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Pair Housing of Macaques in Research Facilities: A Science-Based Review of Benefits and Risks

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Despite the enactment in the early 1990s of regulations requiring social housing of nonhuman primates (NHP), single housing is still prevalent in American research facilities. The publication of the 2011 edition of *The Guide for the Care and Use of Laboratory Animals* has increased emphasis on the implementation of social housing as the default housing method for NHP. Overestimation of the risks inherent in social housing coupled with underestimation of both the benefits of social housing and the risks inherent in long-term single housing has prevented large-scale transitions to social housing. Available caging and housing space often requires research facilities to use isosexual pairs to accomplish social housing. Pair housing presents unique challenges but can be used safely with a thorough understanding of macaque ethology. Here we review literature on the risks and benefits of pair housing macaques in research facilities and provide a concise best-practice approach to pair housing.

Abbreviations: ILAR, Institute for Laboratory Animal Research; NHP, nonhuman primates; USDA, US Department of Agriculture.

In 1985, Congress passed the Improved Standards for Laboratory Animals Act which, among other things, required research facilities "to promote the psychological wellbeing of nonhuman primates"[2] (NHP). After years of input from a spectrum of groups including researchers, animal rights activists, and laboratory animal veterinarians on how to achieve this congressional mandate, the US Department of Agriculture (USDA) adopted regulations requiring research facilities to establish an appropriate plan for environmental enhancement that specifically addresses social grouping. At minimum, the regulations require the written plan to include "provisions to address the social needs of nonhuman primate species known to exist in social groups in nature."[3] To meet the terms of the regulations, research facilities must provide social housing for NHP reflecting currently accepted professional standards in the field.

These regulations exemplify the focus on performance standards that predominates in the United States. Importantly, these types of regulations allow requirements for compliance to evolve over time without the need for lengthy review processes. Reflecting the accepted standard in the late 1950s, one author wrote that "unquestionably, [rhesus macaques] involved in experiments should be housed in individual cages."[19] Since then, the natural history of macaques in the wild has been well-described, and that macaques have specific social needs is generally accepted. Despite the history of NHP being housed in single cages, social housing is the current professional standard for NHP in research facilities and therefore is required for compliance with the Animal Welfare Act unless scientific necessity for individual research protocols or veterinary-related concerns for individual animals necessitate an exemption.[3,24] The Institute for Laboratory Animal Research (ILAR) emphasizes that "social interactions are considered to be one of the most important factors influencing the psychological wellbeing of nonhuman primates. *Knowing that most primates benefit from social interactions, it should be obvious that they can be harmed by a lack of social interaction* [emphasis added]."[23] The International Primatological Society writes "pair or group housing in an enclosure must be considered the norm" for NHP.[25] AAALAC has adopted the position that social housing of social animals is considered the "default method."[4] Although researchers, laboratory animal veterinarians, animal husbandry staff, and IACUC are principally concerned with animal welfare, this new regulatory focus on social housing forces these stakeholders to evaluate their programs closely for methods to provide the social interactions that NHP require for psychologic wellbeing. Despite IACUC oversight of animal programs, specific regulatory or accreditation requirements have initiated enhancement of animal care programs more often than have IACUC reviews, suggesting that stakeholders from within each program should work to improve their animal care practices before external regulations require it.[5]

Despite the enactment in the early 1990s of USDA regulations requiring social housing of NHP, the number of NHP socially housed in American research facilities largely has remained unchanged. In fact, a survey published in 2007 found only 44% of macaques housed in cages or small indoor enclosures were socially housed compared with 38% in a 1994 survey.[8,50] Importantly, the latest survey included grooming-only contact in its definition of social housing, whereas the initial survey only included full-contact pairs as socially housed. This distinction, coupled with a recent report on rhesus macaques finding that grooming-only contact does not provide an equal benefit to full-contact housing,[7] demonstrates the lack of substantial expansion of social housing for caged macaques. The various causes of this lack of change in housing of NHP have been explored in other reports.[5,47,57] In our experience, a general lack of a balanced understanding of the risks and benefits of social housing among stakeholders including researchers, animal care technicians, and laboratory animal veterinarians is the greatest roadblock to transitioning singly housed monkeys into compatible groups. However, pressure on research facilities

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using NIH funding to socially house NHP has been increased by publication of the 2011 edition of *The Guide for the Care and Use of Animals*, which emphasized social housing as the "default" for all social species.[24] Enrichment coordinators, laboratory animal veterinarians, and other stakeholders responsible for maintaining regulatory compliance must develop a thorough knowledge of the risks and benefits of social housing of NHP, its implications for biomedical research, and a best-practice approach to minimize significant injuries to shift the paradigm regarding housing of NHP in research.

Facilities with relatively few primates housed in indoor cages struggle to increase the proportion of NHP that are socially housed.[7] These facilities often must use isosexual pairs to fulfill social needs, given the constraints of available caging, housing space, candidates for social housing, and the need to avoid breeding. Although isosexual pairs are not found in nature and present unique challenges to research facilities, this housing arrangement fulfills the spirit of the regulations requiring social housing. In the current report, we review the current literature on pair housing of research macaques to provide a science-based assessment of benefits and risks associated with both pair and single housing and to provide a concise summary of recommended partner selection, pairing procedure, and postpairing monitoring. In addition, we use examples from our experiences in our AAALAC-accredited facility to demonstrate the feasibility of transitioning previously singly housed macaques into compatible pairs.

Beneficial Effects of Pair Housing

Abstract generalizations regarding the benefits of social housing for NHP are difficult to communicate to investigators. The use of conceptually subjective terms such as 'psychologic well-being' has complicated efforts to convince all stakeholders of the objective benefits of social housing. To reduce the subjectivity in the assessment of psychologic wellbeing, ILAR established 4 criteria by which to judge the success of an institution's plan to promote psychologic wellbeing.[23] These comprise the: ability to cope effectively with day to day changes in the social and physical environment; ability to engage in species-typical behavior such as foraging and grooming; absence of maladaptive or pathologic behaviors that result in self-injury; and presence of a balanced temperament (balance between aggression and passivity) and absence of chronic signs of distress.[23] Although these criteria are themselves somewhat subjective, they do provide some measurable traits of a psychologically well monkey. The literature demonstrates the effectiveness of social housing in addressing each of these criteria.

Ability to cope effectively. There are reports in the literature suggesting that socially housed animals are able to cope more effectively with changes in the laboratory environment.[18,21,67] Rather than being a source of distress, a compatible companion serves as a social buffer during potentially stressful situations. For example, the stress response of rhesus macaques (as determined by T-lymphocyte subsets and serum cortisol concentrations) transferred to an unfamiliar environment was modulated by the presence of a compatible conspecific.[21] Similarly, rhesus monkeys displayed fewer abnormal behaviors when exposed to common laboratory stressors such as the restraint and anesthesia of other monkeys in the room when subjects were pair-housed compared with when the same monkey was single-housed.[18]

Demonstration of species-typical behavior. Studies of wild populations have shown that rhesus and cynomolgus macaques spend 5% to 25% of their time interacting with each other through grooming and other social activities.[12,30,36,70] Singly housed macaques are deprived completely of grooming and other species-typical social behaviors. In a research setting, singly housed rhesus macaques displayed a high degree of affiliative contact with same-sex neighbors through the front bars of cages that did not permit the animals visual contact with each other.[5] These findings indicate the importance to the animal of physical contact with a conspecific.

Although single housing may allow noncontact social interactions, full physical contact provides a greater opportunity for species-typical behavior than does visual-only or protected physical contact, regardless of age.[7,11] For example, rhesus macaques spent significantly more time engaged in affiliative behaviors in full contact than protected contact.[7] In full-contact pairs, female rhesus macaques spent 80% of their time at night and 40% during the day in either physical contact or close proximity.[17] Similarly, female cynomolgus macaque pairs groomed each other 31% of the time.[32] Male macaque pairs also demonstrate species-typical allogrooming (Figure 1). Among compatibly paired adult male cynomolgus macaques[15] and compatibly paired adult male rhesus macaques,[16] the monkeys groomed each other 17% of the time.[15,16] This time allocation reflects a more species-appropriate time budget than does the 0% possible for singly housed monkeys. In addition, the time allocation of socially housed rhesus macaques for time feeding and exploring was closer to that of wild counterparts than was that of singly housed animals.[63] Importantly, these species-appropriate time budgets are maintained in compatible pairs over periods substantially longer than those supported through inanimate enrichment items.[43]

Absence of maladaptive behaviors. Singly housed rhesus macaques spend more time engaged in stereotypic behavior and demonstrate a wider range of maladaptive behaviors than do socially housed NHP.[9] In addition, the occurrence of stereotypies has been positively correlated with the length of time macaques are singly housed.[10] For example, in one study, some form of stereotypic behavior was observed in 89% of singly housed rhesus macaques.[33] Although locomotor stereotypies are most common, approximately 10% of singly caged rhesus macaques develop self-injurious behavior.[41] Social housing can ameliorate these maladaptive behaviors. One study reported halving the incidence of self-plucking in singly housed female rhesus macaques by forming compatible pairs (although the difference was not statistically significant).[17] Correspondingly, pair-housed rhesus macaques spent less time self-grooming and behaving abnormally than did age-matched, singly housed macaques.[62] In another study, self-biting in 7 singly housed rhesus macaques was eliminated completely within 2 mo of transition to compatible pairs.[55] In another study, 6 single-caged rhesus macaques who engaged in self-biting were vasectomized to permit pairing with adult female macaques—3 of the male macaques stopped their self-injurious behavior within a month, whereas the behavior of the other 3 was moderated, but not eliminated.[72] This study[72] not only demonstrates a therapeutic effect of social housing but also shows how a thorough understanding of NHP biology and use of colony management techniques can be used to achieve social housing in research facilities.

Some maladaptive behaviors may not indicate a present source of distress. An example is the long-lasting effect of a lack of maternal contact in infancy. Behavior formed as a coping mechanism in infancy may not change in response to subsequent changes in housing.[35] In addition, NHP exhibiting self-biting should undergo a thorough physical examination to rule out medical causes of the behavior before diagnosing a psychological

Figure 1. A pair of water-restricted adult male rhesus macaques with cranially implanted recording chambers. These monkeys had never been pair housed previously but were introduced successfully after a noncontact familiarization period.

disturbance. Transitioning an NHP to social housing may not modify these types of maladaptive behaviors.

Presence of a balanced temperament and absence of chronic distress. When regulations requiring social housing were first adopted, several publications proposed that a forced living arrangement with an incompatible partner could be the source rather than the cure of chronic distress.[26,32] However, the same stimulus that occasionally causes distress, such as the presence of a partner, might also provide a benefit that outweighs the initial or potential distress.[66] Although socially housed NHP may experience stress, especially in the period surrounding introductions,[13,14,21,31] the importance of social interactions with conspecifics, especially early in life, is well established.[10,33] A compatible partner may at times be a source of stress, but the presence of occasional environmental stresses does not necessarily translate into chronic distress.[23]

ILAR recognizes "the presence of affiliative verses distress vocalizations, facial expressions, postures, and physiological responses" as indices of a balanced temperament and psychologic wellbeing.[23] Numerous studies have investigated the physiologic and behavioral response to single and pair housing. One study found no elevations in heart rate during or fecal cortisol concentration after introduction of adult male rhesus macaques to compatible pairs, and fecal cortisol concentrations were higher when monkeys were singly housed.[16] Some comparisons of serum or fecal cortisol concentrations between singly and pair-housed monkeys have found that pair-housed monkeys have lower cortisol concentrations,[16,58] whereas other studies have not found a significant difference.[15,48,61] However, singly housed NHP develop hematologic profiles suggestive of immunosuppression and experience higher incidences of coronary atherosclerosis.[29,65,68] The evaluation of plasma prolactin concentrations indicates that single housing of female rhesus macaques resulted in higher levels of anxiety.[29] In addition, these singly housed rhesus macaques showed a long-term decrease in norepinephrine that was interpreted to be physiologic evidence of depression that correlated well with behavioral observations that included crouching, huddling, and overall inactivity.[29] Although cortisol is not consistently elevated during single housing, other physiologic and behavior studies have consistently concluded that singly housed macaques experience chronic distress.

Assessment of Risk

Concerns about an unacceptable risk of harm to research subjects as a justification for single housing often are based not on peer-reviewed literature but on personal experience, anecdote, or a failure to scientifically evaluate risk. Although pair housing certainly is associated with some risk, no reports currently in the literature document death or even severe injury requiring euthanasia after an unsuccessful attempt to pair-house macaques.[60]

Balancing any potential risks associated with pair housing are the risks associated with long-term single housing of research animals. Serious forms of stereotypies (such as self-biting) increase with the number of years that NHP are individually housed.[33] In one survey, self-biting was noted in 25% of singly housed macaques with 10% of these developing wounds requiring veterinary intervention.[33] Research subjects displaying this type of psychologic distress may not provide accurate data, complicating efforts to replicate results and leading to greater cost in terms of both animals and time required to obtain meaningful results.[53,67] Social housing, like all other forms of enrichment, is a research variable that should be controlled.[33,41] The responsible conduct of high-quality animal research requires the research community to carefully balance the need to minimize potential confounds to research variables with the need to maximize psychologic wellbeing.

Countering the perception that social housing is associated with greater injuries, one study found that pair-housed rhesus macaques required less veterinary treatment than did singly and group-housed animals.[64] Those results agreed with a retrospective analysis of veterinary records, which showed that the incidence of nonresearch-related veterinary treatment was 23% for single-caged animals compared with 10% for pair-housed animals.[36,47] Another study found that only 3 of 228 (1.3%) paired rhesus macaques required veterinary care due to injuries over the course of 1 y (including during initial pairing) and that none of these injuries were life-threatening, although compatibility rates (as defined by adequate food sharing and absence of serious injury and depressive behavior) were lower than these injury rates may suggest (83% for males and 89% for females).[54] These analyses of veterinary records include treatments for numerous conditions including diarrhea-causing agents common in research facilities, suggesting that pair-housed animals are more resistant to these infectious agents than are singly housed animals.[67] Overall, the data indicate that pair housing of macaques does not result in a greater need for veterinary care.

Macaques can safely be housed in compatible pairs in a variety of configurations, provided that pairs are evaluated during familiarization periods prior to being allowed full contact. Although a large proportion of pairs can demonstrate incompatibility during this period, animals that pass through this stage have a high likelihood of successful pair formation with minimal injuries.[46,55,73] Isosexual pairs can usually be formed with juvenile animals with minimal risk and a high success rate. One investigator transferred a total of 84 female and 22 male juvenile rhesus macaques to same-sex pair arrangements with 100% success with the initial pair selection.[51] Similarly, we have transferred 10 female and 8 male juvenile cynomolgus macaques at our facility into same-sex pairs with 100% success. In addition, adult female macaques are considered relatively compatible in

isosexual pairs. For the current discussion, we have defined success as pairs that remained in full contact at least 2 wk after initial pairing. These success rates do not include potential pairs that were not allowed full contact due to poor interactions during the familiarization period. Several other reports describe the formation of female pairs of both cynomolgus and rhesus macaques without incident and with success rates near 100%.[15,27,51] However, these high success rates are not uniform. One author reported success rates as low as 53% for female pairs, depending on the method of introduction.[69] Although generally not severe, injuries can occur in female pairs.[51,56,73] We have seen female rhesus macaques engage in aggressive contact after pairing but without subsequent injuries requiring veterinary care. Alternatively, juvenile animals can be paired with adults, with rare incompatibility. Because adult animals generally do not exhibit aggressive behavior toward juveniles,[47] the formation of juvenile-adult pairs is particularly attractive for adult animals that may have demonstrated aggression toward peers in the past.

Adult male macaques have the reputation of being too aggressive to be maintained safely in compatible pairs.[57] However, in one study, although adult male rhesus macaques displayed dominance-related behaviors more frequently than did female macaques, male macaques did not engage in more aggressive behaviors more frequently. [45] The author concluded that "aggressiveness is an individual attribute that is (1) independent of dominance status and (2) independent of sex."[45] The distinction of aggression being the trait of an individual animal rather than its sex has important implications, given that male NHP are often preferred as research subjects to avoid interruptions in research associated with the female menstrual cycle. In fact, one author found that fighting occurred within 30 min of formation in 2 of 77 female rhesus macaque pairs that had formed an obvious dominant–subordinate relationship prior to full contact but in none of 20 male pairs familiarized in the same way.[51] A later report recounts the transfer of 817 rhesus monkeys (including 67 adult male–male pairs and 83 adult male–infant pairs) into compatible pairs, with male monkeys being no less tolerant of their companions than were female macaques.[56] Similarly, another study that included 92 female and 28 male adult rhesus macaques found no sex difference in a wounding index based on frequency and severity of wounds when transitioning previously singly housed animals to pair housing.[42] Another investigator achieved 100% compatibility when transitioning 8 previously singly housed adult male rhesus macaques into pair-housing.[16] However, despite a high potential for compatibility of adult male rhesus macaques, high success rates are not universal. One author achieved only a 68% success rate despite the use of a familiarization period.[38] Success in pairing can depend on the species of macaque.[28] Pair housing of adult male cynomolgus macaques has been associated with a lower success rate than that for adult male rhesus macaques.[13,15,20,34] Among adult male cynomolgus macaques that were paired to study effects on testosterone, only 44% of the initial pairs achieved success.[13] The report seems to suggest that the author did not allow a sufficient familiarization period for animals to form dominant–subordinate relationships. However, despite a familiarization period and although 100% compatibility was achieved in adult female pairs, only 53% of adult male cynomolgus monkey pairs were successful in another study.[15] In contrast, other authors report 94%[34] and 100%[44] success in pairing adult male cynomolgus macaques when using a familiarization period prior to full contact. Similarly, only 2 of 31 pairs (6%) of adult male cynomolgus macaques that had passed through a noncontact familiarization period sustained injuries requiring separation.[71]

These high success rates are based on appropriate pair selection during a familiarization period prior to allowing full contact. Animals should be closely monitored for compatibility in a visual-only or protected contact period to minimize the occurrence of injuries after free contact is established. The potential for incompatibility is high during these familiarization periods. In one report, 7 dyads had to be tested to form 5 pairs of adult male rhesus macaques that demonstrated clear dominant–subordinate relationships prior to full contact.[46] One author found 26% of young adult rhesus macaque pairs to be incompatible during compatibility testing prior to full contact.[73] Although pairs that are deemed compatible during the familiarization periods are not guaranteed to be successful in full contact, these periods do provide the opportunity for formation of dominant–subordinate relationships that will obviate the need for aggressive contact. This method of socialization presents a relatively low risk for serious injury and allows behavioral managers to demonstrate a thoughtful, deliberate approach to social housing.

In our facility, NHP are used primarily in neuroscience and behavioral research, which often requires cranial implants, scleral search coils, or controlled access to food or water. Initially, investigators resisted social housing of their subjects because of concerns over potential damage to cranial implants. However, macaques that undergo surgery or have surgically implanted devices can be paired successfully even immediately after surgery. After IACUC review of these protocols and our animal care and use program, we successfully transitioned 18 cranially implanted macaques into isosexual pair housing without injury after providing a noncontact familiarization period (Figures 1 and 2). These included pairs of adult male rhesus macaques, adult male cynomolgus macaques, adult female rhesus macaques, and adult–juvenile rhesus macaques of both sexes. Five of these pairs comprised water-scheduled animals performing behavioral tasks, and 4 pairs had scleral search coils. Among these animals, one pair of adult male rhesus macaques interacted aggressively after free contact, resulting in damage to one animal's head post, which had to be removed. The head post, which the investigator indicated was loose prior to pairing, was damaged when it hit the side of the cage (rather than due to direct contact by its partner), and the 2 animals subsequently again were paired successfully. Comparable to our experience, one author reported 92% compatibility in pairs of adult male rhesus and long-tailed macaques implanted with head restraint posts and scleral search coils.[60] In the cited study,[60] damage to the head restraint post and the eye coil did not occur even in incompatible pairs. Others have demonstrated that pair housing does not interfere with surgical implants.[59] In one study, female cynomolgus macaques were returned to a compatible pair on the same day as a surgical intervention, without changes in social structure or complications with healing.[37] Similarly, adult male rhesus macaques experienced no damage to previously implanted biotelemetry devices when transitioned to pair housing.[16]

Physical injury to animals or surgically implanted devices is not the only concern in pair housing macaques participating in research studies. For instance, the dominant partner may monopolize food, water, or enrichment devices, resulting in malnutrition of the subordinate animal.[40,41] Successful pair housing reportedly has not been associated with weight loss.[52,60] However, we observed weight loss in an otherwise compatible pair in our facility; because the animals in this pair exhibit a

Figure 2. A pair of cranially implanted male rhesus macaques. After a fight with another male monkey, the adult male macaque had been singly housed for several years. He began grooming the juvenile macaque within 20 min of pairing, and the 2 monkeys have remained compatible.

high degree of affiliative contact, they are separated for feeding but remain socially housed. In addition, some parameters important for toxicology studies, such as growth rates and testicular volume, can be affected by social housing, whereas other parameters, such as ejaculate volume and quality and endocrine profiles, are not.[39] Furthermore, social housing can alter a subject's participation in behavioral tasks. For example, one author found that paired rhesus monkeys in behavioral research did not perform certain tasks as effectively as did age-matched, singly housed controls, but performance at other tasks was unaffected.[22] However, another study found that pair housing of water-restricted adult male rhesus macaques with cranial implants and eye coils did not affect task performance.[60] In our experience, motivation to participate in behavioral tasks can fall immediately after pairing but returns to normal after 1 to 2 wk. This potential to alter the rate of data collection should be considered when selecting the most appropriate time to transition animals to social housing, and researchers should be warned to expect suboptimal performances for a period after introduction of pairs.

Establishing Compatible Pairs

Numerous methods of choosing appropriate cagemates exist in the literature, including random selection,[54] algorithms assessing temperament to pair dominant NHP with subordinate animals,[34] and maximization of size disparities to pair larger animals with smaller ones. Although some studies have found that weight or weight difference has no effect on the success of pairs,[28,73] studies comparing success rates after various pair selection methods are few. More research is needed to determine the effect of age, age disparities, weight, weight disparities, species, cage size and layout, the presence of opposite sex animals in the housing room, and other environmental factors on the success of pair housing. In addition, we have found that a singly housed macaque perceived to be especially aggressive toward people may become the subordinate animal when paired; therefore more studies are needed to develop an accurate temperament assessment of macaques that can predict one animal's compatibility with other macaques. However, one study found that observations of the general behavioral characteristics of singly housed adult rhesus macaques were not useful for predicting the ultimate success of social introductions.[38] Although collecting and processing information regarding paired animals demonstrates a thoughtful approach, restrictions to the pool of candidates available for pairing at small facilities or in studies with few subjects may prevent pairing of 'dominant' or large monkeys with 'subordinate' or small monkeys, and these guidelines should not be viewed as absolute requirements for successful pair housing.

To reduce the risk of serious injuries, NHP should be allowed a familiarization period with visual cues to establish dominant–subordinate relationships before having free contact.[40] Although protected contact strategies (in which animals can engage in physical contact through perforated panels, cage mesh, or bars) can be used as an intermediate step prior to full contact,[1] introducing animals directly into full contact was more successful than was a procedure that included a protected contact cessation period in one report.[69] Whichever method is chosen (visual only or protected physical contact), animals must be monitored closely during this familiarization period for the formation of a dominant–subordinate relationship that obviates the need for aggressive contact.[49] To minimize risk and maximize success, new partners should be sought for animals that do not demonstrate a consistent dominant–subordinate relationship or engage in aggressive interactions during the familiarization period. Subordinate animals should display submissive behaviors such as unidirectional fear-grinning, withdrawing, yielding, and presenting, whereas dominant animals should display assertive postures. These behaviors should be seen uniformly in the subordinate and dominant animals.

Because individual and interspecies differences occur in the demonstration of a dominant–subordinate relationship, a slower process can be used when the relationship status is unclear to the observer. If caging permits, pairs can be given additional protected access to each other by using the squeeze mechanism to allow animals to share a single cage.[66] Presentation of a food reward within the reach of both animals that have visual contact can help to make their relationship more clear.[67] Some managers will not proceed to full-contact pairs unless an obvious, consistent dominant–subordinate relationship is observed.[46] However, others will attempt to pair animals even in the absence of clear establishment of rank—as long as there are no noteworthy signs of aggression—because the monkeys may need free physical contact to cement the relationship.[66] Importantly, rank relationships may not be apparent during intermittent observations, and continuous monitoring through the use of video cameras may assist managers in assessing pairs for the presence of these relationships. In our facility, because potential partners are limited by the number of macaques on each study, we have allowed full contact even without an obvious dominant–subordinate relationship in the absence of aggressive interactions during the familiarization period in 3 cases. Among the pairings we have established, we observed aggression after full contact only in these 3, and in all 3 cases minor fighting without serious injury preceded establishment of a dominant–subordinate relationship. Importantly, some individual pairs that appear highly compatible (for example, exhibit high degrees of allogrooming) may not exhibit an obvious, traditional dominant–subordinate relationship.[51] Although monkeys that do not exhibit an unambiguous dominant–subordinate relationship present an increased risk of aggressive contact after pairing, pairing can proceed with caution if aggressive interactions are not observed during the protected contact phase.

Several authors recommend transferring well-familiarized subjects into a new cage to avoid territorial disputes,[34,46,51]

whereas we and other, have paired animals successfully without transfer to a neutral cage.[16] The likelihood of success of male isosexual pairing can be increased by housing the animals in male-only areas to avoid sexual competition triggered by the presence of females,[49,51,54,66] but we have successfully paired adult males in the presence of females without incident. Some colleagues may consider neutral cages and single-gender housing rooms 'gold standards' in pairing macaques, but scientific studies demonstrating that these measures are effective at reducing risk have not been performed. Limited resources and insufficient housing space to accommodate neutral caging and single-sex rooms for pair housing macaques should not be used as justifications for single housing.

Activity of the animals during the first 30 min after pairing is highly predictive of the success of the pair.[34] For example, after separating pairs of same-sex rhesus macaques deemed incompatible during the first 30 min after free-contact introduction, one study reported 98% success in compatibility for at least 6 mo.[73] The dominant animal may assert his or her rank over the subordinate, perhaps aggressively, and a minor fight may ensue, but minor fights are not a sufficient cause to separate animals even if they result in superficial wounds. Low levels of affiliation during the first few hours after pairing may not predict incompatibility.[16] Cages should have sufficient numbers of foraging boards or other enrichment items to accommodate both animals, serve as distractions or tension-relieving mechanisms, and avoid conflict until a relationship between new cage mates is established. The presence of privacy panels allowing animals to avoid visual contact if desired also may help to reduce tension.[51] Trained observers recognize that both minor fighting and rough playing do occur among NHP, and that, although perhaps worrisome to untrained observers, these normal, species-typical behaviors do not merit the separation of pairs. Even monkeys that exhibit aggressive contact when initially paired may become compatible over time if given the appropriate opportunity to cement their dominance relationship. Because previous social contact significantly improves a monkey's ability to be integrated into a new pair if a pair must be broken for scientific or veterinary reasons,[48] research facilities should not hesitate to form new pairs with previously paired animals.

Macaques can demonstrate interpersonal preferences, so that any particular animal may be compatible with some but not all animals. Because macaques have successfully been transferred from an incompatible pair to a compatible pair, [54] an animal's previous incompatibility with 1 or 2 other individual monkeys should not preclude exploring compatibility with other potential partners. In addition, individual animals that have demonstrated incompatibility with one another in the past may be compatible in a different location, in a different cage layout, or in the presence of different monkeys. This phenomenon especially occurs in male macaques that demonstrated aggressive behavior around the time of puberty; these monkeys can successfully be returned to pair housing after a period of months to years.[67] Detailed information regarding attempts at pair housing including the attempted partner, housing situation, and reasons for success or failure should be part of each animal's permanent record. Justification for single housing as a result of repeated incompatibility should be reviewed by the IACUC and attending veterinarian, and these exemptions to social housing should be reconsidered as the environment changes.

Researchers should be included in the institution's plan to transition previously singly housed monkeys to social housing. Such participation by the research staff is key to success in changing the culture of an institution to define social housing as the default method. By engaging the researchers in the process from the beginning, we were able to shift the paradigm for housing NHP at our facility. Despite limitations associated with a relatively small NHP census with no more than 10 animals on each study, we increased the proportion of socially housed macaques at our facility from 12% to 73% in less than 1 y, with no serious injuries or disruptions to ongoing research. Some researchers now advocate for social housing and continuously evaluate singly housed monkeys for compatible partners even across studies and investigators. Because they know the personalities of their subjects, primary investigators and research technicians assist in selecting partners that have the highest chance for success. Coordination among all stakeholders prior to pairing prevents misunderstandings or misinterpretations of behaviors and events that may occur after pairing. The entire team including research staff, veterinarians, and animal care staff must understand the plan to avoid separating potentially compatible animals before the dominant–subordinate relationship has been established. Appropriately trained personnel who understand NHP behavior are essential to the ultimate success of the social housing program, and all staff responsible for monitoring NHP should be trained. A thoughtful discussion of the benefits and risks of social housing of NHP should include awareness that some pairs will be incompatible and some injuries will occur. Issues regarding cost of injury and plans for veterinary care should be discussed prior to initiating pair housing. The success rate that we have observed in our facility may not be universally achievable, and all stakeholders should be aware of the potential for failure of individual pairs. However, facilities housing NHP are obligated to implement a social housing program, document its successes and failures, and modify it to provide as many NHP as possible the opportunity for socialization. The benefits of social housing far outweigh the potential harm, and the risk of injury can be minimized through the use of experienced staff, standard procedures, and a deliberate approach to social housing.

Conclusion

Publication of the 2011 edition of *The Guide for the Care and Use of Laboratory Animals* has renewed emphasis on social housing as the default housing method for NHP in research facilities. Due to limitations of housing space and available caging, social housing is usually implemented as pair housing. Because pair housing, especially of adult male macaques, entails risks and challenges but achieves substantial and important benefits, research facilities must use a thoughtful, science-based approach to establish optimal housing for individual NHP.

References

1. **Abney DM, Weed JL.** 2006. Methods for successfully pair housing adult male rhesus macaques. Am J Primatol **68 Suppl:**59.
2. **Animal Welfare Act as Amended.** 2007. 7 USC §2131–2156.
3. **Animal Welfare Regulations.** 2008. 9 CFR §3.129.
4. **Association for Assessment and Accreditation of Laboratory Animal Care International.** [Internet]. 2011. Social housing: position statement. [Cited 11 October 2011]. Available at: http://www.aaalac.org/accreditation/positionstatements.cfm.
5. **Baker K.** 2007. Enrichment and primate centers: closing the gap between research and practice. J Appl Anim Welf Sci **10:**49–54.
6. **Baker KC.** 1999. Affiliative interactions between singly housed rhesus macaques in adjacent unmodified cages. Am J Primatol **49:**30.
7. **Baker KC, Bloomsmith M, Neu K, Griffis C, Oettinger B, Schoof V, Clay A, Maloney M.** 2008. Benefits of isosexual pairing of rhesus macaques (*Macaca mulatta*) vary with sex and are limited by

protected contact but not by frequent separation. Am J Primatol **70 Suppl 1:**72.

8. **Baker KC, Weed JL, Crockett CM, Bloomsmith MA.** 2007. Survey of environmental enhancement programs for laboratory primates. Am J Primatol **69:**377–394.
9. **Bayne K, Dexter S, Suomi S.** 1992. A preliminary survey of the incidence of abnormal behavior in rhesus monkeys (*Macaca mulatta*) relative to housing condition. Lab Anim **21:**38–46.
10. **Bellanca RU, Crockett CM.** 2002. Factors predicting increased incidence of abnormal behavior in male pigtailed macaques. Am J Primatol **58:**57–69.
11. **Bloomsmith M, Baker KC, Neu K, Griffis C, Oettinger B, Schoof V, Clay A, Maloney M.** 2008. Behavioral benefits of pair housing in adult rhesus macaques (*Macaca mulatta*) do not depend on age, previous duration of single housing, or naturalistic rearing. Am J Primatol **70 Suppl 1:**73.
12. **Chopra PK, Seth PK, Seth S.** 1992. Behavioral profile of free-ranging rhesus monkeys. Primate Rep **32:**75–105.
13. **Clarke MR, Kaplan JR, Bumsted PT, Koritnik DR.** 1986. Social dominance and serum testosterone concentration in dyads of male *Macaca fascicularis.* J Med Primatol **15:**419–432.
14. **Clarke MR, Harrison RM, Didier ES.** 1996. Behavioral, immunological, and hormonal responses associated with social change in rhesus monkeys (*Macaca mulatta*). Am J Primatol **39:**223–233.
15. **Crockett CM, Bowers CL, Bowden DM, Sackett GP.** 1994. Sex differences in compatibility of pair-housed adult long-tailed macaques. Am J Primatol **32:**73–94.
16. **Doyle LA, Baker KC, Cox LD.** 2008. Physiological and behavioral effects of social introduction on adult male rhesus macaques. Am J Primatol **70:**542–550.
17. **Eaton GG, Kelley ST, Axthelm MK, Iliff-Sizemore SA, Shiigi SM.** 1994. Psychological wellbeing in paired adult female rhesus (*Macaca mulatta*). Am J Primatol **33:**89–99.
18. **Gilbert MH, Baker KC.** 2011. Social buffering in adult male rhesus macaques (*Macaca mulatta*): effects of stressful events in single vs pair housing. J Med Primatol **40:**71–78.
19. **Gisler DB, Benson RE, Young RJ.** 1960. Colony husbandry of research monkeys. Ann N Y Acad Sci **85:**758–768.
20. **Goosen C, Van Der Gulden W, Rozemond H, Balner H, Bertens A, Boot R, Brinkert J, Dienske H, Janssen G, Lammers A, Timmermans P.** 1984. Recommendations for the housing of macaque monkeys. Lab Anim **18:**99–102.
21. **Gust DA, Gordon TP, Brodie AR, McClure HM.** 1994. Effect of a preferred companion in modulating stress in adult female rhesus monkeys. Physiol Behav **55:**681–684.
22. **Hotchkiss CE, Paule MG.** 2003. Effect of pair housing on operant behavior task performance by rhesus monkeys. Contemp Top Lab Anim Sci **42:**38–41.
23. **Institute for Laboratory Animal Research.** 1998. The psychological wellbeing of nonhuman primates. Washington (DC): National Academies Press.
24. **Institute for Laboratory Animal Research.** 2011. Guide for the care and use of laboratory animals, 8th ed. Washington (DC): National Academies Press.
25. **International Primatological Society.** [Internet]. 2007. International guidelines for the acquisition, care, and breeding of nonhuman primates, 2nd ed. [Cited 21 March 2011] http://www.internationalprimatologicalsociety.org/docs/IPS_International_Guidelines_for_the_Acquisition_Care_and_Breeding_of_Nonhuman_Primates_Second_Edition_2007.pdf.
26. **Kaplan BJ.** 1986. Psychological stress and behavior in nonhuman primates. In: Mitchell G, Erwin J, editors. Comparative primate biology, vol 2A. New York (NY): Alan Liss.
27. **Kurth B, Bryant D.** 1998. Pairing female *Macaca fascicularis.* Lab Prim Newsl **37:**3.
28. **Lee GH, Thom JP, Crockett CM.** 2005. Factors predicting compatible grooming–contact pairings in 4 species of laboratory monkeys. Am J Primatol **66 Suppl 1:**57.
29. **Lilly AA, Mehlman PT, Higley JD.** 1999. Trait-like immunological and hematological measures in female rhesus across varied environmental conditions. Am J Primatol **48:**197–223.
30. **Lindburg DG.** 1971. The rhesus monkey in north India: an ecological and behavioral study. In: Rosenblum LA, editor. Primate behavior: developments in field and laboratory research, vol 2. New York (NY): Academic Press.
31. **Line SW, Kaplan JR, Heise ER, Hilliard JK, Cohen S, Rabin BS, Manuck SB.** 1996. Effects of social reorganization on cellular immunity in male cynolgus monkeys. Am J Primatol **39:**235–249.
32. **Line SW, Morgan KN, Markowitz H, Riddell M.** 1990. Behavioral responses of female longtailed macaques (*Macaca fascicularis*) to pair formation. Lab Prim Newsl **29:**1–5.
33. **Lutz C, Well A, Novak M.** 2003. Stereotypic and self-injurious behavior in rhesus macaques: a survey and retrospective analysis of environment and early experience. Am J Primatol **60:**1–15.
34. **Lynch R.** 1998. Successful pair housing of male macaques (*Macaca fasicularis*). Lab Prim Newsl **37:**4–5.
35. **Mason WA, Berkson G.** 1975. Effects of maternal mobility on the development of rocking and other behaviors in rhesus monkeys: a study with artificial mothers. Dev Psychobiol **8:**197–211.
36. **McNulty JA, Iskander E, Kyes RC.** 2004. Time budgets of long-tailed macaques (*Macaca fasicularis*) on Tinjil Island, Indonesia. Am J Primatol **62 Suppl:**65–66.
37. **Murray L, Hartner M, Clark LP.** 2002. Enhancing postsurgical recovery of pair-housed nonhuman primates (*M. fasicularis*). Contemp Top Lab Anim Sci **41:**112–113.
38. **Neu KA, Bloomsmith MA, Baker KC, Griffis C, Oettinger BC.** 2007. Is preintroduction behavior associated with the outcome of social introductions in rhesus macaques (*Macaca mulatta*)? Am J Primatol **69 Suppl 1:**46.
39. **Niehoff MO, Bergmann M, Weinbauer GF.** 2010. Effects of social housing of sexually mature male cynomolgus monkeys during general and reproductive toxicity evaluation. Reprod Toxicol **29:**57–67.
40. **Novak MA, Suomi SJ.** 1988. Psychological wellbeing of primates in captivity. Am Psychol **43:**765–773.
41. **Novak MA, Suomi SJ.** 1991. Social interaction in nonhuman primates: an underlying theme for primate research. Lab Anim Sci **41:**308–314.
42. **Oettinger BC, Baker KC, Neu K, Griffis C, Schoof V, Maloney M, Clay A, Bloomsmith M.** 2008. Wounding incidence in isosexual pairs of adult rhesus macaques (*Macaca mulatta*) during introduction and in varying pair housing conditions. Am J Primatol **70 Suppl 1:**71.
43. **Ranheim S, Reinhardt V.** 1989. Compatible rhesus monkeys provide long-term stimulation for each other. Lab Prim Newsl **28:**1–2.
44. **Reaves M, Cohen J.** 2005. Primate pairing under less-than-ideal circumstances. Tech Talk **10:**1–2.
45. **Reinhardt V.** 1987. Are male rhesus monkeys more aggressive than females? Primates **28:**123–125.
46. **Reinhardt V.** 1989. Behavioral responses of unrelated adult male rhesus monkeys familiarized and paired for the purpose of environmental enrichment. Am J Primatol **17:**243–248.
47. **Reinhardt V.** 1990. Social enrichment for laboratory primates: a critical review. Lab Prim Newsl **29:**7–11.
48. **Reinhardt V.** 1991. Agonistic behavior responses of socially experienced, unfamiliar adult male rhesus monkeys (*Macaca mulatta*) to pairing. Lab Prim Newsl **30:**5–7.
49. **Reinhardt V.** 1992. Avoiding aggression during and after pair formation of adult rhesus macaques. Lab Prim Newsl **31:**10.
50. **Reinhardt V.** 1994. Environmental enhancement for research macaques: a survey of institutional compliance. Lab Prim Newsl **33:**1–2.
51. **Reinhardt V.** 1994. Pair housing rather than single housing for laboratory rhesus macaques. J Med Primatol **23:**425–431.
52. **Reinhardt V.** 1995. Social housing of previously single-caged macaques: what are the options and the risks? Anim Welf **4:**307–328.
53. **Reinhardt V.** 1997. Refining the traditional housing and handling of laboratory rhesus macaques improves scientific methodology. Primate Rep **49:**93–113.
54. **Reinhardt V.** 1998. Pairing *Macaca mulatta* and *Macaca arctoides* of both sexes. Lab Prim Newsl **37:**2.

55. **Reinhardt V.** 1999. Pair housing overcomes self-biting behavior in macaques. Lab Prim Newsl **38:**4–5.
56. **Reinhardt V.** 2002. Addressing the social needs of macaques used for research. Lab Primate Newsl **41:**7–10.
57. **Reinhardt V.** 2002. The myth of the aggressive monkey. J Appl Anim Welf Sci **5:**321–330.
58. **Reinhardt V, Cowley D, Eisele S.** 1991. Serum cortisol concentrations of single-housed and isosexually pair-housed adult rhesus macaques. J Exp Anim Sci **34:**73–76.
59. **Reinhardt V, Houser D, Eisele S.** 1989. Pairing previously singly caged rhesus monkeys does not interfere with common research protocols. Lab Anim Sci **39:**73–74.
60. **Roberts SJ, Platt ML.** 2005. Effects of isosexual pair housing on biomedical implants and study participation in male macaques. Contemp Top Lab Anim Sci **44:**13–18.
61. **Schapiro SJ, Bloomsmith MA, Kessel AL, Shively CA.** 1993. Effects of enrichment and housing on cortisol response of juvenile rhesus monkeys. Appl Anim Behav Sci **37:**251–263.
62. **Schapiro SJ, Bloomsmith MA, Porter LM, Suarez SA.** 1996. Enrichment effects on rhesus monkeys successively housed singly, in pairs, and in groups. Appl Anim Behav Sci **48:**159–171.
63. **Schapiro SJ, Bloomsith MA, Suarez SA, Porter LM.** 1996. Effects of social and inanimate enrichment on the behavior of yearling rhesus monkeys. Am J Primatol **40:**247–260.
64. **Schapiro SJ, Bushong D.** 1994. Effects of enrichment on veterinary treatment of laboratory rhesus macaques (*Macaca mulatta*). Anim Welf **3:**25–36.
65. **Schapiro SJ, Nehete PN, Perlman JE, Bloomsmith MA, Sastry KJ.** 1998. Effects of dominance status and environmental enrichment on cell-mediated immunity in rhesus macaques. Appl Anim Behav Sci **56:**319–332.
66. **Seelig D.** 1998. Pair housing male *Macaca fascicularis*: a summary. Lab Prim Newsl **37:**14–16.
67. **Seelig D.** 2007. A tail of 2 monkeys: social housing for nonhuman primates in the research laboratory setting. J Appl Anim Welf Sci **10:**21–30.
68. **Shively CA, Clarkson TB, Kaplan JR.** 1989. Social deprivation and coronary artery atherosclerosis in female cynomologous monkeys. Atherosclerosis **77:**69–76.
69. **Sullivan J, Schulz K, Goecks N, Rosga M, Cruzen C.** 2009. Comparison of introduction strategies: gradual vs protected contact in macaques. Am J Primatol **71 Suppl 1:**14.
70. **Teas J, Richie T, Taylor H, Southwick C.** 1980. Population patterns and behavioral ecology of rhesus monkeys (*Macaca mulatta*) in Nepal. In: Lindburgh DG, editor. The macaques: studies in ecology, behavior, and evolution. New York (NY): Van Nostrand Reinhold.
71. **Watson LM.** 2002. A successful program for same- and cross-age pair-housing adult and subadult male *Macaca fasicularis*. Lab Prim Newsl **41:**6–9.
72. **Weed JL, Wagner PO, Byrum R, Parrish S, Knezevich M, Powell DA.** 2003. Treatment of self-injurious behavior in rhesus monkeys through socialization: a preliminary report. Contemp Top Lab Anim Sci **42:**21–23.
73. **West AM, Leland SP, Collins MW, Welty TM, Wagner WL, Erwin JM.** 2009. Pair formation in laboratory rhesus macaques (*Macaca mulatta*): a retrospective assessment of a compatibility testing procedure. Am J Primatol **71 Suppl 1:**37.