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Comparative Risk of Human Injury/Exposure While Collecting Blood from Sedated and Unsedated Nonhuman Primates

Charlotte E Hotchkiss* and Melinda A Young

Collection of blood samples for research or clinical evaluation is one of the most common procedures performed in nonhuman primates. Several possible methods can be used to obtain samples. In the early days of primate research, manual or physical restraint was used, which was stressful for the animal and risky for the human. As the field developed, chemical immobilization with ketamine or other anesthetics has become the most commonly used method. More recently, training using positive reinforcement has allowed collection of blood samples from unsedated primates that are unrestrained or minimally restrained. Elimination of anesthesia reduces risks to the animal. We wanted to determine whether the risks to humans were different between the sedated or unsedated blood collection. We evaluated injury and near-miss reports in conjunction with blood collection data from 2009 to 2019 at the Washington National Primate Research Center, which houses macaques (*M. nemestrina, M. mulatta, and M. fasicularis*) and squirrel monkeys (*S. sciureus*), and has housed baboons (*Papio* sp.) in the past. Injuries associated with sedated blood collection included those occurring during the sedation procedure and recovery as well as those directly associated with blood collection. Injuries associated with unsedated blood collection included those which occurred both during animal training and during blood collection. Overall, 22 human injury exposures and 5 near misses were associated with 73,626 blood collection procedures. Based on these numbers, 0.026% of sedated blood collections and 0.116% of unsedated blood collections were associated with exposure incidents. In conclusion, our data indicate a very low risk of exposure associated with blood collection. In this data set, the risk was statistically higher for unsedated animals, but the low number of incidents and the variability in the methods of blood collection make the general applicability of this finding questionable.

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Blood collection is a common research procedure. Blood samples can provide a wealth of clinical information needed for veterinary care as well as cells, biomarkers, and reagents required for research. In the early days of nonhuman primate research, manual/physical restraint was used, which was both stressful for the animal and risky for the human. As the field developed, chemical immobilization with ketamine or other anesthetics before blood collection has become the norm. However, anesthetics affect physiologic parameters[15-17,26,38] which could impact the validity of research results. More recently, training using positive reinforcement has allowed collection of blood samples from unsedated primates. These animals are unrestrained or minimally restrained, a refinement that reduces stress to the animals.[1] Elimination of anesthesia is beneficial in that it reduces risks to the animal and minimizes potential confounding effects on research. The impact of this change on human health, in terms of potential for increased exposure to B virus, has not been evaluated.

Personnel who work with macaques in a research environment are well aware of the zoonotic risks of B virus (BV, *Macacine alphaherpes virus 1*, formerly known as *Herpesvirus simiae* and *Cercopithecine herpesvirus 1*).[4-6,10-14,18,19,21,33,34,42] Although rarely pathogenic in the natural host, mortality as high as 80% can occur in infected humans without prompt, appropriate treatment.[13] Postexposure protocols have been established and are effective at preventing infection.[6,20,21,33,34] However, infections continue to occur, and these can result in chronic neurologic deficits and may require lifelong treatment.[24] The antiviral medications (acyclovir, ganciclovir,) used for this treatment and for postexposure prophylaxis can have unpleasant side effects, including pyrexia, diarrhea, leukopenia, nausea, anemia, asthenia, headache, cough, dyspnea, abdominal pain, decreased appetite, and increased creatinine (Product Information, Cytovene (ganciclovir) Genentech, South San Francisco, CA). Despite the serious consequences of exposure to BV, little published information is available regarding the risks of exposure associated with specific husbandry, veterinary, or research procedures.[2,39,43]

Materials and Methods

We obtained animal records from the Animal Research Management System (ARMS), an electronic database that contains records of clinical and research procedures for a colony of nonhuman primates. During time period of this study (July 1, 2009 to June 30, 2019), the colony included primarily macaques (*M. nemestrina*, *M. mulatta*, and *M. fascicularis*), with a small number of baboons (*P. anubis*) and squirrel monkeys (*S. sciureus*); the total colony size (daily census) ranged from 472 to 1,086 animals. All animals were housed in an AAALAC-accredited vivarium, and the University of Washington IACUC approved all research blood collection procedures.

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Washington National Primate Research Center, University of Washington, Seattle, Washington
**Corresponding author. Email: chotchki@uw.edu*

In generating the data, blood collection procedures were considered to have been performed under sedation if the record contained administration of ketamine or tiletamine–zolazepam on the same day. If there was no record of sedative administration, the blood collection was considered to have been performed without sedation. For research blood collections for which the investigator was known to possess his or her own DEA license, IACUC protocols and research records were reviewed to determine whether the collection was performed sedated or unsedated.

Information regarding human injuries and near misses was obtained from reports from the University of Washington Online Accident Reporting System (OARS) with personnel names redacted. Descriptions of the incidents were reviewed to determine whether incidents were associated with blood collection. We identified 27 incidents associated with blood collection and further categorized the specific circumstances of the human injury or exposure (Table 1). Because the incidents associated with blood collection comprised a small fraction of the total number of reported incidents, further investigation was performed, focusing on causes of nonhuman primate (NHP) exposures. All reported incidents were assigned to categories based on the narrative description (Table 2). The safety committees reviewed all incidents monthly. Employees are encouraged to report near misses and safety concerns in the OARS system so that steps can be taken to prevent future injuries. Statistical analysis (Fisher exact test, ANOVA, and Tukey HSD) were performed using R.

Results

During the time period from July 1, 2009, to June 30, 2019, 73,626 blood collection procedures were performed. Of those procedures, 68,994 were performed under sedation, 3,456 were performed unsedated, and 1,176 were performed without animal contact, through an implanted catheter with a tether device. The unsedated blood collection was performed under manual restraint for infants (1,546), in a table-top restraint device (53), either in a procedure cage (1,134) or by skin prick in the home cage (722). One unsedated blood collection was performed in a manually-restrained squirrel monkey that the veterinarian considered too ill to sedate. Approximately 60% of the exposures (13 out of 22) and near misses (3 out of 5) were not associated with the blood collection procedure itself, but rather with ancillary procedures necessary to perform blood collection (Table 1). For sedated blood collection, this included squeezing animals for sedation, the sedation injection itself, and returning sedated animals to the home cage. For unsedated blood collection, injuries occurred while training animals to transfer into the procedure cage and during the blood collection procedure. Ancillary procedures applicable to any type of blood collection include transferring blood from a syringe to a blood collection tube and discarding sharps. Two exposures were associated with failure of safety devices: in one case, a retractable needle did not retract, and in another, a shield broke off the needle.

Medical treatment was given to all personnel who reported injuries. All personnel who received NHP exposures performed appropriate disinfection at the site of exposure[6] and received appropriate medical care. Any personnel who reported near misses discussed the incident with an occupational health specialist. There was no evidence of infection with BV in any personnel.

Overall, 22 personal injury exposures and 5 near misses were associated with 72,450 blood collection procedures. Eighteen out of 68,994 (0.026%) of sedated blood collections and 4 out of 3,456 (0.116%) of unsedated blood collections were associated with exposure incidents. The Fisher exact test revealed a statistically higher risk for unsedated compared with sedated blood collection ($P = 0.019$). The unsedated blood collections could be further categorized as trained animals compared with manually restrained animals. Two out of 1,909 (0.105%) of collections from trained animals and 2 out of 1,547 (0.129%) of collections from restrained animals (primarily infants) were associated with exposures. After this subdivision, no statistical differences were found among the sedated, manually restrained, or trained groups.

Blood collection accounted for a small fraction of exposure incidents. In all, 594 incidents or concerns were associated with animal nonhuman primate care or research during this time period. These incidents are categorized in Table 2, which also demonstrates the variation in the number of reports based on the day of the week. ANOVA indicated a significant difference among days of the week ($P < 0.001$), and Tukey HSD revealed that more incidents occurred on Monday, Tuesday, Wednesday, and Thursday than on Saturday or Sunday. The number of incidents on Wednesday was significantly higher than on Friday. A total of 211 of the incidents resulted in potential NHP exposures (Figure 1). A majority of these incidents (123 out of 211, with 21 out of 22 related to blood collection) were associated with direct animal contact, such as bites, scratches, and needlesticks. However, many (88 out of 211) were due to abrasions, pinches, or cuts from equipment or splashes to the face. The number of exposure incidents due to splashes (33) was higher than expected, given that personnel are required to wear face shields when working near NHP. During this time period, disposable face shields were most commonly used. Five of the reports of splashes specifically indicate that a face shield was worn but that material splashed over the top of or under the bottom of the face shield. The other reports did not specifically state whether a face shield was worn. Further investigation of the specific tasks associated with injuries revealed that a large number of injuries were associated with manipulating animal cages (15%, Figure 2). Ergonomic and strain injuries are not included because the reason for discomfort cannot always be determined; however, a large number of the reports mention moving cages as contributing to discomfort.

Discussion

Many of the procedures performed during routine husbandry, veterinary care, and research involving nonhuman primates include a potential for human injury and exposure to zoonotic infection. The Association of Primate Veterinarians recently issued guidelines for nonhuman primate restraint which state that "Whenever possible, nonhuman primates should be trained, using positive reinforcement principles, to…participate voluntarily with routine experimental practices."[1] The guidelines also point out that one of the considerations in the use of chemical restraint is the safety of the animals and the human handlers. The purpose of this study was to objectively evaluate the relative risk to humans of performing blood collection in animals that have been trained for unsedated blood collection, in comparison to animals that have been chemically restrained.

In this study, we used data from incident reports filed at the time of exposure. This avoids the problems that can occur with questionnaires, such as low response rates, nonrepresentative response rates, and recall bias. However, this does not address exposure incidents that were not reported. Although our institution strongly supports a culture of safety and incident reporting, questionnaire-based studies indicate significant underreporting of NHP exposure incidents nationwide.[2,39,43] Therefore, our data may be incomplete.

Table 1. Potential exposures and human injuries associated with blood collection from sedated or unsedated NHP over a 10-y period (2009–2019).

Sedated or unsedated	Phase of blood collection	Category of injury	NHP exposure	Description
Sedated	Sedation	Bite	no	Bit while restraining infant for sedation. PPE intact.
Sedated	Sedation	Needlestick	no	Needlestick which did not penetrate gloves.
Sedated	Sedation	Abrasion/pinch/cut	yes	Abrasion from cage while squeezing animal for sedation.
Sedated	Sedation	Bite	yes	Bit while squeezing animal for sedation.
Sedated	Sedation	Needlestick	yes	Retractable needle did not fully retract after sedation.
Sedated	Sedation	Needlestick	yes	Needlestick while manipulating squeeze apparatus.
Sedated	Sedation	Needlestick	yes	Needlestick during sedation.
Sedated	Sedation	Needlestick	yes	Needlestick during sedation.
Sedated	Sedation	Scratch	yes	Scratched by monkey while sedating.
Sedated	Sedation	Scratch	yes	Scratched by monkey while sedating.
Sedated	Blood collection	Needlestick	yes	Needlestick while reaching for new needle.
Sedated	Blood collection	Needlestick	yes	Animal moved unexpectedly.
Sedated	Blood collection	Needlestick	yes	Transferring from syringe to blood tube.
Sedated	Blood collection	Needlestick	yes	Animal moved unexpectedly when repositioning needle.
Sedated	Blood collection	Needlestick	yes	Animal moved unexpectedly during second venipuncture.
Sedated	Needle disposal	Needlestick	yes	Removing vacuum phlebotomy tube needle from vacuum phlebotomy tube holder.
Sedated	Needle disposal	Needlestick	yes	Placing vacuum phlebotomy tube needle in sharps container.
Sedated	Needle disposal	Needlestick	yes	Safety shield broke off, and got needlestick while disposing of sharps.
Sedated	Needle disposal	Needlestick	yes	Disposing of needle in poorly-located sharps container.
Sedated	Recovery	Scratch	yes	Scratched by nearby animal when returning sedated animal to cage.
Unsedated/trained	Training	Scratch	no	Scratch while training monkey in procedure cage. PPE intact.
Unsedated/trained	Blood collection	Scratch	no	Scratch while performing blood draw in procedure cage. PPE intact
Unsedated/trained	Blood collection	Bite	yes	Bit while trying to distract monkey from needle during trained blood collection.
Unsedated/trained	Blood collection	Needlestick	yes	Needlestick while collecting blood in home cage.
Unsedated/restraint	Blood collection	Needlestick	yes	Repositioning limb to obtain blood.
Unsedated/restraint	Blood collection	Scratch	no	Scratch while restraining infant for blood collection. PPE intact.
Unsedated/restraint	Blood collection	Bite	yes	Restraining ill squirrel monkey for blood draw.

One consideration in determining the risk of exposure is that perception plays a role in how careful people are. Surveys indicate that personnel performance and perception of risk are impaired when the workload is excessive.[40] A previous study[39] showed that personnel received fewer exposures when working with SIV-infected macaques than when working with SIV-negative macaques, presumably due to increased awareness and caution with known infected animals. Similarly, attitudes toward safety could be different when working with unsedated animals than with sedated animals. Prior reports on NHP exposures have emphasized the high frequency of needlesticks.[39] This current report shows that the risk per blood collection event is low; however, a very large number of blood collection events are performed in an active NHP research facility.

An investigation into the specific circumstances of NHP exposures associated with blood collection reveals factors not previously considered. Although the risk of exposure during the act of blood collection is lower in sedated animals than in unsedated animals, a risk is present both in sedating animals and in returning animals to their home cages after sedation. The process of sedated blood collection involves steps that do not occur in unsedated blood collection: use of the squeeze apparatus, intramuscular injection in an unsedated animal, removal of the animal from its cage, transport to the procedure area, and return of the animal after the procedure. In contrast, animals must be trained for unsedated blood collection, involving direct animal contact both prior to and during the blood collection procedure; these processes are not required for sedated blood collection.

Positive reinforcement techniques (PRT) have been used to train nonhuman primates to cooperate with a number of husbandry, veterinary, and research procedures, including transfers from the home cage, injections, urine collection, blood pressure measurement, saliva collection, vaginal swabs, transfer to restraint chairs, and blood collection.[3,8,9,22,23,25,27,28,36,37,44] Training can reduce behavioral and physiologic indicators of stress associated with these procedures.[7,32,35] However, all animals are not equally trainable; those with an "exploratory" temperament are much more likely to succeed at target training than "inhibited" monkeys.[9] Juvenile monkeys are reportedly less successful at training than adults.[30]

Table 2. All reported injuries or health concerns categorized by type of incident and by day of the week over a 10 y period.

Category	Sun	Mon	Tue	Wed	Thu	Fri	Sat	Total
Abrasion/pinch/cut	9	11	22	29	18	18	8	115
Bite	2	5	5	12	12	4	3	43
Bumps/Contusions	2	8	7	8	10	4	4	43
Concern	4	10	2	17	9	4	5	51
Needlestick	3	5	5	13	9	6		41
Scratch	4	10	14	11	9	9	6	63
Splash	1	9	10	12	7	5	5	49
Vehicle			1		3			4
Ergonomic/strain/sprain	10	23	22	22	16	15	1	109
Other		7	10	4	5	5	2	33
Slips, trips, and falls	5	5	9	8	8	5	3	43
Total	40	93	107	136	106	75	37	594

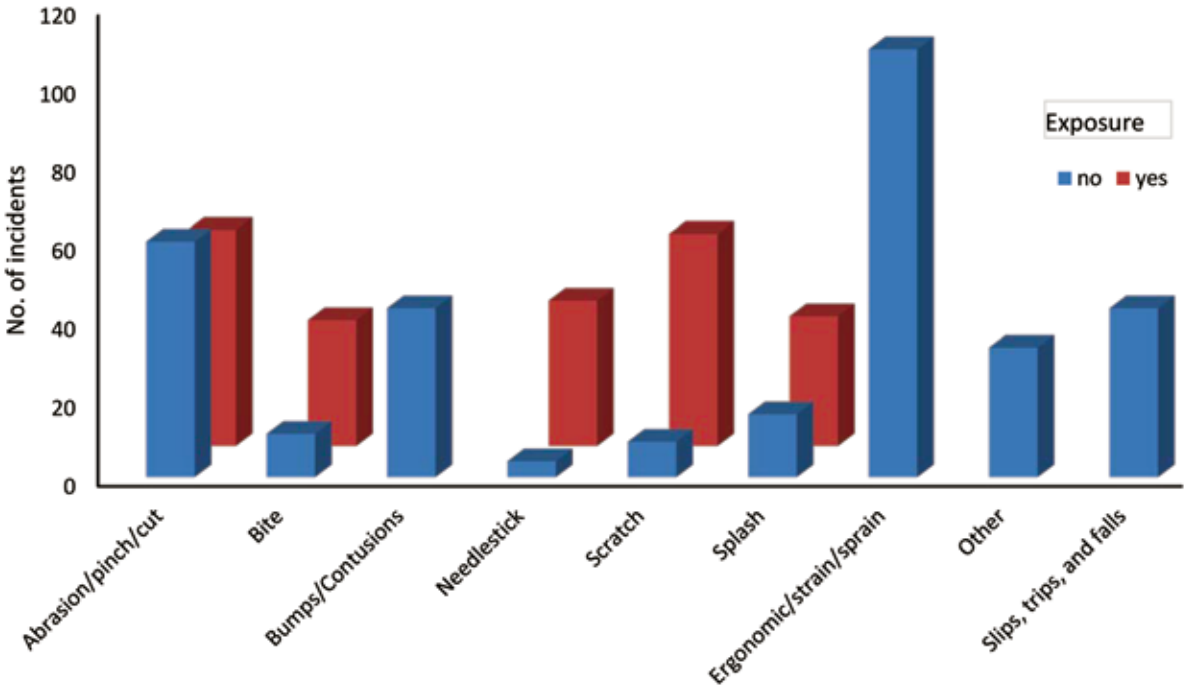

Figure 1. Human injuries reported over a 10-y period categorized by the type of injury and whether an NHP exposure occurred (red) or did not occur (blue).

The time needed for training can be an obstacle to performing blood collection in unsedated NHP and may vary depending on the training technique and the amount of restraint employed. Reported training times for rhesus macaques range from 30 to 60 min[29,31,41] to approximately 200 to 300 min[8] per animal. For a large NHP colony, investing this amount of time in every animal is not practical, particularly when blood collection is often performed in conjunction with other procedures, such as physical examination. On the other hand, if frequent blood collections are needed for research purposes, the time investment may be worthwhile, given the reduction in stress and risk to the animal.

This study examined the relationship of exposure incidents to the number of blood collection events but was not designed to evaluate the number of incidents in relation to time spent in contact with animals and sharps. Assuming that the actual blood collection procedure takes the same amount of time in both situations, an additional 10 to 15 min of time in contact with NHP and sharps is necessary for sedation and recovery each time blood is collected from sedated animals. In contrast, as discussed above, a significant amount of time is needed to train animals for unsedated blood collection, but once that is done, no additional time is needed per collection event. Also, training usually does not involve sharps, making it a lower risk task than sedation.

Exposures and injuries due to blood collection account for a small fraction of the reported incidents and concerns. Our data revealed that moving and manipulating cages contributes to the risks of working with NHP. We also found that the number of incidents of all types varies with the day of the week. We expected a lower number of incidents on Saturday and Sunday as fewer personnel work on the weekend. Our data contained fewer blood collection events on Fridays than on other weekdays. We suspect that the lower number of incidents on Fridays than on Wednesdays is related to fewer animal procedures taking place on Fridays. Why this difference is large enough to reach significance for Wednesdays but not for other weekdays is not clear.

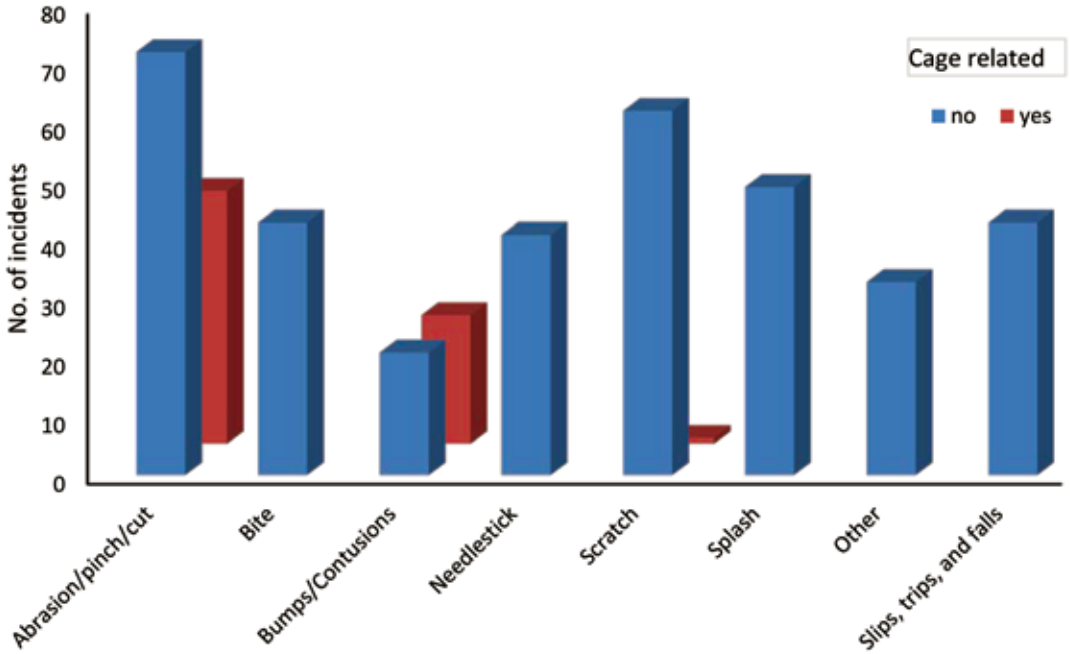

Figure 2. Human injuries reported over a 10-y period categorized by the type of injury and whether the injury was associated with cage manipulation (red) or not (blue). Note that ergonomic issues and strains and sprains are not included, because they often were not associated with a specific event.

In conclusion, although the probability of an exposure differed significantly between sedated and unsedated blood collections, no practical difference in the probability of an incident was associated with sedated (0.026% of blood collections) as compared with unsedated (0.116% of blood collections) situations. In other words, 99.97% of sedated and 99.88% of unsedated blood collections occurred without incident.

Acknowledgments

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References

1. **APV.** 2019. Association of Primate Veterinarians Guidelines For Nonhuman Primate Restraint. J Am Assoc Lab Anim Sci **58:**276–278.
2. **bin Zakaria M, Lerche NW, Chomel BB, Kass PH**. 1996. Accidental injuries associated with nonhuman primate exposure at two regional primate research centers (USA): 1988–1993. Lab Anim Sci **46**:298-304.
3. **Bliss-Moreau E, Theil JH, Moadab G.** 2013. Efficient cooperative restraint training with rhesus macaques. J Appl Anim Welf Sci **16:**98–117. https://doi.org/10.1080/10888705.2013.768897.
4. **Centers for Disease Control and Prevention.** 1995. Publication of guidelines for the prevention and treatment of B virus infections in exposed persons. MMWR Morb Mortal Wkly Rep **44:**96–97.
5. **Centers for Disease Control and Prevention.** 1998. Fatal Cercopithecine herpesvirus 1 (B virus) infection following a mucocutaneous exposure and interim recommendations for worker protection. MMWR Morb Mortal Wkly Rep **47:**1073–1076, 1083.
6. **Cohen JI, Davenport DS, Stewart JA, Deitchman S, Hilliard JK, Chapman LE, B Virus Working Group.** 2002. Recommendations for prevention of and therapy for exposure to B virus (*Cercopithecine herpesvirus* 1). Clin Infect Dis **35:**1191–1203. https://doi.org/10.1086/344754.
7. **Coleman K.** 2012. Individual differences in temperament and behavioral management practices for nonhuman primates. Appl Anim Behav Sci **137:**106–113. https://doi.org/10.1016/j.applanim.2011.08.002.
8. **Coleman K, Pranger L, Maier A, Lambeth SP, Perlman JE, Thiele E, Schapiro SJ.** 2008. Training rhesus macaques for venipuncture using positive reinforcement techniques: a comparison with chimpanzees. J Am Assoc Lab Anim Sci **47:**37–41.
9. **Coleman K, Tully LA, McMillan JL.** 2005. Temperament correlates with training success in adult rhesus macaques. Am J Primatol **65:**63–71. https://doi.org/10.1002/ajp.20097.
10. **Elmore D, Eberle R.** 2008. Monkey B virus (*Cercopithecine herpesvirus* 1). Comp Med **58:**11–21.
11. **Freifeld AG, Hilliard J, Southers J, Murray M, Savarese B, Schmitt JM, Straus SE.** 1995. A controlled seroprevalence survey of primate handlers for evidence of asymptomatic herpes B virus infection. J Infect Dis **171:**1031–1034. https://doi.org/10.1093/infdis/171.4.1031.
12. **National Institute for Occupational Safety and Health.** 2001. *Cercopithecine herpesvirus* 1 (B virus) infection resulting from ocular exposure. Appl Occup Environ Hyg **16:**32–34. https://doi.org/10.1080/104732201456087.
13. **Hilliard J.** Monkey B virus. Chapter 57. In: Arvin A, Campadelli-Fiume G, Mocarski E, Moore PS, Roizman B, Whitley R, Yamanishi K editors. Human herpesviruses: biology, therapy, and immunoprophylaxis. Cambridge. https://www.ncbi.nlm.nih.gov/books/NBK47426/
14. **Holmes GP, Chapman LE, Stewart JA, Straus SE, Hilliard JK, Davenport DS.** 1995. Guidelines for the prevention and treatment of B-virus infections in exposed persons. The B virus Working Group. Clin Infect Dis **20:**421–439. .
15. **Hotchkiss CE, Brommage R, Du M, Jerome CP.** 1998. The anesthetic isoflurane decreases ionized calcium and increases parathyroid hormone and osteocalcin in cynomolgus monkeys. Bone **23:**479–484. https://doi.org/10.1016/S8756-3282(98)00124-0.
16. **Hotchkiss CE, Hall PD, Cline JM, Willingham MC, Kreitman RJ, Gardin J, Latimer A, Ramage J, Feely T, DeLatte S, Tagge EP, Frankel AE.** 1999. Toxicology and pharmacokinetics of DTGM, a fusion toxin consisting of a truncated diphtheria toxin (DT388) linked to human granulocyte-macrophage colony-stimulating factor, in cynomolgus monkeys. Toxicol Appl Pharmacol **158:**152–160. https://doi.org/10.1006/taap.1999.8691.
17. **Hotchkiss CE, Wang C, Slikker W Jr.** 2007. Effect of prolonged ketamine exposure on cardiovascular physiology in pregnant and infant rhesus monkeys (*Macaca mulatta*). J Am Assoc Lab Anim Sci **46:**21–28.

18. **Huff JL, Barry PA.** 2003. B-virus (*Cercopithecine herpesvirus* 1) infection in humans and macaques: potential for zoonotic disease. Emerg Infect Dis **9:**246–250. https://doi.org/10.3201/eid0902.020272.
19. **Jainkittivong A, Langlais RP.** 1998. Herpes B virus infection. Oral Surg Oral Med Oral Pathol Oral Radiol Endod **85:**399–403. https://doi.org/10.1016/S1079-2104(98)90064-6.
20. **Johnston WF, Yeh J, Nierenberg R, Procopio G.** 2015. Exposure to macaque monkey bite. J Emerg Med **49:**634–637. https://doi.org/10.1016/j.jemermed.2015.06.012.
21. **Keller CE.** 2009. B virus (*Cercopithecine herpesvirus* 1) therapy and prevention recommendations. US Army Med Dep J **Jan–March:**46–50.
22. **Laule G, Whittaker M.** 2007. Enhancing nonhuman primate care and welfare through the use of positive reinforcement training. J Appl Anim Welf Sci **10:**31–38. https://doi.org/10.1080/10888700701277311.
23. **Laule GE, Bloomsmith MA, Schapiro SJ.** 2003. The use of positive reinforcement training techniques to enhance the care, management, and welfare of primates in the laboratory. J Appl Anim Welf Sci **6:**163–173. https://doi.org/10.1207/S15327604JAWS0603_02.
24. **Matthews S.** [Internet]. 2018. Lab worker's body is turning numb after catching a deadly rare virus from a research monkey. [Cited 05 October 2018]. Available at: https://www.dailymail.co.uk/health/article-6243417/Lab-worker-caught-deadly-rare-virus-research-monkey.html.
25. **McMillan JL, Perlman JE, Galvan A, Wichmann T, Bloomsmith MA.** 2014. Refining the pole–and–collar method of restraint: emphasizing the use of positive training techniques with rhesus macaques (*Macaca mulatta*). J Am Assoc Lab Anim Sci **53:**61–68.
26. **Paule MG, Li M, Allen RR, Liu F, Zou X, Hotchkiss C, Hanig JP, Patterson TA, Slikker W Jr, Wang C.** 2011. Ketamine anesthesia during the first week of life can cause long-lasting cognitive deficits in rhesus monkeys. Neurotoxicol Teratol **33:**220–230. https://doi.org/10.1016/j.ntt.2011.01.001.
27. **Prescott MJ, Buchanan-Smith HM.** 2003. Training nonhuman primates using positive reinforcement techniques. J Appl Anim Welf Sci **6:**157–161. https://doi.org/10.1207/S15327604JAWS0603_01.
28. **Prescott MJ, Buchanan-Smith HM, Rennie AE.** 2005. Training of laboratory-housed non-human primates in the UK. Anthrozöös **18:**288–303.
29. **Reinhardt V.** 1991. Training adult male rhesus monkeys to actively cooperate during in-homecage venipuncture. Anim Technol **42:**11–17.
30. **Reinhardt V.** 1992. Difficulty in training juvenile rhesus macaques to actively cooperate during venipuncture in the homecage. Laboratory primate newsletter **31:**1–2.
31. **Reinhardt V.** 2003. Working with rather than against macaques during blood collection. J Appl Anim Welf Sci **6:**189–197. https://doi.org/10.1207/S15327604JAWS0603_04.
32. **Reinhardt V, Cowley D, Scheffler J, Vertein R, Wegner F.** 1990. Cortisol response of female rhesus-monkeys to venipuncture in homecage versus venipuncture in restraint apparatus. J Med Primatol **19:**601–606.
33. **Remé T, Jentsch KD, Steinmann J, Kenner S, Straile U, Buse E, Sauerbrei A, Kaup FJ.** 2009. Recommendation for post-exposure prophylaxis after potential exposure to herpes B virus in Germany. J Occup Med Toxicol **4:**1–5. https://doi.org/10.1186/1745-6673-4-29.
34. **Rohrman M.** 2015. Macacine herpes virus (B virus). Workplace Health Saf **64:**9–12. https://doi.org/10.1177/2165079915608857.
35. **Schapiro SJ, Bloomsmith MA, Laule GE.** 2003. Positive reinforcement training as a technique to alter nonhuman primate behavior: quantitative assessments of effectiveness. J Appl Anim Welf Sci **6:**175–187. .
36. **Schapiro SJ, Perlman JE, Thiele E, Lambeth S.** 2005. Training nonhuman primates to perform behaviors useful in biomedical research. Lab Anim (NY) **34:**37–42. DOI: 10.1038/laban0505-37.
37. **Scott L, Pearce P, Fairhall S, Muggleton N, Smith J.** 2003. Training nonhuman primates to cooperate with scientific procedures in applied biomedical research. J Appl Anim Welf Sci **6:**199–207. https://doi.org/10.1207/S15327604JAWS0603_05.
38. **Slikker W Jr, Zou X, Hotchkiss CE, Divine RL, Sadovova N, Twaddle NC, Doerge DR, Scallet AC, Patterson TA, Hanig JP, Paule MG, Wang C.** 2007. Ketamine-induced neuronal cell death in the perinatal rhesus monkey. Toxicol Sci **98:**145–158. doi: 10.1093/toxsci/kfm084.
39. **Sotir M, Switzer W, Schable C, Schmitt J, Vitek C, Khabbaz RF.** 1997. Risk of occupational exposure to potentially infectious nonhuman primate materials and to simian immunodeficiency virus. J Med Primatol **26:**233–240. https://doi.org/10.1111/j.1600-0684.1997.tb00217.x.
40. **Steelman ED, Alexander JL.** 2016. Laboratory animal workers' attitudes and perceptions concerning occupational risk and injury. J Am Assoc Lab Anim Sci **55:**419–425.
41. **Vertein R, Reinhardt V**. 1989. Training female rhesus monkeys to cooperate during in-homecage venipuncture. Laboratory Primate Newsletter **28**.
42. **Weigler BJ.** 1992. Biology of B virus in macaque and human hosts: a review. Clin Infect Dis **14:**555–567. .https://doi.org/10.1186/1745-6673-4-29?cmd=Retrievedb=PubMedlist_uids=1313312dopt=Abstract
43. **Weigler BJ, Di Giacomo RF, Alexander S.** 2005. A national survey of laboratory animal workers concerning occupational risks for zoonotic diseases. Comp Med **55:**183–191.https://doi.org/10.2752/089279305785594153?cmd=Retrievedb=PubMedlist_uids=15884782dopt=Abstract
44. **Whittaker M, Laule G.** 2012. Training techniques to enhance the care and welfare of nonhuman primates. Vet Clin North Am Exot Anim Pract **15:**445–454. https://www.sciencedirect.com/science/article/abs/pii/S1094919412000527?via%3Dihub.https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrievedb=PubMedlist_uids=22998961dopt=Abstract