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Captive Elephant Medicine: Recent Developments

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Several new challenges in elephant medicine have emerged over the past several years. Arguably the most critical is elephant endotheliotropic herpesvirus (EEHV), now recognized as a significant threat to captive Asian elephant populations in range countries, Europe and Asia (Cracknell *et al*. 2007; Reid *et al*. 2007; Richman 2007). Characterized by high mortality as well as stillbirth and abortion, the disease primarily affects juveniles between the ages of 1 and 4 years. Affected animals typically present with mild signs of lethargy which progress within hours or days to cranial and respiratory edema, facial cyanosis, and ultimately death, caused by myocardial failure and damage to the endothelial lining of the microvasculature leading to severe internal hemorrhage. Diagnosis is achieved via PCR testing of whole blood samples from actively viremic animals (Richman *et al*. 1999; Richman 2007). Current treatment recommendations include large doses of the antiviral drug famcyclovir, along with supportive care (Schmitt *et al*. 2000). However, in several cases, elephants have died despite early and aggressive treatment for reasons that remain unclear.

EEHV is a member of the genus Proboscivirus, and little is known about its epidemiology, modes of transmission, or patterns of shedding and latency. Three distinct strains were initially classified: EEHV 1a, found in both Asian and African elephants, EEHV 1b, which is apparently specific to Asian elephants, and EEHV 2, documented both in healthy wild African elephants and in two African elephants in North America who succumbed to hemorrhagic disease. Recently, however, several new strains of EEHV have been recognized, of which some are associated with disease and others are not (Garner *et al.* 2009). The relationships between the new strains are under investigation, and it is still unclear whether they are infective and/or pathologic to both elephant species.

Efforts to establish a databank of elephant serum from North American animals are being performed by several institutions in conjunction with the EEHV laboratory at the National Zoo in Washington, DC in order to identify epidemiological patterns of transmission, seroconversion, and shedding. A recently developed ELISA test from the National Zoo against EEHV1a antibodies allows identification of at least some of animals that have been exposed to the disease. Current estimates indicate that more than 10% of North American elephants are seropositive for EEHV suggesting that seroconversion occurs with subclinical disease (Latimer 2007). It is hoped that measurement of viral titers will eventually help identify animals most likely to shed disease -- information that could be used in managing the movement of captive animals between institutions. A similar databank documenting EEHV titers elephants in Europe and in range countries is planned (Cracknell *et al*. 2007; Reid *et al.* 2006).

Another area of intense research in elephant medicine is tuberculosis (*Mycobacterium tuberculosis*), due, in part to the growing need for better and more reliable methods of diagnosis. Trunk washes, while 100% specific and still the gold standard for diagnosis, have less than ideal sensitivity because elephants only shed mycobacterial organisms intermittently. Diagnostic techniques useful in other species including chest radiographs, skin testing, and interferon gamma levels are either not feasible or not reliable in elephants. (Miller 2007) Although several new serological tests have appeared on the market, their validity remains unproven, and the possibility of false positives using these tests in animals exposed to atypical mycobacteria or even non-mycobacterial cross-reacting antigens

is concerning. (Cousins & Florisson 2005) Because treatment of a positive animal is a signi cant endeavor, and because legislation in several European countries requires euthanasia of any zoo animal with even a suspicion of tuberculosis (*M. tb*), false positives have grave consequences.

Treatment of *M. tb* in elephants still continues to be a conundrum as well. In the United States, treatment requirements are based on older guidelines developed for human with *M. tb*, and evidence now exists indicating that several of these drugs when dosed to produce human serum levels, cause severe toxicity in elephants. The options of utilizing alternative treatment regimes now standard in human *M. tb* therapy, including shorter duration of treatment, intermittent dosing schedules, and the use of other, less toxic drugs, are currently being investigated in elephants (Wiedner & Schmitt 2007).

With several demographic models forecasting the inevitable loss of elephants in captivity due to aging populations and a low birth rate (Wiese and Willis 2004), ongoing research in assisted reproductive technologies has continued unabated (Hermes *et al.* 2007). Reproductive ultrasound of both male and female elephants, used to identify reproductive tract pathology, monitor developing pregnancies, and provide information about breeding soundness and infertility, has become an invaluable technique for institutions committed to breeding their animals (Hildebrandt *et al*. 1998, 2000, 2006).

Improvements in endocrine monitoring now permit tracking of the elephant's estrus cycle (Brown 2000). Elephants are unique in having two surges of luteinizing hormone (LH) during the follicular phase of the estrous cycle, the rst is non-ovulatory and second LH surge induces ovulation. Newer assays for LH and progesterone enable veterinarians and elephant managers to accurately predict the occurrence of this second LH peak and facilitate better planning of both natural and arti cial inseminations. (Dahl *et al*. 2004) A current limitation to using arti cial insemination in Asian elephants is the dif culty of routinely freezing and storing semen for later use, spurring research on sperm physiology, the use of extenders and freezing protocols.

Ironically, the development of an elephant contraceptive vaccine has also been an important recent development (Barber *et al*. 2001; Fayrer-Hoskins *et al*. 2000). Tests of a recently developed zona pellucida vaccine in Africa indicate that use of this immuno-contraceptive may be an alternative to permanent removal from the reproductive pool in areas where elephant populations need to be controlled (Barber *et al.* 2001; Fayrer-Hoskins *et al*. 2000).

A nal area of active investigation is basic anatomy. Gross imaging techniques such as MRI and CT have enabled researchers to produce detailed anatomic maps of elephant joints, limbs, and muscle as well as document locomotion (Tsaopoulous 2008; Hakeem *et al.* 2008). Sophisticated camera recording techniques have unlocked clues about elephant gait and locomotion (Hutchinson *et al*. 2003, 2006; Ren & Hutchinson 2007). Microscopic techniques including histology and scanning electron microscopy have been used to analyze the placenta, the nervous system, and the cushions of the feet (Hoffman *et al.* 2005; Shoshani *et al*. 2006; Weissengruber *et al*. 2006; Witter *et al.* 2007). The potential clinical value of this type of information is high, since anatomic studies that delineate the ranges of normal help in both the recognition and understanding of pathology. As conservation of elephants takes on ever greater urgency, the ability of veterinarians to keep captive populations healthy becomes more important as well.

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Sundara with her mother
Photo courtesy of Feld Entertainment