Response to: Dr. Reich, Pro rebuttal: The treatment of the granulomatous response is beneficial in acute sarcoidosis

Daniel A. Culver*

Cleveland Clinic, Respiratory Institute, 9500 Euclid Avenue, Cleveland, OH 44195, USA

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While the evidence for benefits from CS might arguably be tenuous, the suggestion of harm from CS is an overstatement of the available data. Whether the conception of the systemic granulomatous response as discussed in the latter half of Dr. Reich’s paper is correct or not is unclear right now. There are data available to support alternative hypotheses, and currently this line of reasoning is purely speculative until proven experimentally.

The contention that CS cause mortality is highly suspect for two reasons: the correlation analysis comparing TCS to PBS is irretrievably flawed, and close inspection of the referenced studies does not support the conclusions reached. Major pitfalls in Dr. Reich’s analysis include substantial indiscernible selection bias inherent in comparisons of TCS to PBS, inability to directly relate use of corticosteroids to the outcome (i.e., death), use of chest radiography alone to control for disease severity, lack of accounting for extrapulmonary disease, and racial/ethnic disparities between studies. A review of the five city series that contributes the largest proportion of patients to Dr. Reich’s analysis confirms the fallacy of this approach: the three centers (Paris, Los Angeles and Tokyo) using CS in 2/3 of their patients exhibited lower attributable mortality (0.4–1.8%) than the two centers (New York and London) that limited corticosteroid use to 1/3 of patients (mortality 5%). Review of the TCS where higher mortality is supposedly linked with the use of CS showed that the authors in those clinics typically reserved the use of CS for symptomatic patients, those with progressing disease or extrapulmonary manifestations.1,2 These are the same indications suggested by Dr. Reich to result in lower mortality with ostensibly more circumspect physicians in PBS.

As discussed previously, many of the controlled trials of CS have major methodologic flaws. In spite of this, review of the available controlled trials does not support the contention of Dr Reich that there is a "2–4-fold excess of adverse outcomes (including mortality) in CS recipients vs. controls". Many of the “adverse outcomes” are based on extremely small differences in proportions of patients in various CXR stages after treatment, often strikingly far below the level of statistical significance. None of the authors of these studies claimed that CS were actually harmful—more usually they opined that CS were neither beneficial nor harmful for changing the natural history. Not one of the studies purports to show a difference in mortality. Conflating all of these small numbers together is not a recipe to draw reliable conclusions. In the more rigorous Cochrane meta-analysis of controlled trials of CS, the authors concluded that the CXR was on-balance improved with CS but that the data did not demonstrate benefit or harm for pulmonary function tests.3

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* Tel.: +1 216 444 6508; fax: +1 216 445 8160.
E-mail address: culverd@ccf.org.
I fully agree that the best indication for systemic therapy of pulmonary sarcoidosis is progressive disease, but we all encounter difficult patients with borderline indications. On which side of the fence should we sit? Right now, the bulk of the best evidence favors cautious, titrated treatment, not observation.

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Conflict of interest

None.

References