Mortality vs Case Fatality in the Assessment of Sarcoidosis Lethality

To the Editor:

In this issue of *CHEST* (see page 438), the statement by Mirsaeidi and colleagues¹ that “The age adjusted mortality rate for African Americans was 12 times higher than for Caucasians” may lead one to mistakenly infer a far greater lethality in African Americans (AA) than Caucasians (CA). Assuming equal case fatality, mortality will reflect the incidence ratio; AA to CA = 12-13:1.² Multiple series have shown no AA to CA case fatality difference. In a New York City health clinic in which 79% of patients with intrathoracic sarcoidosis were AA, they constituted 66% of those experiencing an adverse course.³ Unadjusted for incidence, mortality rates can lead to absurd conclusions (eg, sickle cell disease is more and Tay Sachs disease less severe in AA than CA).

More frequent suppressive treatment possibly accounts for a secular increase in sarcoidosis mortality. In an ingenious series of experiments using the Kveim suspension to model the genesis of sarcoidosis, Munro inferred that the disorganized early reaction reflected inefficient cell-mediated immunity, leading to the immunologic fallback of a granulomatous response.⁴ This heterodox conceptual framework furnishes a unifying explanation for absence of an identifiable Kveim immunogen, multiplicity of cellular immune deficiencies associated with sarcoidosis, failure to identify the etiology, assorted identifiable causative agents, and the seeming paradox of favorable outcomes associated with the most intense response.⁴ Numerous case reports of sarcoidosis following therapy with immunosuppressant monoclonal antibodies support this view. Most importantly in this context, corticosteroid suppression in early disease demonstrated a long-term adverse effect: A systematic review showed stage-corrected fatality of intrathoracic sarcoidosis in tertiary care settings was greater than sevenfold that reported in primary care settings and was highly correlated with the propensity to prescribe corticosteroid therapy in each tertiary care setting.⁴ Fatality in a case series of conservatively managed sarcoidosis is < 1%.⁴ Johnston⁵ reported no fatality among 159 people with intrathoracic sarcoidosis in whom the sole indication for treatment (required in four people) was progressive pulmonary shadowing. To the extent

that the authors’ analysis fosters aggressive therapy in AA in the belief that they are at markedly increased risk of death, it may create a self-fulfilling prophecy.

Why was a study (Reference 4 [Rybicki et al] in the article by Mirsaeidi et al¹) with anomalous CA incidence data selected for race correction?¹ It lacks the distinctive age 20 to 40-year peak (Fig 2 in Rybicki et al⁶); the age 50 to 69-year ethnic ratio is < 2:1; and 10.9 is twofold to fourfold the US, UK, and Scandinavian CA incidence estimates. Might the high Vermont CA mortality¹ (at α , 0.05 in a multistate comparison) be a statistical artifact?

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Response

To the Editor:

Fatality rate should not be confused with mortality rate. Case mortality rate defines the proportion of people who die of a certain disease; however, mortality rate is the death rate in an entire population. Our study was not designed to find the racial difference in fatality rates.¹

Assuming equal case fatality for African American (AA) and Caucasian patients with sarcoidosis may not be correct. Sarcoidosis among AAs is usually more symptomatic. They experience more extensive pulmonary disease and a greater need for lung transplant.^{2,3} Therefore, assuming equal case fatality for AAs and Caucasians is doubtful.

The statement of a higher fatality rate in tertiary care settings because of corticosteroid therapy use may lead to significant misunderstanding about the role of steroids in current sarcoidosis treatment. The reason for higher fatality rates associated with sarcoidosis could be related to more severe patients being treated in tertiary centers.

Regarding Dr Reich's concern about the study by Rybicki et al⁴ (Reference 4 in our article), we disagree with Dr Reich about any inconsistent incidence results in the study. Cragin et al⁵ reported a statewide prevalence of sarcoidosis in Vermont. They showed that Vermont had a high prevalence of disease (66 in 100,000 population). Therefore, a high mortality rate for this state would not be surprising.

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