



Report of a Workshop on Large Whale Medical Intervention - Indications and Technology Development

Sponsors: Woods Hole Oceanographic Institution, Center for Coastal Studies, New England Aquarium

Location: Carriage House, Woods Hole Oceanographic Institution, Woods Hole MA 02543

Date: Monday February 7th 2000

Steering Committee: Michael Moore¹, Andrew Stamper², Scott Kraus², Roz Rolland³

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Agenda

- 900 Welcome and Introduction - Michael Moore, WHOI
- 915 Introduction to right whale disease issues including review of recent potential patients
Scott Kraus, New England Aquarium
- 0945 The Federal perspective - Dana Hartley, NMFS
- 1000 Review of need for restraint and sedation during disentanglement efforts- Stormy Mayo
and Dave Mattila, Center for Coastal Studies, Provincetown, MA
- 1030 Break
- 1100 Review of current therapeutics and sedation in marine mammals Andy Stamper, New
England Aquarium and Mike Stoskopf N Carolina State U.
- 1130 Round table discussion 1: drug choice and formulation options for large whales:
sedatives, local anesthetics, glucocorticoids and antibiotics - Chair Andy Stamper
- 1230 Lunch
- 1330 Round table discussion 2: of physical restraint issues for large whales - potential solutions
- Chair Dave Mattila
- 1430 Round Table Discussion 3 : Design of hardware needs given expected drug formulations
- Chair Terry Hammar, WHOI
- 1530 Break
- 1550 Diagnostic priorities – Roz Rolland, Tufts Veterinary School
- 1600 Summary - Michael Moore and Scott Kraus

Executive Summary

The agenda of this workshop was to evaluate the indications for medical intervention in large whales, especially northern right whales, and to develop the technology appropriate for applications that appeared to be clinically and ethically appropriate. A review was presented of ship strike, fishing gear entanglement, reproductive failure and chronic skin disease evident in the populations of NW Atlantic right whales. Then, before proceeding into specific issues we reviewed the need for proposed protocols to be reviewed by the NMFS permit office to facilitate case by case requests for permits for emergency intervention by qualified veterinarians. The current system for physical restraint to enable disentanglement of right whales was then described. The available sedation and antibiotic agents were reviewed in the context of potential application to large whales. Through the workshop a consensus was reached that sedation prior to a disentanglement effort should be seriously considered on a case by case basis. The aim would be to minimize the substantial risk of injury or death to human operators who are attempting to disentangle the whale and to maximize the chance of a complete and minimally stressful disentanglement. The benzodiazepine drug Midazolam has been used successfully in captive free swimming small odontocetes, inducing a certain incoordination but no loss of respiratory control. Therefore the next step is to establish the efficacy and toxicity of this drug in non-endangered mysticetes, such as beached gray whales prior to euthanasia and in entangled humpbacks during disentanglement efforts. At the same time safe intramuscular delivery systems need to be developed that are capable of delivering about 20ml per injection site. The case for use of antibiotics was less clear. Obstacles include the absence of clear diagnostic indication for such therapy, the large volumes required and the frequency of administration. The next steps were therefore defined as: a) testing of Midazolam at doses in the range of 0.02 – 0.04 mg/kg in mysticetes as practical and as permitted by NMFS, b) development of ballistic systems to deliver this drug intramuscularly in animals with up to 25 cm of blubber thickness and c) analysis of available blubber thickness data to select optimal injection sites. Once these two steps are complete the use of sedation prior to disentanglement efforts should then be tested. These developments must be accompanied by further development of physical restraint systems as currently underway at the Center for Coastal Studies. Discussion of these issues included the possibility of head restraint, inflatable dry docks, and the current prototype tail harness. The potential for routine diagnostic evaluation of sedated animals during disentanglement was also discussed. Blood samples allowing surveys of serology were thought to yield the most important information in terms of infectious diseases that may impact the reproductive success of the population. Hematology and serum chemistry panels are also desirable to assess the physical state of the patient, to help to interpret the response to sedation and to establish some baseline values for this species. Therefore a further requirement is to develop a system to obtain blood samples from a restrained whale. Culture and sensitivities of gross external wounds, and possible biopsies thereof, were also suggested to assist in the goal of more complete diagnostics, and to assist in the decisions concerning antibiotic usage.

Background

This one day interdisciplinary workshop, attended by 12 veterinarians 11 whale biologists, an engineer and the NMFS Regional Stranding Coordinator, was convened by Michael Moore, with financial support from the Woods Hole Oceanographic Institution Cecil and Ida Green Technology Innovation Fund. The goal was to examine ways in which veterinary medical techniques could assist in efforts to mitigate right whale mortality. In particular the indications and technology for the use of sedation during disentanglement efforts and antibiotic therapy for wounds after disentanglement were considered.

Scott Kraus reviewed the key features of impacts on right whale survival that have some potential for mitigation. Fifty percent of North Atlantic right whale mortality results from ship strikes and gear entanglement. Ship strikes are the commonest cause of human induced mortality. They also can cause large open wounds resulting in severe scars on some survivors. At least sixty percent of the population has been entangled at least once based upon an analysis of the presence of typical scars. Their skim feeding habit increases the risk of serious entanglement. Disentanglement efforts represent a major chance to mitigate this mortality and morbidity factor. In addition there is a significant un-diagnosed reduction in reproductive success in northern right whales as compared to southern right whales. This has been exacerbated in recent years with the calving index increasing. Right whale calves are born at 4m, growing to 9m in the first year before weaning. Adult females can be up to 13m with males a meter shorter. The recent case of right whale #2030 was discussed. It was found entangled in Spring 1999, partially disentangled in September, but the tightest line remained, cutting through the blubber over the back between the axillae. It died in October as a result of trauma from the entanglement. Permits were sought and granted for antibiotic therapy in Canada, but the permit was not used after the disentanglement effort failed. The ability to safely sedate this animal would have substantially increased the chance of a full disentanglement. Northern right whales also exhibit a variety of chronic skin lesions. Attempts at biopsy of these lesions for diagnosis have failed to date. Thus there is significant entanglement related trauma and undiagnosed skin and reproductive health issues in this population that warrant whatever medical investigation, and treatment that can be delivered ethically and safely. Samples currently available for testing include: epidermal/dermal biopsies, feces, exhaled breath, and ultrasound measures of blubber thickness.

Dana Hartley then discussed the legal aspects of any future medical intervention with large whales. This was material sent to Dana for the workshop from Teri Rowles, an invitee unable to attend the workshop. Entangled whales are not considered stranded unless anchored. Thus free swimming entangled whales are not covered by regional Letters of Agreement for stranding management. Disentanglement of large whales is currently only permitted by the Center for Coastal Studies and qualified members of the Disentanglement Network. This is true for both anchored & free-swimming whales. The stranding network may be allowed to disentangle smaller, anchored cetaceans on a case by case basis under their Letter of Agreement with NMFS. Permit requests for medical intervention would be considered by NMFS on a case by case basis as an emergency action under the Marine Animal Health and Stranding Response Permit. There was discussion on what type of case would qualify for medical intervention under this permit. Initially intervention would probably only be authorized for the more extreme cases, but that as protocols are developed through research (i.e., w/ gray whales), perhaps sedation could be used in "less dire" cases. It was hoped that standard protocols could be submitted to NMFS for peer review so that granting of emergency requests would be facilitated, to allow action by a pre-approved list of qualified veterinarians.

Stormy Mayo then reviewed the current Center for Coastal Studies techniques for disentanglement. The basic approach, developed for humpback whales, is to increase their drag with buoys and drogues to slow them down sufficiently to allow gear removal. This has also been successful in right whales in 3/7 cases in the past 7 years, but the increased stamina, power and irritability of right whales has made this approach at times extremely dangerous to humans and not always successful. To date no serious human injuries have been sustained. A major component of the recent successful disentanglement efforts has been the substantial logistic support received from the US Coast Guard. Systems developed to stop whales include hooks, grapples, floats, boats and drogues. Attachment of satellite-monitored transmitters in buoys to the gear has enabled efforts to continue for multiple days, given adequate weather by keeping track of whales and gear. David Mattila then reviewed current efforts to develop a tail harness for animals where the entanglement involved anterior structures and offered no purchase on the

tail. He also described the concept of a device that was dropped in front of the flukes and had asymmetrical vanes that spun together behind the animal. Discussion ensued on the relative merits of controlling the tail vs./ the head. Tools to approach the latter could include a large hoop net, some form of twitch encircling the rostrum, or a seine net. The idea of an inflatable dry dock type system was also raised. The general assertion that cetacea tend to stop when held was discussed with the hope that this would be applicable to right whales. Experience is equivocal on this point. The general consensus was that physical restraint efforts would be substantially helped with some level of chemical sedation that lasted for periods of up to a few hours. It was agreed that to be effective a sedative has to be given before the animal is stimulated by disentanglement efforts. Sedatives are better at preventing excitement than reducing it.

Andrew Stamper then described the characteristics desirable in candidate sedatives: large margin of safety, low volume, single effective dose, reversible, low cost, no adverse reactions and easy to obtain. Requirements of an antibiotic would be low volume and cost, broad spectrum and bactericidal. Challenges for dose calculation include an accurate prediction of weight, appropriate use of allometric scaling, variation in physiological condition, dive response induced changes in regional blood flow, and pooling of lipid soluble drugs in blubber. There could also be risks to fetuses and suckling calves. Sedation could include the risk of inhalation under water. Challenges for antibiotic therapy include the volume to be administered with the resultant risk of sterile necrosis, the necessary frequency of administration to obtain therapeutic levels, and the potential for adverse reactions such as solar dermatitis with some medications. Delivery systems to discuss include dart syringes, biobullets, lyophilisation, oral, absorption across nasal mucus membranes via instillation into the blowhole and skin patches. Michael Stoskopf then discussed the issue of pharmacokinetics, in terms of partitioning and the chemical nature of specific drugs. He discussed the use of allometric scaling, and concluded that ultimately we need to use all that we know of specific drugs in other species, and then make an empirical assessment of dose, effect and survival to arrive at an appropriate protocol. The potential for antibiotic therapy was discussed, and the concern of the potential for development of multiple drug resistant bacteria was suggested as a barrier to the concept of using antibiotics at all. Others disputed this and the issue was not fully resolved. It was felt that if specific conditions such as *Brucella* were to be diagnosed in the future then the case for antibiotic use would be stronger, but that for entanglement induced wounds, removal of the foreign body was the primary goal, to allow resultant healing.

David Brunson then discussed the nature of Benzodiazepine group: anxiolytic, reversible, mild sedatives and safer than most other drugs. They work well in some species and not at all in others. Jim McBain then offered that in his experience 20ml injection per volume avoided major tissue necrosis. He reported that Midazolam, a Benzodiazepine derivative induced sedation, but not loss of respiratory function in odontocetes – “they appear drunk but functional”. Midazolam was agreed to be the best candidate drug for sedation of large whales. A dose of 0.02 to 0.04 mg/kg was agreed as the best starting dose. This is a water-soluble drug routinely available at 5mg/ml. It can also be theoretically be lyophilized and reconstituted as 20 mg/ml . Thus adult right whales ranging in weight from 20,000 to 60,000 kg would require one to many injections of 20 ml depending upon determination of the optimal dose and estimated weight. It seemed sensible to base our technology discussion on the assumption that multiple 20 ml units would need to be delivered. A brief discussion of immobilization by the use of neuromuscular agents resulted in the conclusion that this was probably not appropriate in these free swimming situations. Not presented at the workshop but relevant to this discussion was subsequent analysis of available necropsy data showing simple relationships allowing estimation of approximate body weight from age, or total length or fluke width (M. Moore pers. comm.).

Candidate situations for testing sedative use in mysticetes were then discussed. Stranded large whales deemed needing euthanasia would seem good initial candidates. Acknowledging that initial doses selected may be lethal, it was suggested that sedation prior to euthanasia has a good ethical basis, thus a relatively high dosage of Midazolam should be given in the first instance, with the resultant impact on heart rate, body and eye movement and survival recorded. It was noted that shocked stranded mysticetes might not be good models for entangled right whales, and that permits should also then be sought for the use of Midazolam on entangled humpback and minke whales. Jim McBain felt that the use of Midazolam in a right whale was unlikely to represent a serious risk of harm.

David Mattila then opened a discussion of physical restraint. Right whales seem to have a unique ability to tow gear, boats and drogues for long periods of time under substantial loads, without slowing down. The Center for Coastal Studies has focussed their efforts on restraint by the tail using small boats and drag systems. Many at the workshop were interested in restraint methods aimed on the head region. Stormy Mayo related that Navy Seals had planned to deploy a cargo net over the head of a right whale in the Delaware River. This had not been attempted. The concern was then raised that there would be substantial drag in trying to deploy a hoop net at the scale required for a right whale. The discussion then moved to the relative size of the whale and the vessel attempting restraint. The group acknowledged that ultimately the vessels best suited for catching large whales are to be found in the catcher boat designs of the whaling fleets. The suggestion was made that any system of restraint be tested on floating dead whales first. In conclusion it seemed that the existing small boat based system, that had been proven to be practical and affordable, could be made substantially safer for humans and whale with a safe sedation protocol.

A discussion was also held on the risk of the capture myopathy syndrome. It was agreed that there was an inevitable risk of this in situations where an animal was severely stressed in handling or chronic entanglement.

Terry Hammar then led a discussion on the possible avenues for drug delivery. Michael Moore demonstrated the prototype injection system designed for use with a cantilevered 40' pole to deliver large volumes (one liter). It was agreed that operator safety would be greatest with a ballistic device. The risk of complications with needles suggested that slugs fired in to the dorsal muscle mass may be the most effective. We agreed to limit the discussion to delivery of one or more 20ml doses or the development of solid "biobullets or biobolts". The question of the ability to lyophilize a drug for delivery was also discussed. Concern was raised that the powder would not be absorbed rapidly enough. Larry Dunn emphasized that the pharmaceutical industry needs to be given specific formulation requests before they can be of assistance. Discussion then covered the possibility of drugs via the blowhole to allow absorption across the nasal mucus membranes. There was no consensus delivering that this was practical, with major concerns of delivery, poor penetration and exhalation voiding any drug introduced resulting in both poor efficacy and potential danger of inhalation by project personnel. The question of attaching a line first, or sedating first was also raised. It was concluded that the specific situation would dictate the precise protocol. This discussion was concluded with a resolution that Michael Moore, David Brunson and Terry Hammar would confer on further development of the available ballistic technology. The systems developed for Discovery tag delivery should also be revisited, as should available information on the biocompatibility of different materials that may be used in drug delivery.

Roz Rolland then briefly discussed the important diagnostic investigations that might be attempted in a sedated whale. Clinical observations before, during and after sedation should

include awareness level, respiration character and rate and expiration/ inspiration interval, and changes in tail, flipper and eye movement. Attachment of an acoustic or electric cardiac monitor by suction cup would also be important if possible. Blood samples should be collected if possible for physiological and health assessment. Desirable parameters include hematology, serum chemistry and serology for a targeted list of infectious disease of concern.

It was also agreed that Beth Turnbull, Roz Rolland, Mike Stoskopf, and Greg Early would assemble a sampling kit for the Center for Coastal Studies for the event where a blood sample could be drawn and cultures and biopsies may be taken. After the meeting Mike Stoskopf provided a prototype design for a pole based blood sampling system. Moore, Hammar, Brunson and Stoskopf will work on this design.

WORK PLAN (written by Michael Moore in writing up the report after the workshop)

1. Moore to submit draft report to attendees for edits. Final report then to attendees for approval.
2. Circulate final report to all invitees and other interested parties, including the Eubalaena email list encouraging feedback and comment.
3. Develop sampling kit for CCS to carry in case the opportunity to collect blood samples cultures and biopsies arises. (Turnbull, Early, Stoskopf and Mattila). Need to submit blood sampling, culture and biopsy protocol to NMFS for addition to CCS permit. Mattila and Stamper/Turnbull to take this lead.
4. Investigate the available ballistic systems to modify for remote i/m delivery of 20 ml fluid or powder 30 cm deep (Moore, Stamper, Brunson, Hammar and Brown).
5. Solicit stranding networks to sedate large whales with Midazolam prior to euthanasia making the observations recommended above. This request should probably be made by Teri Rowles. Data should be collated and reported in peer reviewed literature. Frances Gulland at the Marine Mammal Center in Sausalito will probably get the opportunity to do this on gray whales, so maybe she should be the coordinator of this data set.
6. Prepare and submit to NMFS detailed protocols for use of sedation in disentanglement for potential addition to CCS permit. Administer sedation to entangled humpbacks and minkes. Kraus/ Stamper/ Mattila
7. Assuming work develops as planned add sedation to routine disentanglement protocol for all large whales including right whales.
8. Continue working discussion and research /assess validity of antibiotic therapy in whales.

Pertinent data should be collated and reported in peer review literature.
Suggest a working group be formed to carry out this plan:

Moore, Hammar, Kraus, Early, Mattila, Stamper, Rowles, Gulland, Brunson,

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