practical or ethical in this population, and that these alternative consent methods are also not plausible.

On deciding to undertake a randomized, double-blind trial of olanzapine, midazolam, ziprasidone, and haloperidol to treat agitation, we first consulted our institutional review board. The board has always supported our mission to perform high-quality research in vulnerable populations, and after a full committee review, they approved our protocol pending Investigational New Drug approval. Members of our institutional review board even participated in our community consultation sessions.

Correspondence from the FDA stated that "the study is unapprovable because [you] failed to adequately describe how agitation is a life-threatening situation...failed to adequately describe why patients with agitation are unable to give their consent…and failed to adequately describe why the study could not practicably be carried out without the waiver." We presented facts similar to what Wheeler et al describe, explaining the potentially life-threatening nature of agitation, both because of excited delirium and the potential for missed pathology, but this explanation was evidently not sufficient.

When we were notified of the FDA's decision, the institutional review board shared our disappointment. When our emergency department adopted a clinical protocol standardizing first-line treatment of agitation,[7] the institutional review board fully supported our application to study this protocol under 45 CFR 46.116. Clearly, as the regulations stand, there are gaps that preclude exception from informed consent research in agitation. Recent guidance from the FDA, however, may allow comparative effectiveness trials of drugs to be conducted under 45 CFR 46.116.[8] We hope for future opportunities to collaborate with federal agencies and fellow researchers to overcome these barriers so that we can conduct the research that this population deserves.

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Giant Papillae Versus Lymphoid Follicles of the Conjunctiva

To the Editor:

Trachoma is a cause of blindness that has long been neglected. We were therefore delighted to see material on the diagnosis of trachoma in a recent issue of *Annals*.[1] However, we think the case that prompted the submission of this article is more likely to be allergic rather than infectious in origin, for 2 reasons. First, the reported tearing and itch that were prominent in the history would be atypical for trachoma,[2] but are classic features of an allergic conjunctivitis. Second, the papillary hypertrophy noted by the authors in their description and clearly displayed in their excellent photograph is caused by giant papillae rather than the lymphoid follicles of trachoma. These 2 entities may provoke diagnostic uncertainty; both can cause conjunctival elevation, but giant papillae are relatively translucent, are greater than 1 mm in diameter, and tend to be quite protuberant above the plane of the conjunctival surface, whereas follicles are gray-white, creamy, or yellow, can be as small as 0.5 mm in diameter and still be considered significant,[3] and lie deep to conjunctival

epithelial cells. The surface of the epithelium can be elevated as a consequence of their presence, but not to the extent of the cobblestoning sometimes observed with giant papillae. For the purposes of standardizing population-based surveys to estimate the prevalence of trachoma, intensive training courses are conducted for ophthalmic health care workers.[4,5] For emergency department work, however, reference to the grading card of the World Health Organization simplified system[3] may be helpful.

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In reply:

In the Images in Emergency Medicine article titled "Young Boy With Roughening in the Inner Eyelids," we reported an 8-year-old child with conjunctival hyperemia, increased tearing, moderate itching of the right eye, and intense inflammatory papillary thickening of the upper tarsal conjunctiva of the right eye. The patient was from a city located in the Brazilian Amazon jungle and he was assessed during a national survey of trachoma prevalence in schoolchildren. We considered allergic conjunctivitis within our differential. Giant papillae (papillary hypertrophy) observed in atopic keratoconjunctivitis and vernal keratoconjunctivitis differ from the lymphoid follicles of trachoma. We considered trachoma conjunctivitis because of the intense trachomatous inflammation in addition to lymphoid follicular inflammation, which may explain the exuberant clinical feature mimicking giant papillae. In this case, there was excellent clinical response to antibiotic therapy, and no other treatment was given. Laboratory testing (microscopy of conjunctival scrapings, isolation in cell culture, direct fluorescent antibody, enzyme immunoassay, serology, nucleic acid hybridization probes, and nucleic acid amplification tests)[1] was unavailable for diagnostic confirmation, an admitted limitation of this report. Allergic keratoconjunctivitis was an important part of the differential in this case. Other possibilities included viral and bacterial infections.[2]

The occurrence of trachoma is directly related to low socioeconomic status and poor sanitation conditions, hygiene, and access to water, which favor the dissemination of *Chlamydia trachomatis*, the causal agent of the disease. Although the burden of trachoma has been reduced in Brazil, the disease continues to occur, especially affecting the poorest and most disadvantaged populations in the country.[3]

We appreciate the letter by Talero et al,[4] and we believe that their comments contribute positively to our article, particularly the recommendation of the grading card of the