mutations found in patients experiencing failure raises concerns for the future efficacy of currently recommended second-line regimens based on tenofovir (eg, in WHO guidelines [7]). Combined with the results of other studies [8–11] demonstrating poor sensitivity and specificity of immunological and clinical criteria for detecting virological failure, the findings from these resistance studies raise questions about the sustainability of second-line antiretroviral treatment efforts in resource-limited settings where thymidine analogue–based first-line regimens are still widely used.

The very real occurrence of complex resistance patterns occurring in different viral populations precludes the use of simple algorithms for regimen sequencing after first-line stavudine or zidovudine failure, because there is an increased risk of cross-resistance to other NRTIs. Such studies continue to demonstrate that thymidine analogue–containing first-line regimens do not optimally support a “public health approach” to antiretroviral therapy in resource-limited settings. On the contrary, broad antiretroviral resistance patterns and significant second-line treatment failure should be expected.

It would be instructive to examine the resistance mutations found in each patient in this study, to determine potential second-line regimens for those patients on the basis of available drugs in India. For example, in the Hosseinipour et al study [6], 17% of patients experiencing failure of the first-line regimen had resistance to all NRTIs, leaving only lopinavir/ritonavir monotherapy as their second-line regimen option; additionally, phenotypic analysis showed that 30% of patients experiencing failure were without viable second-line regimens, even when using a 3-drug NRTI-containing option. Guidelines for second-line therapy will now need to be based on a new class of drugs (eg, integrase inhibitors) in combination with a boosted protease inhibitor to have a fully active regimen, because Kumarasamy et al [1] and others [12] have shown that second generation NNRTIs are also likely to be compromised by accumulated NNRTI mutations in a majority of patients. These findings need to be urgently addressed, because we may be embarking on a path to ineffective second-line treatment on a global scale.

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References


The Naming of Strep, with Apologies to T. S. Eliot

To the Editor—Regarding the excellent article on β-hemolytic streptococci by Boyles et al [1], my conclusion is that it is time, altogether, to stop identifying streptococci by hemolytic patterns or Lancefield grouping. Dr Lancefield did her work on group A and B streptococci in the 1930s, and her grouping, together with hemolytic patterns, remains reliable for Streptococcus pyogenes and Streptococcus agalactiae. In contrast, in the case of the other groupable streptococci, the species clearly do not follow so-called Lancefield groupings, nor does it follow hemolytic patterns. For those of us who teach infectious diseases, it is actually an embarrassment to lecture on this subject. Just try explaining to first-year students (or anyone else, for that matter) that individu-
al species of streptococci can fall into Lancefield groups C, F, or G and may be α-, β-, or nonhemolytic.

The following parody on the famous T. S. Eliot poem, “The Naming of Cats” (the basis for the Broadway production of Cats) may be appropriate:

The Naming of Strep is a difficult matter,
It isn’t just one of your holiday games;
You may think at first I’m as mad as a hatter
When I tell you, a strep may have three different names.
First of all, there’s the name that the family use daily,
Such as alpha or beta or gamma—that’s non,
Such as Lancefield Group G or else strep viridans
All of them everyday, sensible names.
There are fancier names if you think they sound sweeter,
Such as bovis, or milleri group or mutants,
All of these also are everyday names.
But I tell you, a strep needs a name that’s particular,
Else how can it keep up its dignity and pride?
Of names of this kind, I can give you a listing,
Pyogenes, pneumoniae or else gallolyticus,
agalactiae, dysgalactiae subspecies equisimilis,
Intermedius, constellatus or just simply canis—
Names that never belong to more than one strep.

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Observational Studies of Salvage Treatment for Persistent Bacteremia: Beware of Survivor Treatment Selection Bias

To the Editor—Jang et al [1] recently published an observational study on the efficacy of linezolid with or without carbapenem in salvage treatment for persistent methicillin-resistant Staphylococcus aureus (MRSA) bacteremia. They found that the MRSA-related mortality rate was lower for patients treated with a linezolid salvage regimen than for patients continually treated with a vancomycin-based regimen (13% vs 53%; P = .030) and concluded that linezolid, with or without carbapenem, produces better outcomes for patients with persistent MRSA bacteremia.

Although they may be right, their manuscript failed to mention a significant limitation of these findings: the survivor treatment selection bias. Indeed, as the introduction of linezolid was treated as a time-invariant factor in their analysis, the authors did not take into account the fact that patients who received linezolid may be different from those who did not, simply by virtue of having survived until the date of treatment alteration [2]. In other words, longer survival may increase the patient’s probability of receiving linezolid and, thus, lead to a survivor selection bias. Of note, in the study by Jang et al [1], there was a trend toward a longer duration of bacteremia in patients treated with a linezolid salvage regimen, with a mean (± standard deviation) of 26.4 ± 38.8 days, compared with 11.8 ± 3.9 days in patients continually treated with a vancomycin-based regimen [1]. Although not statistically significant, which comes of no surprise given the small samples size and the wide dispersion of values, this trend suggests that survivor treatment bias may account for most of the survival benefit attributed to linezolid by the authors. Indeed, if the differences observed were related to the efficacy of the linezolid salvage regimen, one would expect a shorter duration of bacteremia in patients treated with linezolid, compared with patients who continued to receive a vancomycin regimen.

Treatment survivor bias is common in studies published in top medical journals [3] and frequently affects key factors and conclusions [4]. To adequately address this issue, the authors should consider linezolid introduction as a time-dependent covariate in their analysis.

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References