

1) "Failure to monitor animals post-procedurally as necessary to ensure well-being"
1/29-2/1/06—Following an experiment, an animal (#96099) was found with obvious CNS signs. Treatment and diagnostics were initiated, including a CT. PI was instructed by vet to check animal overnight 1/30-31—no indication in records that animal was checked that night or the following night. Animal was found dead on the morning of 2/1. Necropsy was performed, but PI removed the brain prior to carcass being submitted, so no cause of death could be determined.

The following records document that this animal (Buster) presented at 11am on 1/29/06 with signs consistent with an acute hemorrhage resulting from an electrode penetration the previous day. The veterinarian (██████████) was called and instructed the lab on a treatment protocol which we implemented together with LAR staff at 12:30pm (1.0mg/kg Dexamethasone and 20mgs doxycycline for the next 3 - 7 days). Water intake was reduced to minimize cerebral edema. 1/30/06 ██████████ took over the care of the animal at 9:30am. Monitoring by lab staff continued throughout the day (██████). At 8:15pm on 1/30/06 Dr. Basso called ██████████ to report condition of Buster and noted the increased ICP. Diazepam treatment commenced due to suspected seizure. The animal was monitored through the evening - notes in record through 9:50pm from the veterinarian and again at 5:30am from Dr. Basso, in contrast to the allegation that the animal was not monitored. There was no instruction by the veterinarian to maintain a log through the evening. Throughout the day on 1/31/06 animal was monitored, treated and taken for MRI. MRI read by neurosurgeon colleague for possible treatment options. Buster was returned to cage at 7:05pm. The veterinarian indicated in the notes that there would be an exam in the morning. Buster was found dead at 7am and his body was taken to necropsy. Dr. Basso received the brain for histological sectioning from ██████████ at the necropsy, in contrast to the allegation that the PI removed the brain prior to the necropsy. See attached copies of relevant sections of clinical records and necropsy report.

2) 6/19-20/08—During explant surgery, there was screw/drill penetration with some hemorrhage noted during surgery. Animal (#AX25) did not fully recover from anesthesia; research staff was told by vet to call at 10 pm if animal's condition was unchanged or worse. Last check by research staff at 10 pm indicated that animal was unchanged. Animal was found comatose by animal care staff at 7 am the following morning, propped up in a partially squeezed cage. Euthanized later that day. Necropsy revealed focal subdural hemorrhage. Discussed at SMPH ACUC meeting 7/7, 8/4, 9/8/08. Letter sent to PI on 7/8/08 asking for explanation.

Chip was in experiments since 2004. His explant was loosening so we scheduled a minor repair procedure. Drs. [REDACTED] and [REDACTED] attended and provided anesthesia support. In drilling some blood was noted but no CSF. The procedure started with catheterization and intubation at 10:54am. The procedure ended at 12:30pm. Monitoring commenced every 15 minutes until 1:20pm at which time Chip was recovered and moving. At 3:40pm Dr. [REDACTED] noted that Chip was QAR and uninterested in chow. She concluded that this was common for this animal on analgesics. At 7pm upon administration of analgesics by lab staff, some vomit was noted in the cage. Dr. Basso emailed Dr. [REDACTED] at 6:15pm to report on his condition and then called Dr. [REDACTED] and requested assistance/treatment plan - possibly administration of dexamethasone for possible bleed. Dr. Basso indicated that she or students would be back at 10pm to reassess and asked whether she could call [REDACTED] at that time. It is unclear why Dr. [REDACTED] did not come in (or call someone to come in) at 7pm. During this phone call, Basso was told by [REDACTED] to call the veterinarian on call if there was a change in the animal's status. At 10pm Chip's condition was unchanged so no call to the veterinarian was made. It seems that this is the critical issue of concern. A note was added to the clinical record on 6/20 by Dr. [REDACTED] stating that she told Basso to call the veterinarian on call if there was no change or the animal worsened. Basso understood that she was to call the veterinarian on call only if the status changed. Since it takes at least 48-72 hours for life threatening ICP to develop, and this animal was not exhibiting signs of critical ICP, the more immediate concern was aspiration. Therefore, at 10pm, the space in the cage was reduced and the animal was placed on the perch to prevent aspiration. This was not written in the clinical record but was recorded in the lab records.

The veterinarians and my lab staff and I worked closely together for the next day and together made a professional decision to euthanize the animal rather than implement further treatment (see attached email thanking the veterinarians for their help). Necropsy showed an epidural hematoma likely resulting from the drill. This is an unfortunate risk associated with neurosurgical procedures. All procedures were performed as part of an approved protocol, under the supervision of a veterinarian and this was the first time this has happened during a surgery I performed in my 15 years. As presented in the March 6, 2009 information session to the AC ACUC, we implemented a new hand drill with guide tube to minimize the likelihood of such accidents in the future and to ensure successful training of students and fellows on these complicated surgical procedures.

3) "Failure to maintain appropriate animal-related records"

Explant repair ended with animal (#93056) dying under anesthesia on 6/23/03. Although multiple doses of anesthetic were given, there were no records of the times the doses were given. Discussed at 10/3/03 SMPH ACUC meeting.

Corby was my first animal here in Madison. During an experiment after ~2 years, his explant broke. The incident was reported immediately to the veterinarian, Dr. [REDACTED]. She was in charge of the entire emergency wound closure from administering the anesthesia to closing the wound. Therefore, I assumed she would be in charge of the clinical record. There were further problems with this case. At the time of the incident, this animal had not yet received its daily fluid ration. I requested Dr. [REDACTED] provide supportive fluids but she did not. At this time the LAR was insufficiently stocked to care for emergency cases such as this. This was the first in a series of incidents that resulted in formal complaints by me to the director of the LAR (Dr. James Southard) and the chair of the ACUC (Dr. Amy Moser) as well as the Associate Dean for Research of the Medical School (Dr. Paul DeLuca) and my faculty mentoring committee for improved veterinary care for my research animals. See attached letter from me to Dr. Southard and from a former technician in my laboratory ([REDACTED]) who witnessed these events and two others - to be addressed below. These are provided to reiterate that the present conditions for NHP research in SMPH mitigate the likelihood of recurrence of events such as occurred with Corby.

Explicit instructions regarding who is in charge of what aspects of veterinary care and record keeping were not clear across the medical school at this time and to date are not uniform across campus as per [REDACTED].

4) 6/19-6/20/08—Research staff observations were not recorded in the animal's (#AX25) records, but rather in the lab notebook, which is inaccessible to veterinary staff after business hours. PI stated in ACUC meeting of 8/4/08 that the students chronically do not write in the records despite being told to do so, and that PI does not know how to correct this issue.

This is the same case as in Comment 2. Since I arrived in Madison in 2000, our laboratory notebooks are available for access by anyone at anytime. My cell phone number is/was posted in our animal room in [REDACTED] and I can be reached at any time. As indicated at the March 6, 2009 informational meeting the requirements for clinical record keeping have been changing over the course of a number of years at UW Madison. The specifics of what needs to be recorded and when have changed as new veterinarians were hired. Dr. [REDACTED] requirements are different from those of Drs. [REDACTED] and [REDACTED]. The differences between the record keeping styles of the veterinarians are clear in the clinical records for our animals. Furthermore, as recently as fall 2008, [REDACTED] RARC records trainer, stated that the requirements are not uniform across campus.

That said, as noted also in Comment 6, we have had difficulty meeting the changing requirements of clinical records. In spite of my requests to keep clinical records in the rooms where animals are housed, the records are maintained in a room some distance from the animals' housing. Over the years students in my lab understood that the clinical records were maintained by the clinicians, and that we were to maintain our own records. I have since instructed students and post-docs that they are to write in the clinical records all observations as per training with [REDACTED]. Note also that the clinical records for this animal on these days were in the possession of the veterinarians who euthanized and performed the necropsy on this animal. Lab staff did not have access to the records. Furthermore, both Drs. [REDACTED] and [REDACTED] (SMPH veterinarians) indicated satisfaction with the progress my lab was maintaining regarding clinical records prior to the shut-down.

5) Animal (#1640) was inadvertently left in play cage overnight. While there were no ill effects, the incident was not recorded in the animal's record. Discussed at SMPH ACUC meeting 8/04/08.
There are no stated protocols prohibiting an animal from being in the play cage overnight. We can amend the protocol according to the ACACUCs direction.

6) PI repaired skin after explant became dislodged. Records of the anesthesia and repair were not available in the animal's (#AX25) record for a week after the procedure. This occurred after ACUC-mandated records training. Discussed at 11/3/08 SMPH ACUC meeting.

This is the same case as in Comments 2 and 4. I agreed that over the years, laboratory staff had difficulty ensuring that the records were updated in a timely fashion. Often students in the lab were unsure whether they could access the clinical records since they were not veterinarians. We have implemented procedures for handling this concern and have taken further training as instructed by the ACACUC and SMPH ACUC. Note that for this case, the clinical records were in the possession of the veterinarians who euthanized and performed the necropsy on the animal. The records were then filed at the RARC. We did not have access to them to update them.

7) "Failure of animal care and use personnel to carry out veterinary orders" (note: UW-Madison's PHS Assurance includes the Chancellor's Memorandum on Veterinary Authority)
On 4/8/04 PI performed a clinical assessment of an animal (#97098) doing poorly, and ordered a CT scan without consulting a veterinarian. PI then challenged the authority of a veterinarian who refused to allow the animal to be moved after the CT scan due to its unstable condition and who had ordered a necropsy. PI called the IO, the LAR director, and the ACUC chair to dispute the vet's decision. Discussed at SMPH ACUC meeting 4/19/04. Letter sent to PI 5/04. PI requested letter be retracted; ACUC declined to do so.

I believe this refers to monkey 97098 named Quinlan.

As of 1/4/05 my protocol read: "All animals will undergo an imaging procedure post implant to ensure the integrity of the implant. Additionally, daily clinical assessments of the animals' health will be made. If we detect a change in behavior, an imaging procedure either MRI or CT scan will be performed." The Medical School ACUC requested this language be put in my protocol on 10/30/03. This is stated in the Medical School ACUC minutes dated 10/30/03.

Subsequent to the incident with Quinlan the ACUC recommended my protocol be revised to read (bold and underlined statements were added): "All animals will undergo an imaging procedure post surgery to ensure the integrity of the explant. Additionally, daily clinical assessments of the animals' health will be made. If we detect a change in behavior, an imaging procedure either MRI or CT scan will be performed in consultation with the veterinarian."

Dr. [REDACTED] was consulted prior to taking the animal to the Vet School for the CT scan. Shortly after the first incident with Corby, I asked the people in my lab to maintain journals of events and interactions with veterinarians. Attached are two letters, one from a student [REDACTED] and a second from a technician in my lab at the time ([REDACTED]). [REDACTED] arranged the CT scan according to our protocol and consulted with Dr. [REDACTED] regarding this animal's condition.

The CT scan revealed no neurological signs, yet this animal was still unwell on 4/8/04. My technician communicated with the veterinarian again (see attached notes). An ultrasound of Quinlan's abdomen was performed and the Dx according to the radiologist, Dr. [REDACTED] at the vet school was a paralytic ileum. Surgery was contraindicated (Vet school assessment with names of DVMs involved is attached). [REDACTED] and [REDACTED] took Quinlan to [REDACTED] and performed abdominal surgery. By the time I arrived at [REDACTED], Quinlan was dead - his pupils were dilated and fixed. I asked for the brain because I needed it to conclude our studies of this animal and was denied. My reading of the *UW-Madison's Chancellor's Memorandum on Veterinary Authority* includes only live animals. I believed that [REDACTED] was interfering with my research and so I contacted Mulcahy, Moser and Southard to report this behavior.

For the reasons stated above (protocol contained a statement requiring me to perform CT scans after clinical assessment and Veterinary authority is relevant only for live animals) I requested the letter of reprimand indicating that I violated Vet authority be retracted. The committee never interviewed me prior to their writing the letter accusing me of violating vet authority. Please see attached email from Jim Southard (then director of LAR). Note also that his email was referring to developing SOPs for the medical school to care for NHPs. The final document to which he refers never materialized. I publicly apologized to the Veterinarians for speaking unprofessionally (see attached transcript of my statement). The committee indicated they should have interviewed me first and that they were satisfied with my response. Although they did not retract the letter (see attached emails from [REDACTED] acting in her ombudsperson role).

In net, this event points toward the continued lack of consistent and explicit instructions from the committee to PIs regarding responsibilities. I was a member of this committee since 2003 and it.

was about this time that I resigned from the committee for this reason. Please see attached letter of resignation to the committee.

8) In 1/05, animal (#97090) with CNS signs was treated with dexamethasone. After lengthy consultation with veterinary neurologist, MD anesthesiologist, and MD neurologist, it was decided that dexamethasone was contraindicated. Despite veterinary instructions to the contrary, PI treated animal with dexamethasone. This is documented in the animal's medical record.

Mookie had an acute cerebral hemorrhage resulting from an electrode penetration. At the time of the incident a veterinarian was called immediately. According to the clinical record dated 1/12/05, Lasix, not Dexamethasone was contraindicated. Manitol was recommended. The veterinarian Dr. [REDACTED] was treating the animal until 9:40pm with dexamethasone and manitol. Basso was assisting and returned early morning. At 6am Basso repeated the same treatment as the veterinarian gave the previous evening as instructed by the veterinarian. See attached excerpts from the medical records.

9) 6/19-6/20/08—After explant surgery, animal (#AX25) was recovering poorly. Veterinarian instructed research staff to call if animal's condition remained unchanged or worsened. Animal was found comatose the next morning; vet was never called. Discussed at SMPH-ACUC meeting 7/7/08, 8/4/08, and 9/8/08.

This is the same case as cited in Comments 2, 4, and 6. Note that Dr. [REDACTED] (a clinical veterinarian who was present for the procedure) indicated at ~4pm that the monkey was QAR, moved slowly when prompted and was not interested in chow. She concluded that his was normal for this monkey, although the basis for this conclusion is not indicated. No one in the laboratory was contacted to confirm this. Dr. Basso emailed Dr. [REDACTED] ~6:15pm that evening and indicated that the animal looked unwell. Again at 7pm Dr. Basso called Dr. [REDACTED] to report the animal condition: Dr. [REDACTED] neither offered to come in nor sent anyone in to check on the animal. At this time, Basso indicated to [REDACTED] that she or her students would return at 10pm to reassess the animal. Basso was told by Dr. [REDACTED] to call the veterinarian on call if there was a change. A note added to the clinical record the next day by Dr. [REDACTED] indicates she said to call a veterinarian if the animal's condition worsened or if there was no change.

10) On 10/13/08 PI repaired skin (animal # 1640) after explant became dislodged, and did not call a veterinarian before beginning repair, as required by the SMPH ACUC. PI also did not notify veterinarians that the repair was healing poorly, due to haired skin that was curled into incision—it was discovered during a routine walk-through. Repair was re-done by veterinarian, after explant replacement surgery had to be postponed. Discussed at 11/13/08 ACUC meeting.

The ACUC requirement stated, "Soft tissue surgeries may be allowed outside of the [redacted] only with prior RARC veterinary permission and after post-operative monitoring procedures described in your protocols have been amended in consultation with a research animal veterinarian and your staff receives training as described below."

My approved protocol as of November 27, 2008 states: ^{→ after event happened} "3. Small repairs such as chips of the acrylic head holder device breaking without exposure of tissue can occur without any concern for animal well-being. Other issues such as full removal of the explant, a completely broken off explant are extremely rare. In the unlikely event that should happen, the maximum number of times that an explant would require such a repair will be determined in consultation with the Veterinarian who can assess the animal, its well-being and for example, bone integrity. In this unlikely event, animals will be anesthetized immediately with Ketamine (10 - 15mg/Kg, I.M.). The veterinarian will be called, surgical preparation will commence, and any wound(s) will be closed. At this time, an IV catheter may be placed and necessary fluids will be administered. The wound edge will be sutured and the peri-orbital wires may be removed. The animal will be allowed to recover for at least four weeks before a reinstallation of the head holding device and cylinders is performed."

During a routine cleaning of Harish, the explant came off. The animal was bleeding profusely. I anesthetized the animal and removed him from his chair and applied pressure to the wound for hemostasis. I instructed a student to call the veterinarian and to get additional assistance from a student in the lab. The student placed two phone calls. The first was to Dr. [redacted] where the student left a message on a machine. The second was to the LAR office and the student explained to ([redacted]?) that we needed a vet. The initial anesthesia was given at 11:50am. Harish was returned to his cage at 1:10pm. Dr. [redacted] made a detailed note in the clinical record at 12:50.

The complaint made against me here is related to what is described in comment 3 above. In Comment 3 it reads, "Although multiple doses of anesthetic were given...". At the time of the incident described in comment 3, Dr. Chris Parks instructed me that multiple doses of anesthesia should not be given (recall it was Dr. [redacted] who administered subsequent doses, I gave only the first one). With Harish, we had given one full dose at 11:50 and then a half dose at 12:22. The veterinarian still had not arrived and the animal was very light. I performed an emergency wound closure, not a repair of the explant. Dr. [redacted] indicated in the clinical notes that he would reassess later to determine treatment. I never received word on this.

Dr. [redacted] visited me at 3pm or so that day and asked me to "leave the veterinary care to the veterinarians". I agreed and understood that her staff would be monitoring the incision since they were also administering the medications. As can be seen from the relevant sections of the clinical records Harish was monitored by the vet staff through 10/22/08. I was never instructed to do anything further with Harish. I believe this is another example of unfortunate, but poor communication between veterinary staff and investigators indicating clearly who is responsible for what aspects of veterinary care. The attached clinical records have names redacted but lab staff made anesthesia monitoring entries on 10/13/08.

11) "Failure to adhere to IACUC-approved protocols".
PI started a post-operative animal (#1640) on water restriction prematurely (too soon after surgery). Discussed at SMPH ACUC meeting 8/4/08.

Harish was brought down on water on days 6, 7 and 8 after surgery by a new post doc in the lab. Our protocol states, "After surgeries, animals are provided with analgesics (see attached form) and allowed at least one week to recover". When this was discovered, I instructed the post-doc to bring Harish back up on water which was done on day 9 through day 11. For this and other reasons, I terminated the employment of this post-doc in September 2008.

3

12) "Conditions that jeopardize the health or well-being of animals"

Animal (#R99045) reported ill 8/11/03 with CNS signs, died 8/23/03. Necropsy revealed large left frontal lobe abscess, with penetration of the brain by screws in both the left and right frontal regions.

Brain infections are a possible risk of neurophysiology experiments and the procedures used on this animal were all part of an ACUC approved protocol. Although the pathologist concluded that the screws caused the abscess I was present for the necropsy and saw that the bulk of the abscess was located in the infraorbital cortex (ventrally). If the screws were the source of the infection then the bulk of the abscess should have been on the dorsal surface of the cortex. The orbital bone also did not look healthy at the necropsy. Bone erosion is not seen with abscesses that arise from inside the cranium. Finally, this monkey was receiving treatment for a left eye infection ~6 months before its death (see attached clinical notes). For these reasons I submit that the abscess resulted from the orbit rather than the screw. Regardless of the cause of the abscess, the care that this animal received during this time was very poor and this death could have been prevented.

The sequence of events is as follows:

Hanuman's condition was reported to the veterinarian on call as soon as his illness was suspected on 8/2/03. The call was made by laboratory staff because Hanuman worked poorly in the lab that day. The veterinarian, [REDACTED] indicated possible CNS infection (as reported by us). [REDACTED] indicated there was no evidence of CNS infection. On 8/4/03 this animal vomited after drinking some water. By 8/10/03 Basso was convinced of neurological issue and contacted [REDACTED] from the [REDACTED]. Dr. [REDACTED] concurred that the animal had some CNS pathology. The animal continued to decline and was treated for 'dehydration' or 'depression' until 8/11/03. See attached email exchange between Basso and [REDACTED]. Basso made repeated attempts to have [REDACTED] explore treatments for CNS insult. As a result of a conversation with Dr. [REDACTED] (Basso initiated consult with NEI veterinarian who recommended Dex and an antibiotic), this animal was treated with dexamethasone and baytril from 8/11/03 to 8/22/03. On 8/23/03 this animal had paralysis, dilated pupils and postural instability. Dr. [REDACTED] concluded that the animal was dehydrated. I contacted a colleague with ophthalmology experience to determine whether papilloedema was present (assay for ICP). Although she did not have NHP experience, she indicated that the "cups did not look like normal human cups". Dr. [REDACTED] concluded that there was no ICP and treated the animal for dehydration by administering 300cc fluid IV. While holding off the vein, the animal turned blue and stopped breathing.

13) Explant applied 7/24/03, animal (#R98054) reported ill 9/11/03 with CNS signs, euthanized 9/13/03. Brain CT on 9/12/03 indicated possible abscess and screw penetration through dura, although CT report is not in medical record. Animal not submitted for necropsy.

Again the procedures were all part of an approved protocol. The CT scan and MRI were performed by my laboratory as per our protocol. These images remain in my laboratory. These images are and were made available for viewing to anyone requesting them. I continue to insist that it is impossible to penetrate a healthy dura with the screws that are used for this surgery. We believe that the dura may have been compromised by the heat of the drill and this likely precipitated the brain infection. After the imaging procedure and the results apparent, I consulted with neurosurgeon colleagues (Dr. [REDACTED]) and veterinary colleagues (Dr. [REDACTED] and Dr. [REDACTED]) and Dr. [REDACTED]. We developed a treatment plan that included removal of the explant. Dr. [REDACTED] and Dr. Southard then refused to allow us to proceed with this treatment plan indicating that Dr. [REDACTED] did not have the expertise to oversee this kind of 'heroic' treatment. I was told to "cut my losses" and euthanize the animal. I euthanized the animal that afternoon. The veterinarians did not request a necropsy.

14) After experiment on 1/12/05, blood was visualized on probe after it was withdrawn—cerebral hemorrhage suspected. Animal (# 97090) recumbent, taken for brain CT 1/13/05, died during scan. No CT scan report available. Animal, without brain, submitted for necropsy. Unable to determine cause of death.

This is the same case as in Comment 8 (Mookie). Please see attached notes regarding CT scan recorded at the time by Dr. Basso. Since the animal died during the scan as a result of the anesthesia, there is no scan report. Dr. [REDACTED] - the exotic species specialist at the Veterinary school - specializes in birds and reptiles, not non human primates. Dr. Basso consulted with Dr. [REDACTED] in RARC necropsy and requested permission to take the brain and she approved. The slides are available for her at any time and she is aware of this.

15) After experiment on 1/28/06, animal (#96099) was found recumbent in cage on 1/29/06. CNS signs present, including seizures. Cerebral swelling evident on visualization of cylinders. MRI performed 1/31/06. No MRI report in record. Found dead in cage 2/1/06. Animal submitted for necropsy; brain observed grossly by veterinary pathologist, but despite multiple calls, PI did not contact pathologist when the brain was sectioned, so no internal dissection or histopathology was done.

This is the same case as in Comment 1. Note that in Comment 1 it states, "Necropsy was performed, but PI removed the brain prior to carcass being submitted, so no cause of death could be determined". Here it states that the pathologist did observe the brain grossly. As the necropsy report shows, the pathologist did observe the brain on gross dissection and the histological slides are available for Dr. [REDACTED] inspection any time. I coordinated this process with Dr. [REDACTED] for this case and in the past and routinely coordinate this process with Dr. [REDACTED] at the [REDACTED] when she performs necropsies on our animals.

16) Purulent discharge from explant first noted on 8/15/03, after eye coil replacement on 7/24/03; animal (#96089) was on antibiotics almost continuously until euthanasia at end of study on 5/5/06. Animal was not submitted for necropsy, so cause of infection is undetermined.

Weiland was euthanized at the end of the study according to procedures outlined in my protocol. Weiland was my second animal since arriving at Madison in 2000 and was participating in experiments for 6 years+. He had three cylinders. Colonization and possible infection are accepted risks associated with surgical implants of all types as discussed in the approved protocol. My lab staff cleaned this animal routinely and aggressively as per veterinarian discussions/instructions and our protocol and Weiland was under the care of the veterinarians at all times. The veterinarians did not request a necropsy for this animal.

9,

17) Starting 4/24/02, an animal (# 96089) was noted to have 9 eye coil replacement surgeries, with the last one being 4/21/06. Despite multiple instances of eye coil failure, the PI sought no assistance until pressured by the SMPH ACUC. The last two surgeries were done with specific ACUC permission, after specific protective interventions were required. Discussed at SMPH ACUC meeting on 11/1/04, 12/6/04, and 3/7/05.

As with all hardware implants, periorbital eye loops are subject to possible breakage. For a period of time we experienced a higher than normal number of eye loop breakages. As a result we engaged in an aggressive investigation together with our colleagues across the nation to determine what the issue was. I presented our national investigation and the outcome of same to the ACACUC during my information meeting on March 6, 2009. A summary of the steps I took is as follows:

- contacted colleagues across the country to determine if similar failures were occurring
- tested wires from colleagues across the country
- contacted wire company to determine whether alloy was changed
- had surgical technique overseen by Dr. [REDACTED] and Dr. [REDACTED] (latter at the request of the Medical School ACUC).
- had engineers (at NIH and U Rochester) testing the integrity of the wire.
- purchased wire from other companies
- implemented different surgical approaches (soldering, stripping etc...)

As a result of our investigation we discovered that the company changed the alloy and did not inform us. We have not had a series of eye loop failures like this before or since.

18) In response to a standard question during protocol review in 1/09, it was discovered that the PI was using non-sterilized probes, rinsed with tap water, to penetrate the dura and perform physiological readings. When told this was inappropriate, PI replied that, "It is my understanding that tap water is sufficiently chlorinated to kill off any bacteria otherwise it would be unsafe for our consumption". PI then asked for references from reviewers to illustrate their concerns about this practice. (Note: not yet included in minutes, but documented by emails sent by PI.)

Indeed, this was part of an email conversation I had with Dr. [REDACTED] after a protocol review. The phrase in the protocol we were discussing was, "Electrodes are introduced daily for the neuronal recording and behavioral measures. The electrodes and guide tubes are maintained in the same way. Electrodes and guide tubes remain in a glutaraldehyde solution between uses. When preparing for use, electrodes and guide tubes are removed from the solution and rinsed with tap water." Dr. [REDACTED] requested we change this to sterile saline.

Exposing the brain to the chemical in the sterilization solution such as glutaraldehyde would be dangerous. Therefore, electrodes are rinsed before introduction. During my 6 years at the NIH, the SOP was to rinse with tap water. The water from the tap was selected over saline because the force from the tap was sufficient to remove loosely attached particles from the electrodes. It is unclear whether a sufficient force could be obtained from soaking in saline. I wanted to make sure that we are adequately rinsing the glutaraldehyde from the electrodes. Please note that the electrodes we are sterilizing are ~250µm in diameter and are very fragile. They are made of polyethylene coated tungsten so microbial organisms already have a low probability of survival on them. I thought it was important that we discuss the risks associated with each method to determine the best course of action. An additional consideration in this discussion is that according to the Guide for the care and use of mammals in neuroscience research page 80, sterilization procedures can sometimes destroy experimental apparatus. The guide states that flexibility in these procedures is allowed. The autoclave would destroy them and bagging them for EO gas would also.

I would hope that this conversation not be construed as recalcitrance on the part of the PI. It was a discussion. I am happy to rinse the probes however the Vets deem best. I should also point out that not once in my 15 years experience with these procedures have we had a brain abscess result from an electrode penetration.

Summary

This PI has had significant difficulties with the cranial explant model—many more than other investigators using the same model in the same animal care unit with the same veterinary staff.

Two other investigators in [REDACTED] have NHP laboratories and they are less active.

[REDACTED] - 1 paper in 2006 monkey behavior only, no monkey electrophysiology

[REDACTED] - 2 papers in 2002 electrophysiology in monkeys

Michele A. Basso - 9 monkey electrophysiology paper since arrival in Madison (2000).
The model used by [REDACTED] and [REDACTED] is also not the same as ours. Our experiments are more complicated than those of [REDACTED] or [REDACTED]. We have multiple cylinders (up to 3) on our explants. This leaves the underlying support structure less stable and reduces the life expectancy of the explants. We perform recording experiments from very deep midbrain and brainstem structures making each penetration more risky than experiments performed in cerebral cortex for example. To minimize risk, we implement state-of-the-art imaging techniques to identify our locations to improve our targeting precision. We also perform multiple site recording and stimulation experiments (thus the need for 3 cylinders). Our lab and one other in the world has the capability and expertise to perform these experiments.

There is a lengthy history of non-cooperation with veterinary staff, including failure to follow explicit instructions and reluctance to permit necropsies on animals that die with CNS signs.

The evidence cited above and corroborated by the notes in the clinical records, does not support this assertion. Certainly Dr. [REDACTED] and I had many disagreements, largely surrounding the lack of NHP expertise. I apologized publicly for my behavior. I have always maintained excellent working relationships with veterinarians at NIH, at the [REDACTED] Dr. [REDACTED] and now with Drs [REDACTED] and [REDACTED]

There have been multiple instances of proven or suspected brain abscesses, and multiple events involving screws penetrating the dura, leading to either hemorrhage or abscess.

We have had two incidents of brain abscesses. Furthermore, we developed a new hand drill with guiding device to minimize the likelihood of negative outcomes arising from the drills in the future. This will help in training students and post-docs in these complex surgical techniques. I've also implemented new training techniques such as practicing on rodent skulls (much thinner) in advance of monkey procedures.

Animals have been left unattended for hours in compromised condition—the most recent event in June '08 is what triggered the involvement of the All Campus ACUC.

The evidence cited above and corroborated by the notes in the clinical records, does not support this assertion. There have been many times when I stayed with animals well into the early morning hours. Regarding the June incident, if there was any problem it was a miscommunication between me and the veterinarian.

Medical records are often incomplete or inaccessible; despite training, PI insists that it is unclear what needs to be recorded in a medical record.

At the time of the suspension we were working closely and well with Dr. [REDACTED] and [REDACTED] to ensure their needs were met by our lab. We will be certain to keep records complete as outlined by the veterinarians and they will be available at all times.

Recently it was discovered that the PI has been inserting unsterilized materials into brain tissue. This could be a partial explanation for abscessation and chronic inflammation that has affected several research animals.

The discussion surrounded rinsing of sterilized probes. As described in my protocol and discussed with Dr. [REDACTED] and [REDACTED] the procedure we used of sterilizing in glutaraldehyde and rinsing with tap water is the SOP used at NIH where I was trained. We would never insert a

non-sterile object into a monkey brain. Furthermore, there is no evidence that an infection has ever arisen from an electrode insertion in my 15 years working with this preparation.

Sincerely, Janet Welter, DVM, MPH, PhD, DAACLAM Chief Campus Veterinarian