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EDITORIAL

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# A glimmer of hope for the most vulnerable

In this issue of the *Journal of the American Geriatrics Society*, White et al. present data on SARS-CoV-2 antibody detection in skilled nursing facilities (SNFs) residents. While this study raises as many questions as it answers, it is the first glimpse into the natural immune response of frail elders living in long term care settings. The finding that most residents infected with SARS-CoV-2 mounted an antibody response provides optimism that vaccines may be effective even in this vulnerable population.

Substantial morbidity and mortality due to coronavirus disease 2019 (COVID-19) outbreaks in SNFs have been well documented. Although less than 1% of the U.S. population lives in SNFs, this small fraction of the country accounts for approximately 36% of the deaths, topping 160,000 as of February 4, 2021 (https://covidtracking.com/nursing-homes-long-term-care-facilities). It is not surprising the death rates are high since residents of long term care are generally of advanced age with high rates of chronic medical conditions that are known risk factors for severe COVID. High attack rates of COVID within SNFs, often through asymptomatic and pre-symptomatic transmission from staff and visitors during periods of high community transmission pose significant infection control challenges for policy makers in long term care facilities.[1-3] Mitigation of risk has been relatively successful using frequent testing and restrictions of visitors but has come at a significant cost of social isolation as the pandemic persists. Loneliness, depression, and more rapid cognitive decline among SNF residents have been attributed to the COVID-19 pandemic restrictions who are isolated from family and friends.[4,5]

Developing effective methods of treatment and prevention are critical to ending the current pandemic. Protective immunity can result from natural infection or be induced by vaccination. Correlates of immunity are not presently known but it is presumed an effective immune response will entail both induction of serum neutralizing antibody and a balanced cellular immune response. Studies to date indicate that most persons infected with SAR-CoV-2 develop an antibody response and notably mild disease is associated with a weaker antibody response than moderate to severe disease.[6] Additionally, those with mild illness demonstrate robust type I and II interferon responses, whereas, severely ill patients in intensive care show impaired interferon responses.[7] Immunosenescence is a well described phenomenon associated with aging resulting in diminished immune responses to infections and vaccinations.[8] All arms of the immune system, innate, humoral and cellular function are effected with the latter being most significantly affected.[9]

In part because of concerns that older adults would not respond to active vaccination, monoclonal antibody programs were begun with hopes that passive protection of this vulnerable group could be rapidly deployed if SARS-CoV-2 was detected in an institution.[10] However, the recent evolution of COVID variants with reduced susceptibility to convalescent plasma has raised concerns that monoclonal antibodies that bind to a single epitope would be particularly susceptible to development of resistance.[11] Active vaccination has many advantages compared to monoclonal antibody treatment and has already been instituted in many SNFs with the emergency use authorized mRNA vaccines. Data from phase 1 COVID vaccine trials of healthy older adults have shown equivalent antibody response compared with younger volunteers.[12,13] Most importantly, the recent phase 3 mRNA vaccine trials have demonstrated very high efficacy including persons aged 65 and older.[14,15] Although older adults with chronic medical conditions were not excluded from the efficacy trials, very few residents of long term care facilities were included. Therefore, it is not known if the impressive efficacy of the RNA vaccines in the general population will translate into similar efficacy in residents of long term care. The results of the current study published in the *Journal of the American Geriatrics Society* provide hope that they will.

White et al. took advantage of a large network of long term care facilities to gain insights into the immune response of residents with natural infection. By evaluating 669 SNF residents who had both PCR testing and antibody testing for SARS-CoV-2 they were able to show that 86% of PCR positive residents had detectable antibody after infection. The largest percentage of positive antibody tests was noted within 15–30 days (93.6%) although 88.7% of those tested after 60 days was also antibody positive. These results indicate that frail older adults in SNFs are capable of mounting an antibody response. Unfortunately, the methods do not allow

This editorial comments on White et al. in this issue.

  

further nuanced analysis because testing was performed as standard of care within an institution or at the provider's judgment. In addition, the serologic results were not quantitative, represent binding antibody not functional antibody and cannot be trended in individual infected persons over time. A comparison of baseline clinical characteristics of those persons who developed antibody compared with those who remained seronegative after documented infection might provide useful information regarding risk factors for re-infection or vaccine failures. Nonetheless, these results are an important start and should stimulate further studies in the SNF population to rigorously compare immune responses to both natural infection as well as vaccinations. The large phase 3 vaccine trials may provide correlates of protection in the general population but these data will need validation in this special group.

Another striking feature of this study was the finding that 43% of PCR negative residents had detectable antibody in the months following their initial testing. It is well accepted that accuracy of the PCR testing depends on timing during the infection as well as the adequacy of the sample. No test is perfect, and PCR is no exception. Clearly, a single negative PCR test does not rule out the disease. The authors correctly highlight issues with PCR testing and recommend frequent diagnostic surveillance with a low threshold for testing. Older adults with underlying medical diseases not uncommonly have atypical presentations of infection and may exhibit only a change in mental status or deterioration of a chronic condition.[16] Perhaps of equal importance is that a significant proportion of the population studied had asymptomatic or mild infection that went undetected. Residents of SNFs are at extremely high risk because of congregate setting, age, and frailty and as previously noted account a large percent of the COVID deaths in the United States. It is almost difficult to fathom how such vulnerable people could have only mild or absent symptoms, underscoring the complexity SARs-CoV-2 disease pathogenesis. The scientific and medical communities remain humbled by how much is left to learn but resolute to make progress. The study by White et al. represents a small step forward and provides hope that vaccination of frail SNF residents may be a successful strategy to defeat this formidable enemy and end the social isolation that has devasted senior communities.

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## AUTHOR CONTRIBUTIONS

Dr. Falsey is the sole author.

## SPONSOR'S ROLE

None.

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