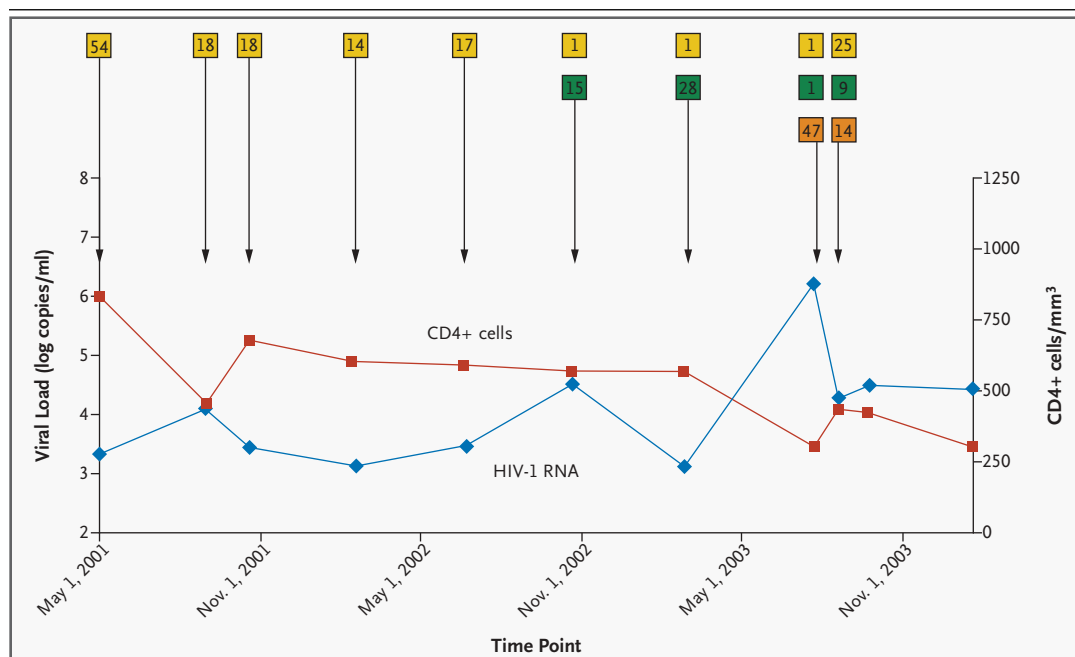
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## Triple HIV-1 Infection

**TO THE EDITOR:** Dual infection with different strains of HIV type 1 (HIV-1) is reported with increasing frequency, attributed mostly to coinfection at the time of the primary infection. However, some patients were superinfected with a second virus after the original seroconversion,<sup>1</sup> which generally accelerated disease progression.<sup>2</sup>

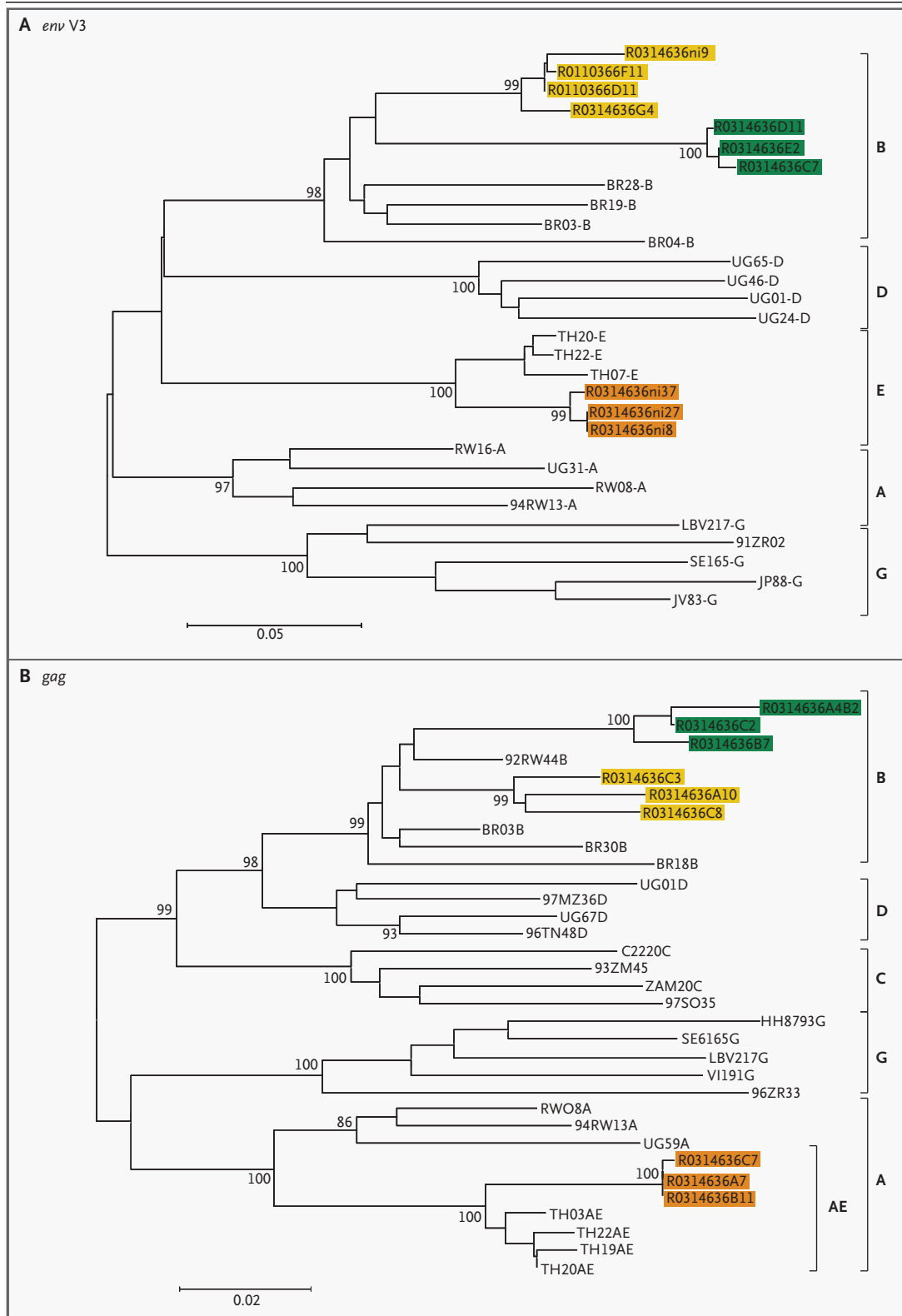
We encountered a case of serial HIV-1 superinfection resulting in a triple infection in a Dutch patient who was originally infected with a subtype B virus. A 35-year-old homosexual man was found to be HIV-1-seropositive in March 2001 and was referred for follow-up. Early in July 2003, the patient

presented with acute onset of fever, rhinorrhea, cough, and arthralgia; the symptoms lasted for approximately one week. A plasma sample drawn during the episode of illness on July 24, 2003, showed an extremely high HIV-1 load with a markedly reduced CD4+ cell count (Fig. 1). Analysis of serial samples for viral genotype provided evidence of a novel HIV-1 infection by a circulating recombinant form 01\_AE of the virus (subtype CRF01\_AE) that dominated the viral population on July 24, 2003 (Fig. 2), and suggested that the patient also harbored a second subtype B virus. An investigation of stored plasma samples indicated that a superinfec-



**Figure 1.** Changes in Plasma HIV-1 RNA Levels, CD4+ Cell Counts, and Viral Sequences in Samples Obtained from a Dutch Patient Serially Infected with Three Strains of HIV-1.

The HIV-1 viral-envelope (*env*) V3 sequences were amplified from plasma with the upstream primer 5'ACAGGCCATGYAMAAATGT3' and the downstream primer 5'CCCCTCCACAATTAARCTRTG3', which can amplify both HIV-1 subtypes B and CRF01\_AE. A reverse-transcriptase-polymerase-chain-reaction analysis was performed as described elsewhere.<sup>3</sup> Fragments were cloned and sequenced<sup>3</sup>; the number of clones obtained is indicated for each subtype of virus (B1 is shown as yellow, B2 green, and AE orange). Additional amplifications with strain-specific primers confirmed the absence of subtype B2 and CRF01\_AE at early time points (data not shown).



**Figure 2 (facing page). Phylogenetic Trees of *env* and *gag* Fragments Obtained from the Same Patient.**

In Panel A, the phylogenetic tree shows the different *env* fragments obtained from the patient at the moment of the second superinfection. Reference sequences were downloaded from the HIV sequence database of the Los Alamos National Laboratory (<http://hiv-web.lanl.gov>). The tree is based on a distance matrix calculated with the use of the Kimura-2-parameter method and constructed with the NJ option available in the Mega software package ([www.megasoftware.net](http://www.megasoftware.net)). Five hundred bootstrap replicates were analyzed. The colors are the same as in Figure 1. In Panel B, the phylogenetic tree shows the different *gag* fragments obtained from the patient at the moment of the second superinfection. The *gag* fragments were amplified from plasma as described elsewhere,<sup>3</sup> with the primers LOUW-1-*gag* 5'TTGACTAGCGGAGGCTAGAA3' and SK39 5'TTGGTCCTTGCTTATGTCAGAAATGC3' and the nested primer set GAG-21 5'GGGAAAAAATTCGGTTAIGGCC3' and GAGAE-3 5'ACTATTTTATTAATCCAGGAT3'.

tion with this second B-type virus (tentatively labeled B2) had occurred between July and October 2002, since the sample obtained on October 22, 2002, was the first to contain B2 RNA sequences (Fig. 1). The patient did not have clinical symptoms nor did his CD4+ cell count decline when he was reinfected with the second subtype B strain, whereas reinfection with a more divergent subtype CRF01\_AE strain resulted in acute viral illness, a prominent rise in viral load, and a decline in the CD4+ cell count. Transient superinfection with a subtype B strain has been reported to produce no symptoms.<sup>4</sup>

It is not clear whether any patient with HIV-1 infection can be superinfected or whether charac-

teristics of the host or viral factors modulate susceptibility to superinfection. The main risk factor for serial HIV-1 infections in this patient was probably his reexposure by way of repeated unprotected sexual contact with other men infected with HIV-1. This unusual case illustrates the potential for repeated HIV-1 superinfection in an HIV-1-infected patient who continues to practice unsafe sex, and it underscores the need for continued preventive efforts aimed at ensuring safe sexual practices even among persons already infected with HIV-1.

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