

Nonhuman primate models for SARS-CoV-2 research: Infrastructure needs for pandemic preparedness

The SARS-CoV-2 pandemic has significantly increased the demand for nonhuman primates (NHPs), the preclinical model most predictive of disease and treatment outcomes in humans, and for biocontainment laboratory spaces adjacent to facilities housing NHPs. Accompanying this requirement for biocontainment and research laboratory space is the need for skilled personnel to work in these facilities.

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The development of COVID-19 vaccines and therapies required extensive testing of their safety and efficacy in nonhuman primates (NHPs) before these new treatments could be used in humans. NHP studies also provided critical insights into the molecular and cellular mechanisms that underlie SARS-CoV-2 infection and pathogenesis. Results from these investigations allowed researchers to further refine and improve diagnostics, therapeutics, and treatments needed for the fight against the pandemic.^{1–13} The use of NHP models in research will continue to contribute to the development of additional acute therapies and the study of post-acute sequelae of COVID-19 (PASC), or long-term COVID.^{14,15}

The significant increase in research studies requiring NHPs as a result of the COVID-19 pandemic has placed enormous pressure on these valuable animal resources (see [previous commentary in this series](#)¹⁶). The pandemic also has significantly increased the demand for biocontainment laboratory spaces adjacent to facilities housing NHPs. Accompanying this requirement for biocontainment and research laboratory space is the need for skilled personnel to work in these facilities. Failing to sustain or expand the current U.S. NHP resources and expertise will negatively affect our nation's ability to respond to emerging infectious disease threats and to identify and develop new medical products to improve health.

Prior to the pandemic, the supply of NHPs, particularly rhesus macaques and marmosets, already was considered inadequate to support biomedical research funded by the National Institutes of Health (NIH).^{17,18} A sustained increase in funding is essential to provide sufficient NHPs for biomedical research across the spectrum of human diseases, particularly emerging

infectious diseases. NHPs have long lifespans and require years to reach sexual maturity, which affects the availability of these animals for breeding and research and creates delays in studies requiring adult or geriatric NHPs.

Through a collaboration between the Office of Research Infrastructure Programs (ORIP) and the National Institute of Allergy and Infectious Diseases (NIAID), the NIH has provided supplemental funding to support the expansion of domestic rhesus macaque colonies at ORIP-supported resources, which is currently underway. This initial investment, however, is likely to be inadequate as research on SARS-CoV-2 and other infectious diseases continues.

The shortage of NHP resources during the pandemic has demonstrated the critical need for increased access to research containment facilities. Research involving specific infectious agents such as SARS-CoV-2 or Ebola virus requires high-containment laboratory facilities that ensure the controlled and safe conduct of research experiments to investigate these agents. Studies of SARS-CoV-2 and related viral variants require the second highest containment laboratory space, Animal Biosafety Level 3 (ABSL-3) or Biosafety Level 3 (BSL-3) facilities. Such facilities will continue to be required for studies to identify virus–cell interactions, processes, and pathways that result in COVID-19 disease, as well as for studies to improve therapies and preventive interventions. A limited number of BSL-3 laboratories are available at NIH-funded NHP facilities and are usually available to support research conducted by government agencies and both nonprofit and for-profit entities. Recently, however, the large number of studies of SARS-CoV-2 infection in NHPs has resulted in a significant

shortage of available space at these laboratories.

Careful investment in biocontainment facility maintenance and improvement will build the foundation for the research necessary to develop new therapies and vaccines for emerging diseases threatening to create a global health crisis. The NIH responded to this critical need through a collaboration between ORIP and NIAID to fund the purchase of equipment and caging, as well as upgrades to existing ABSL-3 laboratories at NIH-supported NHP facilities. This resource investment facilitated the improvements to existing containment laboratories necessary to expedite SARS-CoV-2 research. The modest increase in housing for macaque colonies and breeding that was supported during the pandemic, however, cannot be expected to meet the needs of continuing research into SARS-CoV-2 and other infectious diseases.

The shortage of ABSL-3 laboratory space is not the only challenge to the optimal use of NHP resources for infectious disease research. A shortage of skilled personnel trained to safely work in this controlled containment environment presents another barrier to research on rapidly emerging infectious diseases, such as COVID-19. Veterinarians, animal care technicians, and facility maintenance staff, among others, all need specialized training to ensure a fully functioning and safe containment laboratory environment. The success of any investment in NHP resources and research infrastructure will depend on investment in teaching research teams the skills necessary to operate effectively in a containment setting.

Sustaining and increasing NHP research capacity will require careful preparation

and collaborations to improve existing infrastructure and expand established facilities, expertise, and programs. Such an effort would not only bolster NHP resources available to meet the current demand for SARS-CoV-2 research but also provide resources for research on future emerging pathogens. The NIH is in the process of planning critical NHP resource capacity needed to maintain responsiveness to emerging health challenges and to meet current research needs. A successful response will require several years and investment in NHPs, facilities, equipment and the skilled personnel who do the work.



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