# **2015 GAHP WORKSHOP**

## American Association of Zoo Veterinarians (AAZV)



The Great Ape Heart Project (GAHP) hosted a workshop on September 26 in Portland, OR at the 2015 American Association of Zoo Veterinarians (AAZV) Meeting. The workshop was part of the GAHP's 2012 National Leadership Grant from the Institute of Museum and Library Services (NLG-IMLS). The three-year IMLS grant provided financial support to create a robust, online, cardiac database system to be used by zoo and medical professionals, researchers and other subject matter experts (SME's) as they collectively work to assess, treat and prevent cardiovascular disease in great apes. The primary of

2015 Meeting participants outside the Red Lion Hotel on the River Jantzen in Portland, OR.

to assess, treat and prevent cardiovascular disease in great apes. The primary objective of the meeting was to introduce the GAHP Executive Committee to the new database as well as to update them on GAHP progress and activities to date. The GAHP decided to host the meeting in conjunction with AAZV so that the information could further be disseminated to zoo veterinarians and other participants in the project, while also gaining pertinent feedback for the project.

### **Meeting Content and Presenters:**

Hayley Murphy, GAHP Director: <a href="mailto:hmurphy@zooatlanta.org">hmurphy@zooatlanta.org</a>
Presentation: Welcome address and Meeting Overview

<u>Description</u>: HM summarized the workshop agenda, presented key accomplishments of the 2012 NLG-IMLS grant, and proposed sustainability issues and future directions of the GAHP

including the latest 2015 IMLS grant award.

Marietta Danforth, GAHP Project & Database Manager: Marietta.Danforth@gmail.com

Presentations: GAHP Exam Submission Process & Overview of the design of the GAHP database Description: MD presented the GAHP Executive Committee's 2013 "wish list" for the design of the online database system and summarized how the new database addressed these issues. A demonstration version of the database was presented live from www.gahpdatabase.com. MD went over the cardiac exam submission process and why we request the fields on our submission forms. Submission materials were shared on GAHP USB drives that were handed out to participants and are available for download at <a href="http://greatapeheartproject.org/forms/">http://greatapeheartproject.org/forms/</a>.



Marietta Danforth presenting the GAHP database in the AM session

## Rita McManamon, Karen Terio and Linda Lowenstine, GAHP Pathology Advisors:

ritamcm@uga.edu, kterio@illinois.edu, lilowenstine@ucdavis.edu

<u>Presentations</u>: Improving Ape Cardiovascular Pathology Protocols & Developing the Cardiovascular Pathology Database

**Description:** RM presented the basic and detailed GAHP

Apled flow charter view NV Anterior wall V Ant

Postmortem slides and cardiac ultrasounds are now comparable in the GAHP online database

cardiac necropsy protocols, which were included on the USB drives for participants, and is posted on AAZV's member's only section of their website as well as on the GAHP website. RM & KT explained the value of now having pathology findings in the database alongside cardiac ultrasounds and



Rita McManamon's pathology presentation

demonstrated how the post mortem summary can help us gain a more complete understanding of CVD in the great apes by connecting clinical findings with postmortem evaluations.

#### Gregg Rapoport, GAHP Cardiac Advisor (all species): rapoportg@gmail.com

**<u>Presentation</u>**: Great Ape Cardiac Health Update

<u>Description</u>: GR provided a summary by species of database findings for exams submitted to the GAHP. The summary was compiled during a January 2015 Cardiac Advisors meeting in Detroit and served as an introductory overview of the individual cardiac advisor presentations that followed.

#### Ilana Kutinsky, GAHP Cardiac Advisor (gorillas): ikutinsky@mhgpc.com

**Presentation:** Cardiovascular Disease in Gorillas: current status

**Description:** IK summarized the process for establishing cardiac reference ranges for gorillas, presented possible types of CVD that affect gorillas, explained her current work to define "abnormal" (affected) cases, and touched upon findings from a GAHP field assessment at the Limbe Wildlife Centre in Cameroon.

#### Bill Devlin, GAHP Cardiac Advisor (orangutans): whdevlin@icloud.com

**Presentation:** Orangutan Heart Disease

**Description:** Orangutans are the only apes for which cardiac reference ranges still need to be established. BD highlighted that while the GAHP has 114 echo submissions on orangutans in the database, only 25 of those records are suitable for research purposes. For a reference range publication, we aim to collect exams that: 1. Have both measurements as well as a copy of the echo for exam submissions. 2. Transthoracic exams – Not TEE exams. 3. Exams that did not use medetomidine (alpha2's). 4. Anesthetized exams – not awake (for consistency and best quality). BD then gave examples of affected cases from the 25 exams in the GAHP database.

## Meg Sleeper (presented by Gregg Rapoport), GAHP Cardiac Advisor (chimpanzees): <a href="mailto:margaretmsleeper@ufl.edu">margaretmsleeper@ufl.edu</a>

**Presentation:** Cardiovascular Disease in Chimpanzees **Description**: MS was unable to attend the Portland meeting, so GR presented her talk. The talk provide a literature review, case examples and a review of cardiovascular medications that have been used to treat CVD in chimps.

#### Vickie Clyde, GAHP vet advisor (bonobos):

Victoria.Clyde@milwaukeecountywi.gov

**Presentation:** Cardiovascular Disease in Bonobos

Description: VC presented on behalf of her collaborators, Dr. Sam Wann (GAHP cardiac advisor for bonobos) and Leann Beehler (GAHP ultrasound advisor). VC began with an overview of the types of CVD that are seen in bonobos (hypertension, ARVC/D, and others). She discussed her work evaluating blood pressure in bonobos and the types of devices that have been used in great apes: arm cuffs during anesthesia, finger cuffs during awake training, implantable devices. VC presented findings on obtaining blood pressure from awake bonobos using PetMAP Graphic™ finger cuffs 1. Finger cuff



The PetMAP Graphic blood pressure (bp) monitoring device (shown with a finger cuff) is used for bp monitoring in bonobos

measurements are similar to those taken at other locations 2. ACE inhibitors can lower bp in bonobos over time, and 3. Early treatment may restore normal heart size in bonobos. The GAHP's newest IMLS grant will expand upon the finger cuff work at Milwaukee County Zoo to all bonobo-holding institutions in the US. VC then provided some background to the bonobo cardiovascular database, recommendations for both awake and anesthetized cardiac ultrasounds (emphasizing that alpha-2's should be avoided). VC included early detection and treatment recommendations for CVD, including awake bp monitoring, routine cardiac ultrasounds, restricting dietary salts and caloric intake (increasing fresh browse and produce), and monitoring social stress levels.

Vicky Strong & Sharon Redrobe, Project Lead and Project Director for the EAZA Ape Heart

Project: <a href="mailto:ntxvjs@nottingham.ac.uk">ntxvjs@nottingham.ac.uk</a>, <a href="mailto:sharon.redrobe@twycrosszoo.org">sharon.redrobe@twycrosszoo.org</a>

**Presentation:** EAZA Great Ape TAG endorsed Ape Heart Project based at Twycross Zoo **Description:** VS presented background information about the state of CVD in ape populations in Europe. The Ape Heart Project is a sister-organization to the GAHP and similarly works to raise awareness, standardize approaches for clinical assessments and post-mortem examinations throughout Europe. The project received endorsement from EAZA and the Ape TAG to coordinate data collection in Europe through Twycross Zoo and Nottingham University. More information is available on their website: <a href="http://twycrosszoo.org/conservation/research-at-twycross-zoo/current-research/ape-heart-project/">http://twycrosszoo.org/conservation/research-at-twycross-zoo/current-research/ape-heart-project/</a>

#### Ann Duncan, Chief Veterinarian at the Detroit Zoo: aduncan@dzs.org

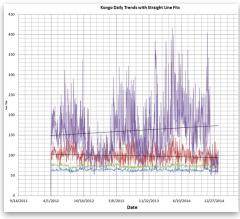
<u>Presentation</u>: Use of Implantable Loop Recorders (ILRs) to monitor cardiac disease in gorillas and chimpanzees

**Description:** AD is one of the first zoo vets to use ILRs in great apes. She presented the advantages as well as the challenges to using the devices. The device that was referenced in her talk was the **Medtronic Reveal™ XT 9529**, which weighs 15 grams and has a 3 year battery life. AD provided background to the gaps in our understanding of arrhythmia in great apes,



Medtronic Reveal XT 9529, which weighs 15 grams and has a 3 year battery life

noting that ECGs are usually only available during a short period when apes are under anesthesia. Zoo veterinarians have successfully adapted human diagnostics and therapies for great apes and ILRs are used to investigate syncope and arrhythmias that occur rarely in humans. The ILRs continuously produce a



Output from the Reveal ILR shows heart rate variability as well as heart rates by day/night and activity levels.

bipolar ECG lead and record arrhythmia episodes, including start time, duration and an ECG. They also monitor daytime Heart Rate, Nighttime Heart Rate, Heart Rate Variability, and Activity levels. The ILR device has a loop memory and can store 27 minutes of data. AD "interrogates" the implants

every 2-4 weeks using a Carelink programmer, which takes about 45 seconds. They use a cell phone to transmit the Carelink results. AD presented information on the surgical placement of the devices in both gorillas and chimpanzees (and how they differed), the mapping of the device, the reports that are generated by the device and the work that goes into sorting through the data from the reports.

#### Pam Dennis, GAHP epidemiologist:

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<u>Presentation</u>: Metabolic Syndrome as a Risk Factor for Heart

Disease in Great Apes

**Description:** PD provided an update on her research in collaboration with Dr. Mary Ann Raghanti on metabolic syndrome in gorillas. PD presented criteria for metabolic syndrome in humans, which involves any three of the following: abdominal obesity, hypertension, triglycerides >150mg/dL, HDL <40 mg/dL men; <50 mg/dL women, fasting plasma glucose 100-110 mg/dL. She then showed preliminary findings in healthy captive gorillas, captive gorillas affected with CVD, and apes housed at a sanctuary in Cameroon.



Collaborators Mary Ann Raghanti & Pam Dennis

### Suzan Murray, GAHP Executive Committee: MurrayS@si.edu

**Presentation:** Update on Brain Natriuretic Peptide in Gorillas

**Description:** SM provided an update on her work investigating BNP values in gorillas. In humans, BNP is one of several diagnostic tests utilized to not only diagnose cardiac disease (Left Ventricular Hypertrophy in particular). The Initial goal of her study is determine whether BNP can be validated for use in gorilla clinical care, and her initial findings suggest that this is possible. The general trend she has seen can be put into three categories:

BNP less than 125 pg/ml – generally healthy, non clinical (normal human levels less than 100) BNP over 350 pg/ml – mostly clinically ill male gorillas – the majority of which are now deceased

Middle ground – either older females (over 30 years) or male gorillas currently on treatment The next step is to perform more in-depth statistical analyses and publish the findings.

Deb Schmidt, GAHP nutrition advisor: <a href="mailto:schmidt@stlzoo.org">schmidt@stlzoo.org</a>

**Presentation:** Great Ape Nutrition Project

**Description:** DS presented her pilot project to identify nutrition correlations to CVD using ape serum to look at fatty acids (profile), vitamins A, D, & E, minerals (profile, and lipoproteins (cholesterol, triglycerides, LDL, HDL). Her start up funds are from Mazuri and Saint Louis Zoo.

Ben Brainard, GAHP Anesthesia Advisor: <a href="mailto:brainard@uga.edu">brainard@uga.edu</a>
<a href="mailto:Presentation">Presentation</a>: Anesthesia and the Ape: A tender tale</a>
<a href="mailto:Description">Description</a>: BB reviewed anesthesia concerns as they relate to great ape CVD. He addressed adequacy and safety concerns, and in particular, explained how alpha-2 drugs



Ilana Kutinsky, Ben Brainard, Gregg Rapoport & Pam Dennis presented findings from GAHP exams performed in Cameroon

affect the interpretation of cardiac exams. In addition to this presentation, BB participated in the afternoon panel discussion and provided a write-up for the GAHP to distribute to zoos on the use of alpha-2's.

## **Problem Solving and Panel Discussion Sessions**

**AM SESSION**: The AM session consisted mainly of GAHP Executive Meeting Members, therefore discussion focused on GAHP logistics, such as sustainability and data access.

**Sustainability** - Funding options such as "pay-to-play" were discussed, whether or not zoos are willing to contribute financially in the future, and examples of projects for which this has happened were discussed (e.g. Elephant Herpes-EEHV project). Once the database is well-populated, another suggestion was to open it up to PhD students: 1. To get information published and 2. To gain funding to cover the use of the database.



GAHP Executive Committee Members: Kristen Lukas, Tom Meehan, Hayley Murphy, Pam Dennis & Linda Lowenstine

**Data & Access** – Questions from the vet and path advisors were presented to clarify whether necropsy reports can be freely shared between the GAHP and the SSP advisors in either direction. It was noted that we need to better emphasize the GAHP's endorsement by the SSPs to zoos so that they understand that their submissions can be used for future research.

A point was raised by a research facility veterinarian about that institution's inability to contribute to the database, and it was clarified that their access to SME's and feedback on cardiac exams is still available, they just need to make it clear that the exam cannot be entered into the database as a submission.

Another point raised was keeping track of projects within the project – if someone doesn't publish their findings in "X" years, then it needs to be handed over to someone else to publish. In the publications discussion, crowd-source funding for research was discussed, including O-search and experiment.com.



PM Session Panelists - Ann Duncan, Ben Brainard, Gregg Rapoport, Ilana Kutinsky, Bill Devlin & Hayley Murphy

<u>PM SESSION</u>: The PM session was a continuation of the morning meeting, but also open to AAZV members. The majority of talks were presented in the PM session and were followed by a panel session, consisting of Hayley Murphy, Ben Brainard, Gregg Rapoport, Ilana Kutinsky, Bill Devlin, and Ann Duncan, to discuss the following topics:

**Diagnostics**: Examinations- awake vs anesthetized, Effect of anesthesia, BP, Blood work, Clinical picture

**Treatments**: Drug classes, Benefits vs risks of treatment, treatment before or after systolic dysfunction

#### Key points and comments that came out of the panel session:

- Difficulty in establishing orangutan Reference Ranges:
  - Orangutans tend to not be anesthetized as much as other apes, partly because they tend to be exhibited in smaller zoos where veterinarians may not be as experienced in great ape anesthesia and partly because of other health issues that may re-focus the concern away from the CV system. Respiratory issues appear to be more pressing as a veterinary concern.
- Are there recommendations about how frequently to anesthetize and examine a great ape. Is there a difference in the recommendations once an ape is diagnosed with CVD?
  - Hayley Murphy pointed out that the answer to this is complicated.
  - Each SSP should have guidelines in their Animal Care Manuals from the appropriate SSP veterinary advisors addressing this.

- General comments from the audience that management staff are often hesitant to anesthetize apes and the message is getting lost how valuable anesthetized exams are and why they are so beneficial
- Hayley Murphy noted that she is hesitant to put in writing to another zoovet to echo again in 6 months if it requires anesthesia, because then there is a written record suggesting a vet do something they may not have ability to do.
- One zoo vet participant noted: we do our gorillas q18 months with anesthesia to monitor because we see changes that quickly and have animals deteriorate within that time period. We have not had issues with it.
- Other said an exact time frame would be potentially harmful to the zoovet in that they will be held responsible for doing it or not doing it.
- O HM- pointed out that written recommendations from the GAHP should maybe be more general but follow up phone calls with SME's could be more specific, then that leaves the individual zoo clinician to decide what is best for their situation and to record appropriate information in the animal's records.
- Awake echo options
  - Hayley Murphy Doing echoes on non-anesthetized apes can be useful for monitoring a diagnosed cardiac issue and monitoring the response to treatment, but these examinations are often not complete or diagnostic. The keeper staff and even some vets have gravitated towards awake echoes as this idea that we don't have to anesthetize the apes anymore and this is not true. There is a lot of value to performing anesthetized exams that you cannot get from awake exams.
- A question was presented to the audience: Do the vets want treatment advice from the GAHP cardiologists?
  - There was an overwhelming yes. It was asked because it is ultimately the zoo
    vet who will decide the treatment, but the overwhelming response was they
    want to hear what the GAHP has experienced and/or recommended and make
    their decision based on that.
- Anesthesiology questions: What are some of the protocols for general anesthesia in great apes that are recommended and are being using.
  - Ben Brainard Discussed the drawbacks of using an alpha-2 agonist (in most cases that is medetomidine). Stated that medetomidine has its place as an anesthetic agent in apes, particularly when you need a reversible agent. Drawback is the cardiovascular side effects of hypertension that last approx. 20-30 minutes and then the compensatory hypotensive effect that is predominant.
  - He likes Telazol™ (tiletamine / zolazepam combo) as an anesthetic in apes. Ben Brainard discussed the use of premedication's containing a benzodiazepine in order to maximize the dissociate effects of the tiletamine.
  - Many zoo vets do not like the prolonged anesthetic recovery times seen with Telazol. Ben Brainard explained that Telazol lasts so long likely due to the metabolites of the zolazepam, which are active like the diazepam.
  - Hayley Murphy: personal experience- uses a low dose of 2.5-3 mg/kg Telazol and finds that recoveries are quicker with most apes sitting up within 2 hours of end of procedure.

 It was noted that using hand injection dramatically reduces the induction dose needed and therefore tends to lead to shorter recoveries also.

- Medetomidine may cause a normal heart to look diseased on echo so BB doesn't recommend using it for exams that require echo and don't use on apes with cardiovascular disease
- Question presented: When is it beneficial to start treatment?
  - Gregg Rapoport noted that there are differences in the literature on when to initiate treatments of CVD. Everyone on panel agreed that there are aspects of an abnormal echocardiogram that we all think are worth treating, but disagreement exists between the veterinary cardiologists and the human/MD cardiologists in some areas. All panelists agreed that when you see a heart with systolic dysfunction, treatment with ace inhibitors is appropriate.
  - o More disagreement exists when there is no systolic dysfunction, but just thickness in the heart. All agreed that if cardiac thickening is due to hypertension, that treatment has been shown to be therapeutic. However, the literature is not clear on the benefits of treatment when there is no clear cause of the hypertrophy.
  - o Bill Devlin: in humans thickening of the ventricle is not normal and it is treated with an ace inhibitor. If we wait bad things are going to happen if the therapy has low risk why not treat. Some use ENALAPRIL 5-20mg 2x per day. LISINOPRIL is a once daily ACE-I 2.5 to 40mg daily.
  - o Ilana, we don't know what normal is so we were very generous in describing and setting our "normal" for the male gorillas. LVH is bad and ace-inhibitors treat LVH and ace-inhibitors extend life in humans. We all came from the dimension that it is hypertension driven but it may not be; it may be familial and it may be better treated with beta-blockers. We just don't know yet.
  - Ben Brainard warned that animals on ace inhibitors have a dramatically magnified hypotensive effect to inhalant anesthetics and in humans they stop these drugs before anesthesia to avoid profound hypotension.
  - O Hayley Murphy: Pointed out that this discussion was very beneficial. The goal was to point out to zoo clinicians that this is not an exact science. Wanted the zoo vet to realize that since all the SMEs are not in agreement; it is up to the zoo clinician to ultimately make decisions for his / her animals. Wanted to aid in making informed decisions and then clinicians need to use their best clinical judgment on a case-by-case basis.
  - Ilana Kutinsky stressed again that there is no disagreement among SMEs on treatment of hearts that have systolic impairment
  - Gregg Rapoport: there are a lot of things we don't know, even the pharmacokinetics of the ace inhibitors in the apes is unknown. As we get better and better about collecting data we will be able to answer some of these questions. Some animals are being treated and some not, which also will be informative as time progresses.
- Zoo vet question posed: Isn't hypertension presumed? The chicken and the egg thing. Because the lesions are there.
  - Hayley Murphy at Zoo Atlanta, we have been monitoring blood pressure in non-anesthetized apes for a while now and we do not see a consistent

hypertension (as defined by human reference ranges). We also do not have a lot of cardiac disease though so this doesn't really prove anything. Cautioned audience from jumping to conclusions until we have more data.

 GAHP is helping with finger cuff BP study to improve our blood pressure understanding.

#### ILR questions:

- Ann Duncan we are treating 2 gorillas with ace inhibitors and beta blockers for ventricular wall thickening we are doing the human based therapy in treating the thickening before we have systolic dysfunction.
- Ilana Kutinsky: ILRs have a ton of info you can get from them. The apes don't tell you how they are feeling or that their activity has dropped off etc, so this is a way to monitor some of those variables. The newer ILRs have been used to see the HR come down when on beta-blockers but they are difficult to interpret and they are not useful in a healthy animal. If you see the occasional VPC in a healthy animal, it will not change your day-to-day management.
- Marietta Danforth: FYI the ILR data they are talking about isn't "GAHP data" that is in the database, but I'm keeping track of which zoos have ILRs in place and trying to recommend those who inquire about ILRs to get in touch with zoos that are already using them (such as Detroit and Lincoln Park Zoos, Columbus and National Zoos, and Omaha).
- Hayley Murphy: Also be aware that the apes can remove them easily and destroy them - bite them and hand them back. The devices cost around \$6000.
   And you can't just implant it and leave it there – there's a lot of additional work involved to get what you need out of them.
- One last question: Where to run blood samples for primates? More and more labs are not taking NHP blood for routine CBC/Chem. VRL does the viral stuff, ABL was also mentioned. Another vet said they've used Cornell to run samples and that they do the cholesterol and triglycerides. Some have had success with their local hospitals.

## Thank you

Thank you to all the presenters, Executive Committee Members, and participants of this meeting. The workshop would not have been possible without the financial support of the Institute of Museum and Library Services (IMLS NLG: LG-26-12-0526-12). A special thanks goes to Allison Tuttle and Adine Nicholson for helping to organize the workshop and allowing us to be part of the 2015 AAZV Meeting in Portland.



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