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**Elephant Endotheliotropic Herpesvirus Hemorrhagic Disease
Management Guidelines for Asian and African Elephants**

Updated June 2026

Disclaimer:

These guidelines have been summarized to the best of our knowledge and are based on limited research in elephants and available information in domestic animal and human medicine. **Many of the suggested treatments need to be scientifically validated in elephants and the application of these recommendations remains the responsibility of each institution.**

We strongly recommend that you use this information and the data in the literature to create your own institutional EEHV protocol. Utilize and reorganize this document to suit your needs and resources. The website www.eehvinfo.org should be consulted for further protocols, training recommendations, recommended treatments, and clinical findings, among other information, PRIOR to an elephant becoming ill with EEHV. Preparation for an EEHV case is an essential part of elephant welfare and care. The following document should be evaluated, modified, and adapted based on each clinician, and the resources and preferences of each individual institution.

In addition, individual institutions are encouraged to create their own “Fast Plan”, Emergency Care Flow Chart, and Treatment tables and summaries.

Contents

OVERVIEW OF EEHV AND EEHV HD	3
COMMUNICATION PLAN	3
EEHV SURVEILLANCE TESTING AND PREPARATION	4
CLINICAL SIGNS ASSOCIATED WITH EEHV HD	9
DIAGNOSTIC TESTING: SAMPLE COLLECTION WHEN EEHV HD IS SUSPECTED OR CONFIRMED	10
TREATMENT OPTIONS.....	12
INTENSIVE CARE OF THE EEHV HD PATIENT	13
NECROPSY	22
RECRUDESCENCE	22
APPENDIX 1: PROPOSED CASE DEFINITIONS	23
APPENDIX 2: ANTIVIRAL DRUGS	25
APPENDIX 3: BLOOD GAS ANALYSIS AND LACTATE MONITORING	27
APPENDIX 4: LIST OF SUPPLIES.....	32
APPENDIX 5: EMERGENCY FLOW CHART AND FAST PLAN.....	35

OVERVIEW OF EEHV AND EEHV HD

Elephant Endotheliotropic Herpesvirus Hemorrhagic Disease (EEHV HD) is a rapidly fatal disease affecting Asian and African elephants and is caused by several similar, but genetically distinct novel herpesviruses. EEHV is endemic within the Asian and African elephant populations and has been the cause of morbidity and mortality in elephants both in the wild and under human care. EEHV HD occurs primarily in elephants between 1-15 years of age. The clinically detectable course of EEHV HD is sudden and death can occur hours after the first clinical signs are observed, without clinical signs (sudden death), or the elephant may exhibit clinical signs for a week or more prior to death. This is a particularly devastating disease for elephant care teams, veterinary teams, and conservationists, and it is a serious threat to all populations of elephants. Adult elephants can develop disease associated with an EEHV infection and clinical signs are generally less severe presumably due to a pre-existing adaptive immune response. In North America, EEHV 1 is the most common species associated with EEHV HD in Asian elephants. EEHV 4 and EEHV 5 have also been implicated in causing disease, but less frequently. EEHV 2, EEHV 3, and EEHV 6 have been associated with illness and death in African elephants. Elephants can survive an acute episode of EEHV HD through a combination of timely diagnosis, rapid treatment, and innate and adaptive immunity.

Understanding the current knowledge and the significant gaps in information about the viruses and the diseases they cause is crucial for making informed decision about initiating and adjusting the treatment based on the condition of the individual patient and the herd, as well as adapting the response of the team.

EEHV emergency drills should be conducted once or twice a year to ensure that the response is swift and accurate. Assigned tasks and responsibilities, identification of deficiencies and successes, and debriefing and addressing areas of concerns will create stronger teams.

North American institutions are encouraged to register to gain access to the North American EEHV Advisory Group's Resource Database, developed to centralize human and material resources, optimize response teams, and provide support to organizations. For further information on EEHV and EEHV HD, please use the links listed here:

<https://eehvinfo.org>

<https://eehvinfo.org/about-us/eehv-information/>

<https://eehvinfo.org/publications/>

COMMUNICATION PLAN

In the event of a suspect EEHV HD case, rapid and effective communication must occur between the veterinary team, the animal care staff, and the administration. Each institution should establish their communication tree so that accurate information is relayed with minimal loss of time. A plan for 24-hour care should be established.

Enter the contact information for your institution below and establish your communication plan here. Consider including contact information for:

- Elephant team: Curator, Elephant Managers, Elephant Trainers, additional support staff
- Veterinary Staff: Veterinarians, Veterinary Technicians, additional staff
- Director, other
- Other key support staff
- Contact for Public Relations and Human Resources
- Diagnostics contact information
- Sample shipping information
- Resources contact list
- Consulting veterinarians with EEHV experience
- Consulting elephant managers with EEHV experience
- Pharmacies

Name Role / Institution	Emergency phone information	Alternate phone information	Email address / Physical address

EEHV SURVEILLANCE TESTING AND PREPARATION

In 2013, researchers demonstrated that viremia was present up to twenty-eight days before elephants show clinical signs of illness from EEHV HD. This breakthrough led to the recommendation to monitor at-risk elephants via EEHV qPCR on blood on a regular basis, to detect viremia early and start aggressive treatment before elephants show outward signs of illness. Most cases of EEHV HD survival since then have been diagnosed and treated prior to outward detection of clinical illness.

Routine monitoring of the herd allows for early detection of shedding (in trunk secretions) and potential hemorrhagic disease in younger elephants (as a viremia). In herds with recent changes in dynamics and with at-risk individuals, analysis of weekly trunk wash secretions is one way to know when the virus is being shed in the herd. The amount of viral shedding by one elephant required to result in a primary viremia in another elephant, and the viral incubation period are both unknown, but initial detection of EEHV on whole blood qPCR has been seen in some animals as much as 8-10 weeks after a herd mate shedding event.

Based on our current knowledge, the highest risk period for calves and young adults to develop EEHV HD is estimated to be between 1 and 10 years in Asian elephants and 1 to 15 years in African elephants. At risk animals should be tested routinely. Whole blood EDTA samples should be collected for a CBC and EEHV testing via qPCR at least once weekly. Institutions may decide to test twice weekly, as the viral load can increase exponentially very rapidly and maintaining a once weekly qPCR testing schedule can result in delayed detection of EEHV HD.

If EEHV is detected on whole blood qPCR, the recommendation is to increase the frequency of qPCR and CBC evaluation, until a determination of the condition of the animal is established.

All elephants should have EEHV serologic testing performed at least once, and in at-risk elephants, this should be repeated every 6 months. Young elephants can lose maternal immunity by 2-3 years of age, although some can lose it earlier. If an elephant is not challenged by the virus during the protected period, its risk of developing EEHV HD is increased. EEHV antibody titer information is an essential tool to inform surveillance and treatment plans. However, these time frames for enhanced monitoring are estimates, and longer periods of monitoring are recommended based on exposure to EEHV, herd status, and the immune status of each at-risk individual. Older animals that are seropositive can be monitored quarterly (or as deemed by the attending veterinarian) via a CBC, serum chemistry panel, and regular trunk washes qPCR testing for epidemiologic purposes. A comprehensive and updated surveillance plan document can be accessed here: <https://eehvinfo.org/clinical-management/eehv-routine-monitoring/> Up to date information on serologic testing can be found here: <https://eehvinfo.org/clinical-management/serology-in-eehv-surveillance-and-case-management/>

Collating serology, qPCR testing results, and crossmatching

Results for serology, qPCR, and crossmatching for each elephant should be kept updated. Examples of tables summarizing the information are provided here for Asian and African elephants:

Status of the elephants (at your institution and consider adding historical information as well)

Elephant ID	EEHV 1a	EEHV 1b	EEHV 4	EEHV 5a 5b	Serologic status Pan EEHV EEHV 1a EEHV 1b EEHV 4	Has developed EEHV HD and outcome (survivor, deceased)

Elephant ID	EEHV 2	EEHV 3	EEHV 6	EEHV 7	Serologic status Pan EEHV EEHV 2 EEHV 3 EEHV 6	Has developed EEHV HD and outcome (survivor, deceased)

Crossmatching

Crossmatching elephants is an essential part of EEHV preparedness. To ensure readiness for a potential EEHV HD case, crossmatching should be performed between at-risk animals and all other elephants at the facility as well as with donor elephants at neighboring facilities. After treatment with blood product, crossmatching should be repeated on any donor animal. Post-transfusion crossmatching should be performed at least 72 hours after treatment with blood

products. Results should be reported in the Crossmatching Database section of the EEHV Resource Database, to expedite response with blood product. Further information for crossmatching techniques can be found here:

<https://docs.google.com/document/d/1F3U7zjQgop3C1gBvWCGTCscCrKkNLR6I/edit>

Elephant ID / Crossmatch					

Blood Products Collection and Banking

Blood products play a pivotal role in treating EEHV HD. Large volume blood collections should be attempted periodically on any adult donor elephant to create a bank of products readily available during an emergency crisis. Whole blood is preferably collected into sterile, closed-system collection bags containing citrate-phosphate-dextrose-adenine solution (CPDA-1). Some collection bags come with a plasma transfer bag already connected. If the collection bag does not include this additional bag, sterile, empty plasma transfer bags should be maintained in your inventory for plasma separation and storage. If collection will be done using dry collection bags, the collection line should be primed for at least one hour with adenine-citrate-dextrose (ACD) solution.

Whole blood and plasma can be stored or collected to be used immediately. Fresh blood products are always superior to frozen banked products as they provide active platelets and clotting factors. Immediate separation of plasma from blood cells by a blood bag centrifuge preserves more beneficial factors than slow physical separation by gravity overnight. *Immediate freezing of plasma after centrifuge separation results in “fresh frozen plasma”*. Fresh frozen plasma stored for over one year becomes frozen plasma, which can be stored frozen for up to 5 years in a manual defrost freezer. It is not recommended to store plasma bags in ultralow freezers (-80°C) as the bags will be prone to splitting, resulting in complete loss of the contaminated plasma.

Penciclovir-fortified blood products may be used (see details in Appendix 2). The use or effectiveness of penciclovir-fortified plasma has not been thoroughly investigated, though it has been administered to several elephants of both species without adverse effects noted.

When indicated, platelets (freeze-dried or fresh platelet-rich plasma) can be supplemented to treat thrombocytopenia.

Behavioral training:

Successful diagnosis and treatment of EEHV HD depends largely on the ability to access the animal for visualization, sample collection, and treatment, including oral medication, rectal fluids and medication administration, and intramuscular injections. Prioritize the milestones to be achieved.

By one year of age, most of following behaviors should be a part of routine daily husbandry. Several documents are available which provide time ranges by which to achieve these behaviors (EEHV Caretaker Preparedness packet; AZA). These goals should be adjusted for each institution with the understanding that treatment will be enhanced the earliest a calf (and its dam) can respond to operant conditioning.

- Isolation from dam/other elephants
- Restraints / tethers / ERD
- Lay down
- Voluntary injections (IM and SQ)
- Voluntary blood collection
- Urine collection
- Body temperature measurement (fecal bolus, rectal, oral cavity)
- Blood pressure measurement (cuff on base of tail) if used
- Open mouth / Oral examination
- Acceptance of oral and rectal medications
- Acceptance of rectal fluids / rectal palpation
- Auscultation of the heart
- Cardiac ultrasound
- Body weight measurement
- Veterinarian / calf interactions
- Trunk washes

Daily Elephant Assessments:

Elephant care staff are most familiar with the elephant and are most likely to notice even subtle abnormalities in behavior. Any abnormalities should be reported as defined in your communication plan. It is better to have countless false alarms than to have one sick elephant go undetected. The appearance of clinical signs is an indication that internal damage has already occurred. The following observations should be conducted daily by the elephant staff:

- Overall attitude, demeanor, activity level, responsiveness
- Any change in behavior, training, mentation
- Mouth inspection including mucosa and tongue looking for discoloration, swelling, ulcers, blood blisters, hemorrhage, etc.
- Eye inspection looking for redness or small hemorrhages in the conjunctiva or sclera.
- Overall appearance looking for swelling of head / face, neck, trunk, front limbs and ventral abdomen (SC edema)
- Assessment of appetite (decrease or loss)
- Assessment of water consumption
- Assessment of urination (frequency, amount, color, etc.)
- Assessment of gastrointestinal system (defecation), frequency (increased or decreased), number of boluses, size of boluses, consistency of boluses, discomfort, diarrhea
- Assessment of musculoskeletal system: gait, mobility, joint range of motion, stiffness, lameness, muscle tremors, muscle weakness.

Monitoring vital signs:

Routine monitoring of physiologic parameters such as body weight, body temperature, pulse rate, respiratory rate, and blood pressure will help to establish normal values for each individual

elephant. This will yield a baseline of information for comparison to use when an elephant is a suspect for EEHV HD or other disease problem.

- Body weight is measured with (fill in here with your own protocol). Note that recent intake of water will cause fluctuations in body weight.
- Body temperatures are taken by inserting a digital thermometer into the center of a freshly voided fecal bolus, or during a rectal clean out by holding onto the thermometer while far into the colon. Temperatures higher than 100° F (37.8° C) should be considered elevated. However, once baseline temperatures have been developed for each elephant, you will fine tune what is considered an elevated temperature.
- Oral cavity temperatures may be recorded using a handheld temp gun and aiming at the same oral landmark for each elephant. These attempts should be made in the morning and prior to an animal eating. Note that there may be too much variation in baseline values to consider this technique reliable.
- Pulse rates may be taken by palpating an ear artery. The value is determined over 1 minute (either count for 60 seconds or count for 15 seconds and multiply by 4). An alternative would include using readings from the blood pressure monitor placed on the tail.
- Attempts can be made to record blood pressure by using human or animal blood pressure monitor and placing the cuff over the tail (using always the same location). While some institutions have been successful in establishing ranges and trends, others have struggled to get readings and consistency.

Record any changes from baseline values for temperature, heart rate, respiratory rate, blood pressure (if possible) and body weight and communicate information with veterinary staff.

Parameter	Expected African elephant ranges (given as guidelines)	Expected Asian elephant ranges (given as guidelines)	Your elephant's range when healthy
Systolic blood pressure (mmHg)	179	134 +/- 4 (range 93-172)	
Diastolic blood pressure (mmHg)	119	95 +/-3 (range 62-140)	
Fecal bolus temperature	95-98.7°F 97.6-99°F	97-99°F	
Oral cavity temperature (oral gun)			
Heart rate (beats / minute)	25-50 28-32	25-40 standing 30-60 lying down	
Respiratory rate (breaths / minute)	4-12	4-7 standing 10-15 lying down	

Where more than one normal range is listed, different values from different sources have been identified

Elephant care international, Dos Santos 2020

CLINICAL SIGNS ASSOCIATED WITH EEHV HD

Clinical signs are often absent, subtle, or non-specific at the beginning of an EEHV HD illness. In case of a confirmed or suspected EEHV HD case, the above list of observations should be performed multiple times during the day to record any change, improvement or worsening in condition. If the elephant can travel to the scale, body weight should be monitored daily to help assess hydration status. For further details on case definition, see discussion in Appendix 1: Proposed Case Definition.

Clinically, the following signs may indicate a possible EEHV infection:

Early clinical signs:

- Dullness, change in mentation
- Intermittent lameness or stiffness
- Decreased appetite
- Changes in water consumption
- Changes in feces: diarrhea or constipation
- Abdominal discomfort (colic)
- Changes in training / behavior
- Changes in sleeping patterns
- Swelling of temporal gland

Severe clinical signs:

- Lethargy
- Loss of appetite
- ** Edema / swelling of head / face, trunk, front limbs and ventral abdomen (SC edema)
- Continued or worsening lameness or stiffness
- Muscle tremors
- Oral lesions:
 - Hyperemia (dark, red oral mucosa)
 - Vesicle formation or ulcer formation
 - Petechiae / ecchymoses (hemorrhage)
 - **Cyanosis (blue discoloration) and inflammation of the tongue progressing from the tip towards the pharynx.
 - Ulcers or blood blisters in the oral and pharyngeal cavity.
- Ocular abnormalities:
 - Scleral injection
 - Bruising or redness of the ocular conjunctiva,
- Vulvar or preputial mucosa petechiae or ecchymoses (hemorrhage).
- Decrease in frequency of urination and defecation.
- Discoloration of urine (red to red brown).

** Presence of edema or cyanosis should warrant initiation of treatment immediately.

The following physical examination findings may be associated with EEHV HD:

- Tachycardia
- Cardiac arrhythmia

- Heart murmur
- Changes in blood pressure from baseline
- Hypoxia (< 95% measured pulse oximetry)
- Alteration in body temperature
- Evidence of fluid accumulation on ultrasound (abdomen, pericardial)

DIAGNOSTIC TESTING: SAMPLE COLLECTION WHEN EEHV HD IS SUSPECTED OR CONFIRMED

Because of rapid onset and progression of the disease, treatment should be initiated based on hematologic and clinical findings rather than an absolute diagnosis. If an elephant is showing clinical signs consistent with EEHV HD, blood samples should be collected as soon as possible for diagnostic purposes. When possible, trunk wash samples should be collected from each elephant in the herd for epidemiologic purposes.

Blood samples:

In a suspected EEHV HD case, high priority sample collection includes:

- Whole blood in EDTA for EEHV qPCR and CBC
- Serum or plasma for biochemistry, lactate analysis, and serology.

Additional samples include

- Whole blood in citrate for fibrinogen, D-dimer, and coagulation testing
- Banking extra serum and plasma (potential penciclovir levels)
- Whole blood banking in EDTA for future qPCR analysis

If possible, additional samples may be collected for current research requests. Use this link to access active protocols. <https://eehvinfo.org/clinical-management/research-protocols/>

Whole blood EDTA should also be collected from any potential blood donors in the herd for EEHV qPCR testing.

All blood samples should be processed as soon as possible. In-house CBC, PCV, and total protein should be analyzed and compared to the elephant's baseline values. Serum may be analyzed in-house or submitted to an outside lab for chemistry. The results of the EEHV qPCR from NEHL will not be available for at least 24 hours. Initial treatment decisions in that first 24 hours, before qPCR results are available, should be made based on CBC results and the elephant's history and serology status. Other samples may be run at the veterinarian's discretion.

One of the early changes in affected animals is a leukopenia with monocytopenia. The presence of leukopenia and monocytopenia in an animal with any level of viremia is significant and warrants immediate initiation of treatment. The presence of band heterophils in an elephant is abnormal and should be considered a significant finding for possible EEHV HD or other disease processes. Thrombocytopenia is often present and is noted to varying degrees. As with clinical

signs, the CBC profile may worsen for a few days even after initiation of therapy. Follow-up CBCs are important in tracking recovery or decline of the animal's condition. As the animal enters the recovery phase, a rebound leukocytosis and thrombocytosis lasting several days to weeks may be seen.

Urine samples: For a EEHV HD suspect or confirmed EEHV positive case, urine samples should be collected for urinalysis. Urine can be collected free catch into a tube or off the floor.

Trunk Wash: Depending on the institution, trunk washes of EEHV HD suspect and herd mates should be collected and sent out or analyzed in house with qPCR for herd surveillance. Knowing which elephants were shedding what virus may be helpful epidemiologically.

Shipment of EEHV PCR Samples

National Zoo Elephant Herpesvirus Laboratory (NEHL)

1. For EEHV routine surveillance or for suspect case:
 - Whole blood in EDTA (0.5 to 2 mL) for EEHV qPCR, sent on ice packs in cryovial
 - Serum (> 1 mL), sent on ice packs
2. Necropsy tissue samples (prioritize liver, heart, and other grossly affected organs)
 - Shipping on dry ice is preferred. Another option is using a sufficient amount of ultralow freezer packs
3. Use preprinted Fed Ex labels for:
Erin Latimer
National Zoo Elephant Herpesvirus Laboratory
Smithsonian's National Zoo
3001 Connecticut Avenue, NW
Washington, DC 20008
(W) 202 633-4252
(F) 202 633-8717
4. Email Lab coordinator (latimere@si.edu) to notify of sample shipment.
 - Email that a routine sample, clinical suspect, or postmortem sample has been shipped, share Fed Ex tracking number(s).
5. Weekend
 - For Saturday delivery, call / text cell (703-855-9611) to arrange for shipment of samples.
 - For Sunday testing, discuss options with lab coordinator (latimere@si.edu, 703-855-9611). Options include staff driving/flying samples to DC or using couriers.

Serological Testing:

The Baylor College of Medicine has developed serology tests to detect antibodies against EEHV in Asian and African elephants. A minimum serum volume of 100-200 uL is necessary (if amount is limiting, please contact Dr. Ling) for either the African or Asian elephant panels. The following link will provide information about the tests, directions for online submission, and payments. <https://orit.research.bcm.edu/EEHVSerologyTestingService>. Please contact Dr. Paul Ling (paul.ling@bcm.edu) with any further questions.

Samples are submitted to the following address:
Baylor College of Medicine

Attn: Paul D. Ling, Ph.D., Professor
Department of Molecular Virology and Microbiology
Jewish Building 919D
One Baylor Plaza
Houston, Texas 77030

TREATMENT OPTIONS

It is essential to remind all parties involved that treatments selected and prescribed are recommended based on the expertise of the attending veterinarian in charge of the case. The treatment plan for an EEHV HD case is dynamic and will change often in response to the animal's condition. The affected animal should be under intensive care, and round-the-clock monitoring is needed. **Many of the suggested treatments need to be scientifically validated in elephants and the application of these recommendations remains the responsibility of each institution.**

Initial treatments for EEHV HD are fluid therapy and antiviral therapy. This disease progresses rapidly with death likely resulting from viral-mediated vascular damage, multifocal hemorrhage, coagulation disorder, hypovolemia, multi-organ dysfunction, and myocardial damage. The goal of therapy is to provide aggressive supportive care to maintain tissue and organ perfusion while the body (or antiviral medication) attempts to fight the infection. **Sedation may be necessary to facilitate treatment in EEHV HD cases and to manage pain.**

The first line of treatment is rectal fluids. The rectal mucosa of elephants is capable of absorbing large amounts of fluid, with the excess being excreting. Lukewarm fluids administered at a slow rate via a soft hose or tubing can be very effective at keeping an animal hydrated. If condition deteriorates, intravenous (IV) fluids can be added. Elephants have a lower serum osmolality when compared to other mammals. Commercial crystalloid fluids are **hypertonic** for elephants therefore administration rate and dose should be adjusted accordingly and monitored closely. Colloid fluids can also be used, and small amounts can be beneficial. Consider the associated adverse effects that may depend on dose and specific product administered (e.g. acute kidney injury, impaired hemostasis, and platelet dysfunction). Administration of IV crystalloid or colloidal fluids should always be paired with rectal fluid administration to maintain hydration status.

Blood products are an essential part of any EEHV HD treatment protocol. They can be stored or collected fresh and administered IV through appropriate blood filters. **Elephants do have specific blood group antigens, so crossmatching is necessary before blood or plasma administration.** Penciclovir-fortified products can also be given to aid in treatment.

Antiviral drugs work to inhibit viral replication, but by themselves, do not correct the damage done by the virus to the animal's cells. It is important to treat the virus as soon as possible to prevent further viral replication and subsequent endothelial cell and tissue damage. EEHV is a unique herpesvirus, and data is currently unavailable to determine which antiviral drug (if any) is most effective at combating the disease. The two primary drugs that have been used to treat EEHV HD in North America are famciclovir and ganciclovir. Famciclovir has been used in more cases, and it has the convenience of being administered via oral or rectal routes with no reported

side effects. Absorption in healthy animals is good through oral and rectal routes, however, animals clinically affected by EEHV HD may not have effective absorption and distribution of the drug due to hemorrhagic and cardiovascular effects of the disease. Ganciclovir is a drug used in human medicine to treat beta herpesvirus infections. It is administered twice a day, intravenously, slowly over 20-30 minutes to achieve adequate blood levels, but does have potentially more risk of side effects. In addition, extravasation of ganciclovir can cause severe tissue irritation, phlebitis, and necrosis. ***Currently, there is no evidence to support efficacy of either of these drugs against EEHV; however, their use in the absence of adverse effects is likely to continue until more clinical data are available.**

Other therapies, such as analgesics, antibiotics, anti-inflammatories and gastrointestinal protectants are often used in EEHV HD cases for additional supportive care.

To inform treatment choices, further drug information, doses, decision trees can be found in the following chapters: Chapter 95 in: Fowler's Zoo and Wild Animal Medicine 9th edition, 2015; Chapters 19 and 32 in: Zoo and Wild Mammal Formulary 2nd edition, 2026.

INTENSIVE CARE OF THE EEHV HD PATIENT

Medical record

Detailed, accurate medical records are important to inform treatment options and advance understanding of this disease, future EEHV research, and further management options. All observations (activity pattern, appetite, sleeping pattern, restlessness, lethargy, dullness, and any change in clinical signs), treatments, and responses should be documented as thoroughly as possible.

Physical exam

Perform q4-6hrs while in the acute disease phase, then twice daily

- Body posture and mentation
- Edema (eyes, head, neck, ventral abdomen)
- Temperature – fecal bolus
- Changes in color or ulceration of oral mucus membranes
- Auscultation of calves less than 3000 pounds (heart rate, murmurs, arrhythmias, gut sounds)
- Respiratory rate and effort
- Production of urine or feces
- Lameness or stiffness
- Abdominal discomfort or signs of colic
- Blood pressure (tail cuff, 9-13 inch)
- Ultrasound assessment of thorax and abdomen daily to evaluate for cardiac contractility, development of pericardial/abdominal effusion, and splenomegaly
- Clinical signs seen as disease progresses
 - Dribbling saliva due to swollen tongue
 - Reduced trunk movement
 - Ataxia

- Recumbency
- Difficulty in auscultation of heart
- Weak, thready pulses
- Unresponsive to commands
- Sand eating
- Slight aggression towards keepers
- Discharge from trunk
- Decreased urination
- Increased sleeping

Diagnostic testing

- **Blood should be collected at least once daily for repeat testing**
 - EEHV qPCR
 - Treat if > 5,000 - 10,000 vge/mL
 - Test daily to adjust treatment regimen
 - Rapid elevation warrants treatment even if no clinical signs and CBC normal
 - Complete blood cell count
 - Leukopenia and thrombocytopenia precede clinical disease
 - Rapid decline in monocytes (monocyte: heterophil ratio < 1)
 - Lowest levels of both parameters correlate with peak viremia
 - Both show a dramatic rebound when clinical signs start to improve
 - Packed cell volume (PCV) and total solids
 - Serum biochemistry
 - Coagulation panel
 - Blood gas analysis (CG8 / CG4) and emphasis on lactate
 - Serum amyloid A (4 x higher in viremic animals)
 - Colloid oncotic pressure
 - Blood culture to rule out bacterial septicemia (e.g. salmonellosis)
 - Urinalysis – specific gravity, protein, crystals (specifically in African elephants but also important in Asian elephants)
 - Bank all samples (serum, plasma, and heparinized whole blood)

Rectal administration of fluids

This procedure is essential for any calf showing signs of illness, prior to EEHV diagnosis. Administer tap water using tubing or garden hose connected to the faucet after careful removal of distal fecal boluses. A gravity-driven funnel or a gastric pump may also be used.

- Administer at minimum of 3-4 times a day, up to every 2 hours.
- A bolus treatment of 10-20 mL/kg is often used.
- Hold tail down for one minute after fluid administration.
- Fluids must be given one hour prior to the administration of rectal famciclovir.
- Reduce fluid therapy when urine specific gravity decreases and crystals return.
- Pre-treat the rectum with a mixture of sterile lube and lidocaine to decrease irritation of the tissue, thus increasing compliance.

Antiviral treatments (see discussion in Appendix 2)

- Famciclovir
 - 15mg/kg orally or rectally 3-4 times daily

- Make into a watery paste for rectal administration
- Wait at least one hour after fluids to administer famciclovir
- Rake out excess water in the rectum before rectal administration of meds
- Ganciclovir
 - 5mg/kg given in IV slow administration over 20-30 minutes, twice daily. Dilute in one liter of fluids.
- Acyclovir (Used most commonly in Thailand)
 - 15mg/kg IV BID or 8 mg/kg IV TID.
 - 45 mg/kg orally TID
- Valganciclovir (Asian elephant PK study only, not yet used in an EEHV HD case)
 - 10 mg/kg PO X 2 loading doses, then 7 mg/kg PO TID
- Reduction of frequency and dosage of anti-viral treatments during recovery phase should be incremental and based on viral load and CBC response.
- Can administer 5-15 mg/kg famciclovir to plasma donor (orally or rectally) one hour before plasma collection to produce penciclovir-fortified plasma

Intravenous catheter placement

Placement of a temporary IV catheter in the aural vein during standing sedation is described below. Elephant plasma is hypo-osmotic relative to standard crystalloid intravenous fluids, hence, standard intravenous fluids given to elephants work like hyperosmotic saline used in large animal medicine. A relatively small volume of fluids can make a difference to the elephant's response. Minimally 2mL/kg seems to give visible results.

- Venous access is normally achieved using the vasculature on the caudal aspect of the ear.
- The skin should be prepped with chlorhexidine scrub using standard aseptic procedures. A 14-16 ga, 3" intravenous catheter should be placed and stabilized with Tegaderm™, tape, and skin staples (possible in an animal in standing sedation).
- Fluids can be given through a large animal IV line, using a fluid pump or fluid bag under pressure to speed delivery. It is helpful to use at least one extension set between the fluid administration line and the catheter to facilitate changing fluids and administration of medications along with the IV fluids.
- Extended Use MILACATH® (Mila International) catheters have been suggested when longer term placement is needed, when blood pressure is low, or when vasculature has been damaged due to prior treatment.
- Elephants in an intensive care environment can be subject to secondary infections, such as MRSA. Attention to hygiene and biosecurity is very important in elephants being treated for EEHV, particularly due to their immunocompromised status. Frequent hand washing, prompt removal of waste products, and regular sanitizing of equipment are recommended. Any handling of the intravenous catheter or associated fluid lines should be done with gloves.

Intravenous fluid therapy

Intravenous fluids are recommended to support circulation and hydration. An initial bolus of IV fluids (0.3 to 4 mL/kg in a calf) can be given to a dehydrated or "shocky" elephant as a resuscitative measure; this bolus could be repeated up to three times with re-evaluation of the patient and vital signs after each bolus.

Asian elephants have very low serum osmolality and are hyponatremic and hypochloremic compared to other mammalian species. African elephants are thought to have similarly low serum osmolality. The normal osmolality of Asian elephants ranges from 258-269 mOsm/L (median 261 mOsm/kg; Hall et al 2012).

- Crystalloid fluids have an osmolality as listed:
 - 5% dextrose: 252 mOsm/L
 - Lactated Ringers Solution: 273 mOsm/L
 - Normosol®-R, Plasma-Lyte: 294 mOsm/L
 - 0.9% sterile saline: 308 mOsm/L
 - Thus, commercial fluids such as Plasma-Lyte or Normosol®-R are actually hypertonic for elephants. These fluids could be used in elephants as you would use actual hypertonic solutions in other species; in other words, very small amounts (one liter per 1,000 lbs; one liter per 450 kg) are given through an IV catheter and followed afterwards with large amounts of rectal fluids.
- Isotonic crystalloid bolus
 - To be given to dehydrated calves or in cases of shock
 - 0.3-4 mL/kg - small volumes only
 - Can give 3 boluses with evaluation of vital signs after each bolus
 - Follow up with rectal fluids

Intravenous whole blood and plasma transfusions:

Plasma:

Fresh plasma (that was not previously frozen) or fresh frozen plasma transfusions are highly effective volume expanders. They also provide clotting factors, albumin, and essential proteins to combat infection. Additionally, animals with active EEHV HD illness likely do not have antibody to the virus and plasma transfused from an antibody positive donor may be beneficial. They are a key component to EEHV HD treatment recommendations. Crossmatching is essential and should be completed in advance (link [to protocols](#)).

Fresh plasma: Never frozen plasma that is separated and refrigerated at 4° C within 6-8 hours of collection is called *fresh plasma*. It is the best product to use as it contains all the coagulation factors, albumin and immunoglobulins. Coagulation factor activities decrease with time, and it is best used within 30 days of collection.

Fresh frozen plasma: Plasma that is separated and stored at -20° C within 6-8 hours of collection is called *fresh frozen plasma* and has a shelf-life of one year from collection with kept frozen. In Asian elephants, fibrinogen concentrations remain stable and while factor VIII decreased by 16%, IgG by 37%, fresh frozen plasma retains excellent therapeutic potential. Coagulation factor activities of other factors are likely decreased. In small animals, fresh frozen plasma retains on average 50% of the baseline coagulation function after thawing.

Frozen plasma: After 1 year of storage at -20° C or if there is a delay of more than 8 hours from collection, the product becomes *frozen plasma*, with a shelf-life of 5 years. In small animals, when thawed, frozen plasma retains most factors with reduced function (except factors V and VIII that are labile). A delay of more than 8 hours from collection to freezing of plasma, or freezing for up to 5 years, results in further reduction of clotting factor activities.

- Using a 20-16 gauge, 6cm length catheter will reduce perivascular leakage
- Plasma transfusion

- Fresh plasma has more beneficial factors than fresh frozen plasma, fresh frozen plasma is more beneficial than frozen plasma, and frozen plasma is more beneficial than no plasma at all.
- Plasma should be EEHV-screened as PCR negative prior to administration
- Administer after minor (and major) crossmatching using a filtered infusion set (size filter: 170 – 260 microns; changed at least after 4L – Equine recommendation)
- Dose: 0.5-2 mL/kg body weight (up to 10mL/kg)
- Administer the first 100 mL slowly (1 drops per second) to monitor for anaphylaxis – monitor every 5 minutes for clinical signs of reaction: heart rate, respiratory rate and temperature. Mild signs can be treated with antihistamines and by decreasing rate of transfusion. More severe reactions should be addressed by stopping the transfusion. If no reaction is seen after the first 100 mL, the transfusion rate can be increased, and vital signs checked every 15 minutes.
- Clinical improvement has been noted with doses as low as 0.5 mL/kg
- Once the EEHV type is identified, consider strategic plasma transfusion to provide a certain amount of antibodies in animals that are seronegative.
- Penciclovir-fortified plasma and whole blood can also be given to aid in treatment.

Whole blood transfusion:

Whole blood transfusion can be given after major crossmatching and EEHV PCR testing. Whole blood transfusions are indicated if the animal is anemic, PCV <12% or has severe thrombocytopenia.

- Collection and administration techniques are standard and require the use of a blood filter (170 – 260 microns) changed at least after 4L (Equine recommendation).
- Whole blood is administered following the same monitoring protocol as plasma transfusions.
- Whole blood stored at 1-6° C (33.8-42.8° F) will last at least 20-30 days with decreasing coagulation factor function. If not used, plasma can be collected from unused blood and stored (becoming frozen plasma, good for 5 years).

Platelets:

Plasma contains no cells and therefore when prepared routinely, this product does not provide thrombocytes. Platelet rich plasma is prepared by differential centrifugation of fresh whole blood, within 2 hours of collection; it requires special centrifugation specs and blood collection bags. The product has a shelf-life of 5-7 days when stored at 3.5 – 4.5° C. The resultant volume is small, but the concentration of platelets may be 3-5 times that of whole blood.

Sedation

The following protocols can be accessed via the EEHVinfo.org website:

<https://eehvinfo.org/clinical-management/sedation-for-eehv-management/>

Sedation is routinely used to administer treatments especially when drugs are administered IV. Reversal of the sedation may not be necessary to preserve analgesia and to allow for sequential sedations. Butorphanol reversal specifically may not be needed if calf is showing signs of pain.

Staff should not be afraid to sedate a calf for treatment but must be prepared with the proper tools and support staff to be successful. The following drug doses have been used successfully for standing sedation in elephant calves. Sedation protocols should be included in the institutional EEHV preparedness plan including contingency plans in the event of anesthetic complications. Anesthetic dosing and drug administration must be under the direction of an experienced veterinarian. Reversal agents may be administered to hasten recovery from sedation; however, consideration must be given to the need for repeated sedation events as well as reversal of analgesic properties. It is not always necessary, or advised, to reverse the sedatives unless complications arise.

These are dosage guidelines recommended by the EEHV Advisory Group based on many years of experience and published data. Attending veterinarians must make medical management decisions based on sound clinical judgement.

Asian Elephant Calf Standing Sedation (ZIMS 2025)

- Butorphanol 0.044 mg/kg (0.016-0.07 mg/kg) IM
- Detomidine 0.02 mg/kg (0.01-0.031 mg/kg) IM

African Elephant Calf Standing Sedation (ZIMS 2025)

- Butorphanol 0.02 mg/kg (0.009-0.05 mg/kg) IM
- Detomidine 0.014 mg/kg (0.008-0.025 mg/kg) IM

In some instances, it may be necessary to provide light sedation (lower end of dose) or standing sedation (higher end of dose) to the dam or other herd mates to facilitate safe administration of therapy to a calf with EEHV HD. Reversal agents may be administered to facilitate reintroduction to the calf but is generally not necessary. The following are recommended dosages based on years of experience and published data.

Adult Asian Elephant

- Butorphanol 0.02 mg/kg (0.006-0.07 mg/kg) IM
- Detomidine 0.016 mg/kg (0.006-0.031 mg/kg) IM

Adult African Elephant

- Butorphanol 0.018 mg/kg (0.009-0.023 mg/kg) IM
- Detomidine 0.016 mg/kg (0.009-0.022 mg/kg) IM

Reversal agents

- Atipamezole 5 times detomidine dose
- Naltrexone 2.5-5 times butorphanol dose

Oxygen therapy

Supplemental oxygen should be administered where possible, especially based on blood gas data. 2-4 liters/min via flexible tube passed into one nostril (if tolerated) or via an opened mask.

Analgesia

Pain is often associated with the EEHV HD. A few options are available.

- Butorphanol 0.008-0.015 mg/kg IM every 3-4 hours has been used in Asian calves. Avoid reversing sedation to maintain analgesia.
- NSAIDS
 - Analgesia and anti-inflammatory action
 - WARNING: *Use contraindicated in humans with peripheral edema and hemorrhage. Due to potential toxicity, evaluate risk if there is severe dehydration, shock or renal insufficiency.*
 - Flunixin 0.15-0.5 mg/kg IV/IM SID (endotoxemic dose)
 - Meloxicam 0.03-0.06 mg/kg IM, PO, SC SID
 - Phenylbutazone 3 mg/kg q48hrs, 1-2.5 mg/kg PO/ IV/ IM SID

Antibiotics

Antibiotics have no effect in treating EEHV however, the animal's immune system will be severely compromised, and secondary opportunistic infections associated with a compromised gastrointestinal tract and leucopenia may further compromise the patient. Options include:

- Cefotiofur sodium (Naxcel®): 1.1 mg/kg IV BID
- Cefotiofur crystalline free acid (Excede®): 6.6 mg/kg SC every 5 days
- Enrofloxacin: 2.5 mg/kg PO/ rectal SID
- Marbofloxacin: 2 mg/kg IV / IM / SC SID
- Amoxicillin: 11 mg/kg IM SID
- Penicillin G Procaine: 20,000-50,000 IU/kg IM/ IV BID-TID
- Other choice per clinician's preference and/or bacteria and sensitivity test

Gastroprotectants

- Omeprazole: 1mg/kg PO SID)
- Famotidine: 0.5-1mg/kg IV slow
- Pantoprazole:
 - Asian elephants (ZIMS 2026): 0.13 mg/kg-0.99 mg/kg IV SID
 - African elephants (ZIMS 2026): 0.05-0.2 mg/kg IV SID
 - Domestic horse (Plumb's): 1 mg/kg IV SID or 2 mg/kg SC SID
- Sucralfate
 - Foals: 20-40 mg/kg PO every 6 hours, used with acid-suppressive drug such as omeprazole

Mesenchymal Stem Cells Administration

Mesenchymal stem cells are derived from adult tissues such as blood, adipose tissues, placenta or umbilical cord. These cells are a potential emerging therapy for EEHV used for their anti-inflammatory effects, their ability to decrease cytokine storms and to protect endothelial cells, which may help improve clinical outcomes. Stem cells have been safely administered to both African and Asian elephants, including calves with EEHV. These cells can be used to treat different individuals of the same species.

Stem cells do not have an immediate effect, but they likely support the body during the recovery phase. It takes around 24hrs to process from frozen cells to an actual treatment. Stem cells need inflammation to be effective so need to time administration appropriately, but early in process

ideal since they need time to work (around 5-7 days for effect). Typical dose is 100-500 million cells (ideally 1 million cells/kg). No crossmatching is necessary. Administration will differ based on clinical resource but typically infusion is over 5 mins as a slow IV injection, given via an intravenous catheter and blood filter (18-20 microns). Treatment can be repeated in 5-7 days based on clinical appearance. Hypersensitivity reactions can occur to the components of the media the cells are grown in but are rare and treated as any other hypersensitivity reaction. Adverse effects include transient tachycardia, tachypnea, fever, lethargy, and anorexia.

There is a fee associated with preparation and shipping of stem cells, and a submission form requesting target treatment animal information and body weight. More information can be provided upon request by contacting the following individuals:

Vet Stem (<https://vetstem.com/>) located in San Diego, CA has stored Asian and African elephant stem cells that are available for shipping to individual institutions as needed.

Contact information:

Kristi Hauta khauta@vetstem.com
858.218.8660 (office direct)
858.748.2004 (customer service at Vet Stem)

Valerie Johnson processes elephant stem cell via Michigan State University

Contact information:

Valerie Johnson DVM PhD DACVECC
Michigan State University
736 Wilson Rd
East Lansing MI 48824
John7670@msu.edu

Immune stimulants and antioxidants

To support and stimulate the innate immune response to EEHV infections, immunostimulants have been studied and shown to elicit response in Asian calves. ZelNate® DNA immunostimulant is a veterinary product developed for use in cattle and available in the USA. It has been shown to induce innate antiviral immune response in Asian elephant blood cells in vitro. This product could head-start immunity and aid calves fight off infections with EEHV. The proposed dose is 2 mL IM on days 0, 4, 7 and 12. Further clinical investigations are needed to evaluate the clinical efficacy of this drug in the management of EEHV HD as well as any potential side effects.

Antioxidants include vitamin C (6 mg/kg IV SID), selenium (0.06 mg/kg SC), and vitamin E (5-15 IU/kg IM). Vitamin C will also help support the immune system.

Acid-base balance and lactate monitoring

Acid-base balance and lactate monitoring are essential parts of EEHV HD management. Please see Appendix 3 for an extensive discussion, further information and references.

Additional treatment options to be considered as dictated by condition of the patient

- **Vitamin B complex** (2 mg/kg in IV fluids) can be administered to support erythropoiesis (with or without iron supplementation) and to support neurologic and other cellular functions, etc., as indicated. Manufacturing of B vitamins by the body

may be significantly altered secondarily to the changes present in the gastrointestinal tract.

- **Diuretics** – mannitol 0.25-2 g/kg 20% solution slow IV, furosemide 0.25-1 mg/kg IM / PO BID
- **Probiotics:** consider using equine products or other choices per clinician's choice
- **Pentoxifylline:** lower dose has been used in elephants; titer to effect - must balance side effects vs desired effects.
 - Asian elephant (ZIMS 2026): young elephant 0.73 mg/kg PO BID
 - African elephant (ZIMS 2026): 1.7 - 4.78 mg/kg PO BID (dose used in adults)
 - Domestic horse (Plumb's): 8-10 mg/kg PO BID
- **Glucocorticoids**
 - i. The administration of a *single* corticosteroid injection for the purpose of membrane stabilization, though reported in clinical practice outside the United States, remains a subject of considerable controversy. Careful deliberation of the risk-benefit considerations is essential. **In the USA, this treatment is not endorsed and is considered as contraindicated by many.**
 - ii. Dexamethasone 0.05-0.1 mg/kg IV/ IM

References:

McCain S., P. Bapodra-Villaverde, and C. Sanchez. 2026. "Elephants." In: *Zoo and Wild Mammal Formulary*. 2nd ed., edited by Alicia Hahn, 309-325. Hoboken, NJ: John Wiley & Sons, Inc.

Howard L.L. 2026. "Elephant Endotheliotropic Herpesvirus Hemorrhagic Disease (EEHV HD) Treatments. In: *Zoo and Wild Mammal Formulary*. 2nd ed., edited by Alicia Hahn, 497-504. Hoboken, NJ: John Wiley & Sons, Inc.

Zuba J.R., and K.R. Mama. 2025. "Elephants." In: *Zoo Animal and Wildlife Immobilization and Anesthesia*. 3rd ed., edited by Gary West, Daryl Heard, and Nigel Caulkett, 925-964. IA: Wiley Blackwell.

Thitaram C, Bansiddhi P, Pakamma A, Arintasai K, Khammesri S, Sirikul C, Kosaruk W, Brown JL, Vongchan P. Long-term biochemical stability of fresh-frozen plasma from Asian elephants (*Elephas maximus*) stored at -20°C: Implications for emergency transfusion protocols for elephant endotheliotropic herpesvirus hemorrhagic disease. *Vet World*. 2026 Jan;19(1):125-134.

ZIMS Anesthesia Summaries for African Elephant (*Loxodonta africana*). (2025, Aug 07). Species360 Zoological Information Management System. Retrieved from <http://zims.species360.org>.
Filters: Weight range 500-3000 kg; Weight range 5000-7000 kg

ZIMS Anesthesia Summaries for Asian Elephant (Elephas maximus). (2025, Aug 07). Species360 Zoological Information Management System. Retrieved from <http://zims.species360.org>.
Filters: Weight range 300-1500 kg; Weight range 3000-6000 kg

ZIMS Drug Usage Extracts for African Elephant (Loxodonta africana) and Pentoxifylline. (2026, June 18). Species360 Zoological Information Management System. Retrieved from <https://zims.Species360.org>
Filters: All_ages_combined_Males_Females.

ZIMS Drug Usage Extracts for Asian Elephant (Elephas maximus) and Pentoxifylline. (2026, June 18). Species360 Zoological Information Management System. Retrieved from <https://zims.Species360.org>
Filters: All_ages_combined_Males_Females.

ZIMS Drug Usage Extracts for Asian Elephant (Elephas maximus) and Pantoprazole. (2026, June 18). Species360 Zoological Information Management System. Retrieved from <https://zims.Species360.org>
Filters: All_ages_combined_Males_Females.

ZIMS Drug Usage Extracts for African Elephant (Loxodonta africana) and Pantoprazole. (2026, June 18). Species360 Zoological Information Management System. Retrieved from <https://zims.Species360.org>
Filters: All_ages_combined_Males_Females.

NECROPSY

While the case fatality rate of EEHV1 in North America has decreased from 83% (1987 to 2013, n=23) to 50% (2014 to 2024, n= 24), it is still possible that an elephant will die from EEHV HD, even if detected early and treated aggressively. In the case of death or euthanasia due to EEHV HD, a complete necropsy is important to helping to advance our understanding of the disease and further decrease the fatality rate in the future. Elephant Necropsy protocols can be found at this link: <https://eehvinfo.org/necropsy/>

RECRUDESCENCE

After a primary infection with an EEHV species, the virus remains latent in the body with periodic recrudescence as evidenced by intermittent low-level viremia and/or viral shedding in trunk wash secretions. Further details on how to manage these cases can be found using this link: <https://eehvinfo.org/clinical-management/treatment-options/identifying-and-managing-cases-of-eehv-recrudescence/>

APPENDIX 1: PROPOSED CASE DEFINITIONS

The following definitions are proposed in the publication listed below for Asian elephants in North America (Senner et al). Extrapolation to other EEHV viruses and to African elephants is at the clinician's discretion.

Non-fatal cases: Elephants were included as EEHV1 HD survivors if they met three criteria:

- 1- A whole blood sample positive for EEHV1 via PCR or qPCR, with qPCR values above 1,000 vge/mL, or cycle threshold (CT) value below 38
- 2- The presence of at least one clinical sign (see table 1A below)
- 3- Documentation of at least one abnormal laboratory finding (see table 1B below)

Fatal cases: Elephant were included as EEHV1 HD deaths if they met two criteria:

- 1- Confirmation of the presence of the virus (either perimortem blood sample or at least one postmortem tissue positive for EEHV1 via PCR or qPCR, or the presence of virus inclusions was documented on the histology of at least one tissue).
- 2- The presence of lesions compatible with hemorrhagic disease (vasculopathy, hemorrhage, or edema) in more than one organ from a gross or histologic exam)

Table 1. Clinical signs of illness (A.) and laboratory abnormalities (B.) documented during EEHV HD and the proportion of EEHV1 cases (N=16) that each factor was identified in. Inclusion as a non-fatal EEHV HD case required the presence of at least one clinical sign of illness and one laboratory abnormality.

A. Clinical Signs	Proportion of Cases (%)
Change in behavior (decreased training compliance, decreased social activity, decreased general activity level)	93.75
Musculoskeletal discomfort (lameness or stiffness in one or multiple limbs, may be intermittent)	68.75
Edema (head, neck, legs, or trunk)	62.5
Mentation change (subdued behavior, lethargy, confusion, ataxia)	62.5
Oral or vaginal mucosal lesions (hyperemic mucosa, vesicle formation, ulceration, petechiae, ecchymoses)	62.5
Alteration in sleeping pattern or activity (more or less sleep than usual)	31.25
Decrease in water or food intake	31.25
Ocular abnormalities (scleral injection, icterus of sclera, retinal hemorrhage)	31.25
Cyanosis (tongue, mucus membranes)	18.75
Abdominal discomfort (stretching, rolling, "colic" like behavior)	6.25
B. Laboratory Abnormalities	
Leukopenia (WBC decreased below normal range for individual elephant)	75
Monocytopenia (Absolute monocyte count below normal range for individual elephant)	62.5
Thrombocytopenia (absolute thrombocyte count below normal range for individual elephant)	50
Anemia (packed cell volume PCV <25%)	25
≥ 2% immature neutrophil/heterophil (band) cells present	12.5

Reference:

Senner PW, Bapodra P, Bercier M, D'Agostino J, Faust LJ, et al. The population-level impact of elephant endotheliotropic herpesvirus-1 hemorrhagic disease (EEHV1-HD) mortality and

treatment in Asian elephants (Elephas maximus) in North America. In: Proc 21st Int Elephant Conserv Res Symp; 2025. p. 609-622.

APPENDIX 2: ANTIVIRAL DRUGS

From Goodman and Gilman, Plumb's and peer-reviewed papers.

Various antiviral drugs have specific or broad activity against herpesviruses including herpes simplex (types I and II), cytomegalovirus, Epstein-Barr, varicella-zoster, equine herpesvirus and feline herpesvirus.

Acyclovir:

Valacyclovir is acyclovir's prodrug.

Famciclovir

Famciclovir lacks intrinsic antiviral activity but is rapidly converted after oral absorption into penciclovir (active antiviral compound).

Ganciclovir:

Ganciclovir is similar in structure to acyclovir; valganciclovir is ganciclovir's prodrug.

Spectrum of activity:

Penciclovir and acyclovir have similar spectrum of activity and potency against human simplex herpesvirus (HSV) and varicella-zoster. Penciclovir has demonstrated potent in vitro antiviral activity against FHV-1.7 Penciclovir is considered a virostatic agent and therefore does not affect latent virus and does not necessarily clear the virus. Viral resistance may occur by mutation of viral thymidine kinase or DNA polymerase.

Ganciclovir has inhibitory activity against all herpesvirus and is especially active against cytomegalovirus (CMV).

Metabolism:

Famciclovir has a longer half-life and better oral bioavailability than acyclovir.

Penciclovir and acyclovir are phosphorylated intracellularly by a viral thymidine kinase (TK) and subsequently by host cell enzymes to become inhibitors of viral DNA synthesis (and to a much lesser extent cellular DNA polymerases). In cells infected with susceptible herpesvirus, viral thymidine kinase phosphorylates penciclovir to penciclovir monophosphate. Penciclovir monophosphate is then converted to penciclovir triphosphate, which inhibits herpesvirus DNA polymerase via competition with deoxyguanosine triphosphate, thereby selectively inhibiting viral DNA synthesis. Although penciclovir triphosphate is approximately one-hundredth as potent as acyclovir triphosphate, it is present in infected cells at much higher concentrations and for more prolonged periods.

Ganciclovir is monophosphorylated intracellularly by viral TK during HSV viral infection and by viral phosphotransferase encoded by UL97 gene (CMV infection). It inhibits viral DNA synthesis. Ganciclovir diphosphate and ganciclovir triphosphate are formed by host enzymes.

The triphosphate preferentially inhibits viral rather than host cellular DNA polymerases. Incorporation into viral DNA causes eventual cessation of DNA elongation.

Bioavailability:

In human studies, oral bioavailability of acyclovir (10%-30%) and ganciclovir (6%-9%) are low; for both, their prodrugs (valaciclovir and valganciclovir have better oral absorption). In contrast, famciclovir is well absorbed orally (bioavailability ~75%) and is converted rapidly to penciclovir in the liver.

In elephants:

EEHV have both the TK and UL97 genes, but we lack evidence of their function. We also do not know the IC₅₀ for EEHV of any of the antiviral drugs currently considered.

Pharmacokinetic studies for famciclovir (as well as measures of penciclovir), ganciclovir, and acyclovir are available in Asian and African elephants, however no pharmacodynamic studies are yet available. Pathologic changes both in structure and function of the tissues caused by EEHV HD may influence absorption, metabolism, activation, and excretion of the antiviral drugs. Acyclovir oral bioavailability is low in elephants (6%) and declines with increased doses.

Decreased appetite during EEHV HD often limits oral administration of drugs. Rectal administration of famciclovir and acyclovir to healthy elephants has been shown to high yield plasma levels that are equivalent to therapeutic levels in humans. Ganciclovir is administered intravenously.

Penciclovir-fortified plasma (or whole blood) is obtained by treating a healthy crossmatched elephant with famciclovir and collecting blood one hour later to extract plasma or administered whole. This technique has been suggested as one way to provide elephants in EEHV HD with penciclovir (thus avoiding the extra step of famciclovir metabolism into penciclovir). However, higher doses of famciclovir recommended (30 mg/kg PO once) may cause side effects in the donor. One alternative would be to administer famciclovir rectally at a lower dose since rectal absorption seems to be superior to oral bioavailability.

In many domestic species and in humans, these drugs are associated with a variety of adverse effects spanning from none to myelosuppression, urticaria, neurological deficits, hepatic necrosis, and renal tubular necrosis (especially famciclovir in cats) and we recommend close monitoring of renal and hepatic functions and adjusting of doses accordingly.

APPENDIX 3: BLOOD GAS ANALYSIS AND LACTATE MONITORING

Blood Gas Analysis

Arterial blood gas analysis allows assessment of oxygenation, ventilation, and acid-base status, providing significant information regarding the metabolic status and respiratory function of the patient. During an EEHV HD crisis, profound metabolic changes are expected to occur, necessitating targeted interventions to correct the resulting disturbances. Accurate interpretation of the primary alterations along with the physiological corrections, will allow clinicians to implement more effective, targeted treatments.

In elephants, aural arteries may be the most accessible peripheral vessels. Local anesthetic mixture of lidocaine (2.5%) and prilocaine (2.5%) cream can be applied to desensitize the skin 20-30 minutes prior to blood collection or catheterization. While arterial blood is required to assess pulmonary function, mixed venous blood may be used for acid-base analysis. Paired arterial and venous samples can be used to estimate oxygen extraction ratio.

Vacutainer tubes are not acceptable for blood collection and samples should be collected aseptically and anaerobically using pre-heparinized syringes. Make sure to expel excessive heparin from the syringe pre-sampling) and to expel any air bubbles and cap the syringe after the sample is collected for accurate measurements. To maintain accuracy of the parameters, samples should be analyzed within 10 minutes of collection or stored in an ice bath for no longer than 2 hours.

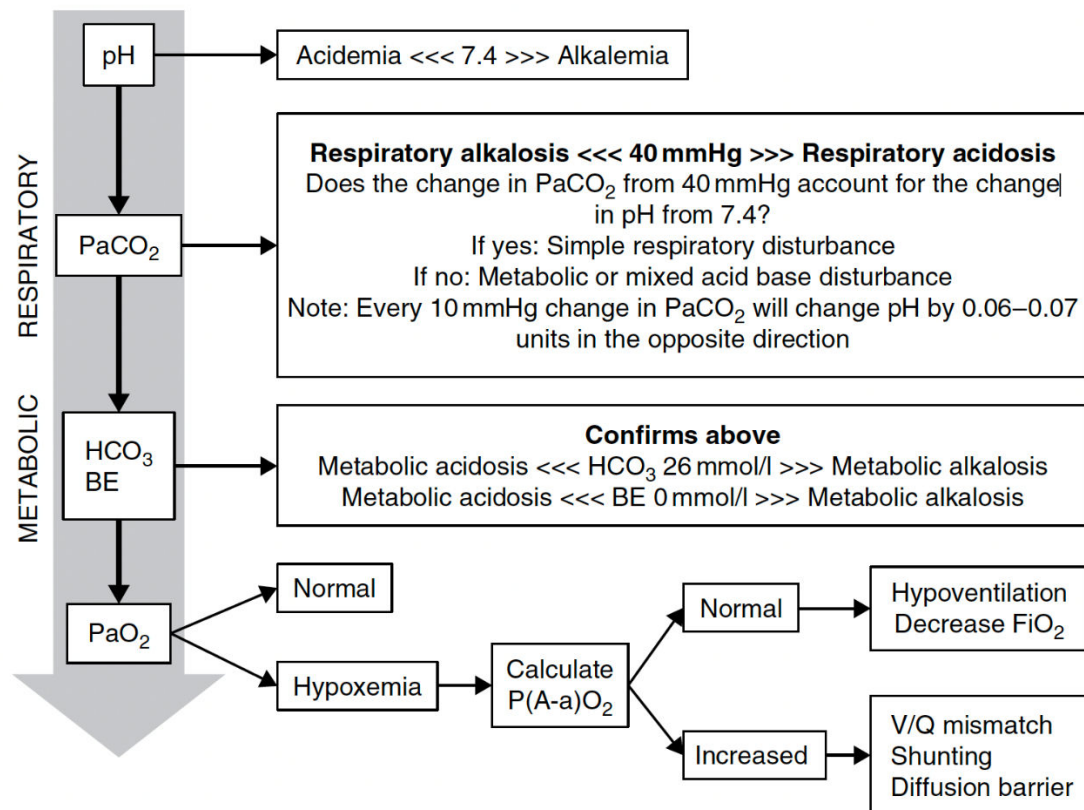
These simplified steps will guide an interpretation of the possible disturbances seen during the course of the disease (for further details, please refer to additional references). Ranges provided below are “expected ranges” and individual ranges should be determined for each elephant when healthy for accurate interpretation. Values are also given for standing elephants as changes will occur in recumbent animals (Isaza R. et al, 2003).

- 1- Confirm the origin of the blood sample (arterial, venous, mixed). Evaluate oxygenation based on sample type.
- 2- Determine the pH disturbance:
 - a. Normal (between 7.35 and 7.45)
 - b. Acidemia: pH less than 7.35 and severe if less than 6.8
 - c. Alkalemia: pH greater than 7.45 and severe if greater than 7.8
- 3- Evaluate oxygenation: What is the PO₂ value in the arterial sample?
 - a. Normal range: 80-100 mmHg in an animal breathing room air (Arterial O₂ saturation 95-100%)
 - b. Hypoxemia is present if PaO₂ is less than 80mmHG and is considered severe if less than 60 mmHg
- 4- Assess alveolar ventilation: What is the CO₂ value?
 - a. Normal range: 35-45 mmHg
 - b. Respiratory acidosis due to hypoventilation:
 - i. A rise in PCO₂ results in a drop in pH due to an increase in hydrogen (H⁺). In anesthetized horses, pH will decrease by 0.06-0.07 units (from a 7.40 base) for each acute increase of 10 mmHg in PaCO₂. (Blaze and Robinson, 1987)

- ii. Can be caused by central nervous system depression (general anesthesia, head trauma, encephalitis), as compensatory response to metabolic alkalosis, thoracic wall trauma, neuromuscular dysfunction, restrictive pulmonary diseases (pleural effusion, pneumothorax, upper airway obstruction, etc.)
 - c. Respiratory alkalosis due to increases in respiratory rate or tidal volume, or both:
 - i. A decrease in PCO_2 results in a rise in pH due to a decrease in hydrogen (H^+).
- 5- Evaluate the metabolic component:
 - a. What are the base excess and bicarbonate values?
 - i. Bicarbonate normal range: 22-28 mmol/L
 - ii. Base excess normal range: -4 to 0 mmol/L
 - b. The base excess is the amount of acid that needs to be added to bring the pH to exactly 7.40. Bicarbonate is the main buffer in the extracellular space; however, the effect of CO_2 may cause shifts in bicarbonate unrelated to a metabolic acid-base disturbance. Base excess and bicarbonate provide the same information as the bicarbonate, but base excess measurement factors out the CO_2 effect on bicarbonate and thus any respiratory effect on metabolic acid base status. Look at the base excess value whenever available.
 - c. Metabolic acidosis: when bicarbonate is less than 15 mmol/L
 - i. A decrease in bicarbonate (HCO_3^-) results in a decrease in pH due to an increase in (H^+).
 - ii. This can be due to too much acid (lactate, uremic acids (sulfates and phosphates), etc.) or a loss of base (buffer) bicarbonate (loss during small bowel (secretory) diarrhea, or during renal tubular acidosis (no associated azotemia)). Use anion gap to differentiate between the 2:
 - 1. Cations are represented by sodium, potassium, and unmeasured cations (magnesium and calcium).
 - 2. Anions are represented by chloride, bicarbonates and unmeasured anions which include albumin. Albumin has a net negative charge and represents in a healthy patient the major unmeasured anion contributes net negative charge to the plasma.
 - 3. Anion gap is the difference between unmeasured anions minus unmeasured cations. But to actually have a value, it is also calculated as $(\text{Na}^+ + \text{K}^+) - (\text{HCO}_3^- + \text{Cl}^-)$
 - d. Metabolic alkalosis: when bicarbonate is greater than 25 mmol/L
 - i. An increase in (HCO_3^-) results in an increase in pH due to a decrease in (H^+).
 - ii. Can be caused by treatment with loop diuretics, severe vomiting (loss of hydrogen and chloride ions limiting the patient's ability to excrete bicarbonate, excessive administration of sodium bicarbonate)
- 6- Determine the primary disturbance:
 - a. When a substantial disturbance is present, a concurrent respiratory disturbance in the opposite direction will occur to move the pH closer to normal range. If both a respiratory and a metabolic disturbance are present, it is important to determine which one is primary.
 - i. If both disturbances are in the direction of the pH change, then both are primary disturbances.

- ii. If one disturbance is an alkalosis and one is an acidosis, the primary disturbance is likely the one in the direction of the pH change.
 - iii. If the pH is within the normal range, the side where the side of pH that is trending represents the primary disturbance.
- 7- Look for evidence of compensation; physiologic responses to acid-base disturbance are described chronologically:
- a. Buffering: the major extracellular buffer pair is bicarbonate/carbonic acid ($\text{HCO}_3^- / \text{H}_2\text{CO}_3$) reacting with hydrogen ions to form carbonic acid that is subsequently converted into water and CO_2 : $\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$
 - b. Compensation: the respiratory system will attempt to compensate for metabolic acid-base abnormalities, and the renal system will attempt to compensate for respiratory acid-base abnormalities.
 - i. CO_2 is eliminated by alveolar ventilation (within minutes)
 - ii. The kidneys will regulate the generation and excretion of HCO_3^- (hours)
 - c. Correction: last phase aimed at rectifying the pathophysiologic process that caused the abnormality

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Lactate Measurement

In physiological conditions, lactate is produced daily from various organs, metabolized in the liver, kidney (and other organs), and excreted by the kidneys. Conversion of pyruvate to lactate allows the production of energy without oxygen. Hyperlactatemia can occur in critically ill patients secondary to insufficient oxygen delivery, due to decreased tissue perfusion and/or inadequate oxygenation, increased glycolysis (sepsis) in patients with cellular inflammatory response, or impaired lactate clearance. Lactic acidosis is a major factor for acidemia. Monitoring lactate levels has become a hallmark in the management of critically ill patients and is often used to guide treatment decisions, assess the patient's response to therapy, and serve as a prognostic marker. It is an important parameter to monitor during an EEHV HD crisis.

If available to the institution, lactate can be measured using a point of care lactate meter (e.g., Lactate Plus meter or i-STAT with CG4 cartridges) on arterial or venous whole blood. Establishing individual baseline ranges for each elephant at different physiological states will enable more informed interpretation of the lactate fluctuations. In many domestic species, lactate level in healthy animals, ranges between 0.5-1.5 mmol/L at rest and persistently elevated lactate levels (> 4 mmol/L) are associated with poor prognosis. While further research is needed to establish ranges, preliminary data indicate lactate levels in healthy elephants are below 1 mmol/L and range between 1 and 3 mmol/L in mildly ill animals and in males in musth.

In conjunction with the rest of the parameters analyzed during the course of an EEHV HD crisis, repeated monitoring of lactate levels will guide clinicians' decision to adjust fluid resuscitation and cardiovascular support.

Cited and Additional References:

Blaze CA and Robinson NE. 1987. Apneic oxygenation in anesthetized ponies and horses. *Vet Res Commun* 11:281–291.

Guedes A. Blood Gases. In: *Interpretation of Equine Laboratory Diagnostics, First Edition*. Edited by Nicola Pusterla and Jill Higgins. Pages 57-65. Published 2018 by John Wiley & Sons, Inc.

Hall NH, Isaza R, Hall JS, Wiedner H, Conrad BL, Wamsley HL. Serum osmolality and effect of water deprivation in captive Asian elephants (*Elephas maximus*). 2012. *J Vet Invest*. 24(4) 688-695.

Heard DJ, Jacobson ER, Brock KA. Effects of oxygen supplementation on blood gas values in chemically restrained juvenile African elephants. 1986. *JAVMA* Vol 189(9):1071-1074.

Honeyman, Virginia L., Glenn R. Pettifer, and Doris H. Dyson. "Arterial Blood Pressure and Blood Gas Values in Normal Standing and Laterally Recumbent African (*Loxodonta Africana*) and Asian (*Elephas Maximus*) Elephants." *Journal of Zoo and Wildlife Medicine* 23, no. 2 (1992): 205–10.

Hopper K, Rezende ML, and Haskins SC. 2005. Assessment of the effect of dilution of blood samples with sodium heparin on blood gas, electrolyte, and lactate measurements in dogs. *Am J Vet Res* 66: 656–660.

Isaza R, Behnke BJ, Bailey JK, McDonough P, Gonzalez NC, Poole DC. Arterial blood gas control in the upright versus recumbent Asian elephant. *Respir Physiol Neurobiol*. 2003 Mar 3;134(2):169-76.

Magdesian KG. 2004. Monitoring the critically ill equine patient. *Vet Clin North Am Equine Pract* 20: 11–39.

Noel PG, Couetil L, and Constable PD. 2010. Effects of collecting blood into plastic heparinised vacutainer tubes and storage conditions on blood gas analysis values in horses. *Equine Vet J Suppl*, 91–97.

Rose RJ, Rosedale PD, and Leadon DP. 1982. Blood gas and acid–base status in spontaneously delivered, terminally induced and induced premature foals. *J Reprod Fertil Suppl* 32: 521–528.

Still J, Raath JP, Matzner L. Respiratory and circulatory parameters of African elephants (*Loxodonta africana*) anaesthetised with etorphine and azaperone. *J S Afr Vet Assoc*. 1996 Sep;67(3):123-7. PMID: 9120854.

Tennent-Brown BS. Interpreting lactate measurement in critically ill horses: diagnosis, treatment, and prognosis. *Compend Contin Educ Vet*. 2012 Jan; 34(1):E2. PMID: 22271469.

Zager E, Fletcher DJ, Goggs R. Evaluation of the association between strong ion acid-base disturbances and mortality in dogs: a retrospective study. *Vet Med Sci*. 2018. 4(3):206–17.

APPENDIX 4: LIST OF SUPPLIES

Please create your own list that meets your institution, resources and facilities. The following recommendations can be found in the Resource Database section of the EEHVinfo.org website.

For facilities housing elephants at-risk for EEHV, the North American EEHV Advisory Group recommends maintaining adequate supplies on hand for at least four (4) days of treatment. Products will need to be rotated in these supply bins in order to ensure that all items remain in-date.

Supplies should be organized in such a way that items are relatively easy to find in an emergency. Maintain a list in each bin of the supplies that should be found there. For any supplies that will be a last-minute grab (e.g. multi-parameter monitor), make sure that there is a checklist to keep track of what still needs to be packed. It is also recommended to keep several copies of drug dosage charts, ICU sheets, EEHV protocol, etc. in each bin. Ensure that each bin is well labeled so that supplies are easy to locate in a crisis.

Here is a list of recommended supplies:

Elephant Barn supplies:

- Assortment of ropes, slings, and belly bands
- Flashlights
- Obstetric lubricant
- Mortar and pestle
- Towels
- Inner tubes (various sizes)/gym mats- to be used for cushioning and support in the event of a full immobilization procedure

Clinic Supplies:

Diagnostic Supplies:

- Syringes, luer lock (2 boxes each of 60, 35, 20, 12, 6, 1 mL sizes)
- Needles (1 box each, long and short, of 14g, 16g, 18g, 20g, 22g, 25g)
- Butterfly catheters (1 box each)
- Vacutainer adapters
- Blood tubes- serum separators, EDTA, lithium heparin, citrate, royal blue top
- Blood tube racks & cooler
- Lancet supplies
- Lidocaine/prilocaine cream

Drug administration/supportive care:

- Famciclovir powder or tablets- minimum 3-day supply for an adult elephant
- Ganciclovir 500 mg vials- 25 vials/box (12,500 mg/box)
 - 1L sterile water to mix dose of ganciclovir if stocking lyophilized powder form
- Gram scale, measuring cup, empty gel capsules

- Other drugs- Butorphanol, detomidine, naltrexone, atipamezole, flunixin meglumine, ketoprofen, ceftiofur CFA, vitamin C, vitamin E, vitamin B complex, emergency drugs (epinephrine, doxapram, sodium bicarbonate, lidocaine, atropine, dexamethasone SP)
- Sterile lube tube (for mixing with famciclovir for rectal administration)
- OB suits, OB sleeves, duct tape, and lube
- Exam gloves (all sizes)
- Towels (10-12)
- Hot packs for ears
- 10-22 GA catheters (long & short)
- Injection caps and T ports - standard & large bore
- Bacteriostatic saline (IV catheter flush) & syringe labels
- White tape (1-inch, 2-inch, 4 inches; 5 rolls each)
- Vetwrap (2 & 6", multiple rolls each size)
- Elastikon (2 & 4", multiple rolls each size)
- Tissue glue
- Tegaderm
- Alcohol and scrub
- 4x4 gauze (6 packages)
- Bandage scissors
- Large Animal IV line (6 complete sets)
- Large Animal IV extension set (6 complete sets)
- Standard IV administration set (6 complete sets)
- Standard Extension set (6 complete sets)
- 1L & 5L fluids (all in stock)
- IV pump(s) & IV pole(s)
- 1L & 3L pressure bags
- Ropes/wire to hang bags
- Extension cord
- Blood filters
- Large animal surgery pack & sterile gauze packs
- Scalpel blades: 10, 15
- Sterile gloves (6.5, 7, 7.5)
- Lidocaine
- Drapes
- Sharps container
- Suture (0, 1, 2 prolene or similar with cutting needle)
- Flashlights/head lamps
- Portable surgery lights
- Plasma (stored from herd, keep on ice)
- Hetastarch

Sedation/anesthesia:

- Butorphanol (minimum 4 bottles, 5 ml/bottle, 30 mg/ml)
- Detomidine (minimum 3 bottles 5 ml/bottles, 10 mg/ml)
- Naltrexone (minimum 4 bottles, 50 mg/ml, 30 ml/bottles)
- Atipamezole (minimum 13 bottles, 10 ml/bottle, 5 mg/ml)
- Emergency drugs
- Anesthesia clipboard

- Stethoscope
- Thermometer
- Calculator
- Pole syringe/Jab stick
- Oxygen tanks (E tanks) and large animal demand valve
- Oxygen tanks (H tanks) and Zubinator
- Portable anesthesia machine
- ET tubes (24, 22, 20, 18, 16, 14), tie gauze, & cuff syringe
- Stylets, cake spatulas, endolight
- Laryngoscope w/long blade
- Y piece (nasal administration)
- Ropes/seatbelt straps (open mouth)
- Blocks (open mouth)
- Endoscope and associated equipment (intubation)
- Multi-parameter monitor (with all leads)
- Pulse oximeter
- Blood gas analyzer & cartridges
- Coagulation analyzer & cartridges

Miscellaneous:

- ICU flow sheet, pens, Sharpie markers, clipboard, watch
- Towels with hobble ropes (face cover)
- Ultrasound & large tub of ultrasound gel
- Doppler
- Ophthalmoscope (1) & ophthalmoscope extra battery
- Trash bucket & trash bags
- Folding table
- Extra batteries (all sizes)
- Pericardiocentesis supplies:
 - 60 cc regular tipped syringes
 - 3 way stop cocks (2)
 - 5 1/4" IV catheter, smallest gauge available
 - 10" spinal needles
 - Sterile urine cup to save for culture
 - 50 ml conical vials for storage of fluid

APPENDIX 5: EMERGENCY FLOW CHART AND FAST PLAN

EEHV-HD Emergency Flow Chart

Treatment initiation is based on:

- EEHV qPCR value and rate of viral load increase
- CBC
- Clinical Signs
- 1-15 years of age
- Serology status

Start rectal administration of fluids immediately

Collect baseline information

- Blood sample
- History
- Physical exam

Supportive therapy (may require sedation)

- As indicated by condition:
- IV fluids
- Plasma / fortified plasma / whole blood
- Crystalloids

Additional treatments as indicated by condition:

- Oxygen supplementation
- Antiviral drugs
- Antibiotics
- Analgesia
- Immune stimulants and antioxidants
- Gastroprotectants
- Stem cell administration
- Miscellaneous

EXAMPLE OF AN EEHV HD FAST PLAN

Initiate treatment if:

- Clinical signs are present. They may be subtle at first.
- When CBC changes are present (changes in morphology of WBCs, decreased WBC count, decreased platelet or monocyte count) as compared to individual's normal range, with or without clinical signs.
- EEHV viremia is present ($> 5,000$ vge/mL) on whole blood qPCR
- Rapidly increasing EEHV viremia vge/mL on whole blood qPCR
- The serological testing shows low or absent antibody titers

Interventions:

1. Collect baseline information
 - a. Blood collection:
 - i. EDTA (purple top tubes): EEHV qPCR, CBC, (preferably in-house), and banking.
 - ii. Lithium heparin (green top tubes) blood gas analyses (CG8. lactate)
 - iii. Red or tiger top tube: serum biochemistry, serology, banking
 - iv. Citrate (light blue top tubes): fibrinogen, coagulation parameters
 - b. Temperature, pulse, respiratory rate
 - c. Physical findings
 - d. Blood pressure
2. Administer rectal fluids (10-20 mL/kg rectally, 8-minute duration from average barn hose). Pre-treat the rectum with a mixture of sterile lube and lidocaine to decrease irritation of the tissue and increase compliance.
3. Administer famciclovir (15 mg/kg) 3-4 times daily
 - a. Orally or rectally (crushed pills mixed with OB lube). If given rectally, allow a minimum of one hour before or after administration of rectal fluids.
4. Standing sedation with butorphanol and detomidine given at the same time.
 - a. Asian elephant calf:
 - i. Butorphanol 0.044 mg/kg (0.016-0.07 mg/kg) IM
 - ii. Detomidine 0.02 mg/kg (0.01-0.031 mg/kg) IM
 - b. African elephant calf:
 - i. Butorphanol 0.02 mg/kg (0.009-0.05 mg/kg) IM
 - ii. Detomidine 0.014 mg/kg (0.008-0.025 mg/kg) IM
 - c. Provide supplemental oxygen via nasal cannula when possible.
 - d. Reversal may be omitted to provide analgesia as duration of action of drugs is often sufficient for procedures.
 - e. If reversal is elected:
 - i. Naltrexone: 2.5 times butorphanol dose
 - ii. Atipamezole: 5 times atipamezole dose.
5. Place IV catheter (under sedation) in ear vein (with T-port and/or injection cap) and place second IV catheter if possible after the first is secured.

- a. Plasma: first choice is EEHV-negative, crossmatch compatible fresh plasma (never frozen) as indicated by condition. Administering thawed fresh frozen plasma is second choice, and if neither are available, thawed frozen plasma can be used.
 - i. 0.5-2 mL/kg (do not exceed 10 mL/kg)
 - ii. Consider fresh penciclovir-fortified plasma if time allows.
 - b. Whole blood (possibly penciclovir-fortified) if anemia is present.
6. Administer IV fluids rate of 0.3-4 mL/kg/hour (~ 3-4 liters in a 1000 kg calf)
 - a. Administer further rectal fluids after IV fluids
7. Administer elephant mesenchymal stem cells IV
8. Consider administering following ancillary therapies as indicated by condition:
 - a. Ceftiofur sodium (Naxcel® 1.1 mg/kg IV SID) or ceftiofur crystalline-free acid (Excede® 6.6 mg/kg IM every 7-10 days)
 - b. Anti-inflammatory drugs: flunixin meglumine 0.25 - 0.5 mg/kg IV/ IM but if renal function is compromised, use lowest dose or meloxicam 0.03 - 0.06 mg/kg IV/IM/PO
 - c. Vitamins and mineral supplementation
 - i. Vitamin C: 6 mg/kg IM / IV
 - ii. Vitamin E: 5-15 IU/kg IM / SC (foal dosage; to achieve this dose, do not overdose with selenium if using combined product)
 - iii. Selenium: 0.06 mg/kg IM / SC (foal dosage)
 - iv. Vitamin B complex (formulation containing 100 mg/ml of thiamin): 2 mg/kg thiamin or 5ml per liter of IV crystalloids.
 - d. Famotidine: 0.5 mg/kg IV slow
 - e. Omeprazole: 0.7-1.4 mg/kg PO
 - f. Colloids (0.25-0.5 mL/kg) as indicated by albumin levels.
 - g. Ganciclovir 5 mg/kg diluted in one liter of crystalloid fluids IV BID (20-30 minute slow IV administration, avoid perivascular leakage)