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The Horse (*Equus caballus*) as an Animal Research Model for Human Diseases

Abstract

Horse and man have a long-standing relationship that validates a dependency on man's part to use horses in many aspects of ancestral and present life. The relationship has evolved from horses being used as a food source to a form of sport and recreation. However, it is the equine species' role in medical research that people should really be applauding. Horses naturally acquire many of the same diseases that plague humans such as osteoarthritis, autoimmune uveitis, and diabetes mellitus type two; therefore, equines serve as an accurate animal model in investigating these diseases for advances in medical knowledge and eventually for a proposed cure.

Keywords: horse, animal model, medical research

The human- horse relationship has a long and varied history. The relationship between horses and humans has existed for over 5500 years (Anthony, 2007). This long-standing relationship between horse and man validates a dependency on man's part to use horses in many aspects of ancestral and present life. Horses first served humans as a food source, then in agriculture and warfare; presently, horses serve humans in police work, racing, and most currently in riding therapy for individuals with mental and physical disorders (Anthony, 2007). After the invention and mass production of cars, horses by fault became a source of entertainment and sport (Edenburg, 1999). In contrast to many other domestic ungulates (cows, goats, and sheep), which are kept mostly for breeding, meat and milk production, and/or wool production, horses rapidly acquired a "mixed status" in terms of their interaction with humans. Many past and present products were and are derived from horses, including meat, milk, hide, hair, bone, and pharmaceuticals extracted from the urine of pregnant mares (Olsen, 2006). Although horses are historically and presently most known for their athletic ability in a multibillion dollar industry, the role they used to and currently serve in medical research proves far more beneficial for all humankind.

The horse's contributions to modern medicine are often outshined by their high earnings in the race world; however, this piece is devoted to informing the public of past and present medical explorations that would not have been possible without the equine species. Horses have actually been utilized as an animal model in medical research for an extremely long time. In the 18th century, Stephen Hales made the first measurements of blood pressure on a fourteen year old mare (Booth, 1977, p. 794). Furthermore, another more tragic story exists about a horse called Jim who helped prepare an antitoxin in 1901 for diphtheria (Lou & Davis, 2001). The animal gave over thirty quarts of the antitoxin and inevitably saved many lives. Despite the lives he saved, Jim's blood was contaminated with tetanus and also caused thirteen children to die (Lou & Davis, 2001, p.1017). This bittersweet incident resulted in some paramount and necessary biological regulation such as the Biologics Control Act of 1902, and ultimately in the creation of the Food and Drug Administration (FDA) (Lou & Davis, 2001, p.1018). These animals provided the medical world with principal techniques and regulations that are still employed today. Many more ground breaking research projects involving human diseases exist today that use horses as the research model. The equine research model is involved in current projects observing osteoarthritis, uveitis, and type two diabetes.

Osteoarthritis stands as the most common form of arthritis and the leading source of chronic disability in humans in the United States. This degenerative joint disease has no cure, only treatment for the symptoms exist (McIlwraith et al., 2010). Equine models of osteoarthritis (OA) have been used in McIlwraith's study to investigate the pathogenic pathways of the disease and also to evaluate macroscopic and microscopic scoring systems as well as propose new scoring systems for naturally occurring equine OA. Proper scoring systems result in better diagnoses, which could be the difference between prescribing the patient successful or disappointing treatment.

Peffers et al. executed a study in 2010 using the equine model to study the SOX9 transcription factor which is essential for the formation cartilage extracellular matrix (ECM). The loss of ECM is a characteristic of osteoarthritis (Peffers et al., 2010, p.1502). Osmotic loading regulates SOX9 gene expression cartilage cells (chondrocytes). The study included examining SOX9 gene regulation through static and cyclical hyperosmotic conditions in normal and OA equine chondrocytes. Peffers et al. revealed that osmotic loading of SOX9 mRNA depends on the type of osmotic stimulus and the phenotype of the cartilage cells (p.1507), and the response of chondrocytes from OA cartilage is considerably different from that of normal cartilage. These results signify that this variation as well as changing the osmotic environment and inappropriate responses of the local cell population may be important in disease progression (p.1508).

The horse is an appropriate model for addressing specific uncertainties related to human osteoarthritis; furthermore, there is abundant tissue in the equine joint to harvest for multiple measurements (McIlwraith et al., 2010, p. S93). Even though, the equine species requires unique facilities and trained employees, control of the subjects' activity level and other interventions are completed with ease (McIlwraith et al., 2010, p. S103). Because osteoarthritis occurs spontaneously in the horse, genetic or surgical models are unnecessary, which saves money and time that would be spent altering the animal to better emulate the human disease. Synthetic models, although necessary when authentic models do not exist, can result in undesired side effects or results that stray from the actual events in the human disease.

An additional disease where the horse serves as an invaluable model is autoimmune uveitis. This disease damages vision in humans because T cells are able to cross the blood-retinal barrier (Hofmaier et al., 2011, p. 2314). Equine recurrent uveitis (ERU) is an autoimmune disease that resembles the human condition in terms of immunopathology and physiology (Hofmaier et al., 2011, p. 2314). An experiment done in April of 2011 by Hofmaier and colleagues investigated the molecular mechanisms contributing to the disease in the horse model, such as the changes in the matrix enzymes in spontaneous uveitis. This study implicates a change in functional protein to protein interactions (p.2315). This newfound information fortunately hones in on specific protein interactions that can eventually be manipulated and perhaps result in a reversal of the disease symptoms (p.2319). Another study exists that benefitted from the equine model to represent the human condition while experimenting uveitis. The purpose of the 2011 study done by Eberhardt et al. was to gauge retinal glial cell function in ERU. Essentially every retinal disease produces a reaction where astrocytes are proliferated, and this study aimed to measure specific functions of this reaction in regards to autoimmune uveitis (p.697). Moreover, the research by Eberhardt et al. with the equine model provided the first report of aquaporin protein AQP5 involvement in a retinal disease (2011, p.698). In ERU and human autoimmune uveitis T cells secrete proinflammatory cytokines after blood– retinal barrier breakdown occurs; this research linked the cytokine release to reduced expression of the aquaporin protein in this disease (2011, p.699). Anytime new protein interactions are discovered more in depth research must be implemented to reach the ultimate goal which is alleviation of the disease and its consequences. Without the equine model that produces an almost identical condition in the retina as autoimmune uveitis, these intricate protein interactions may not have been observed (2011, p.705). Scientific research is an on-going process, and it is only because of an appropriate animal model that the small victories can be discovered to make head-way in medical therapies.

A third disease that plagues humans, and horses can aid in researching is non-insulin-dependent diabetes mellitus (NIDDM). This epidemic of modern society plagued an estimated 221 million people worldwide in 2010 and that number will only increase without researching the similar condition that occurs in the horse (Hodovance, Ralston, & Pelczer, 2007). Horses and humans have a very similar aging process; both species have a tendency to gain weight as they age which can result in an imbalance of hormones, specifically abnormally high insulin and blood glucose levels. The condition in the horse is known as equine metabolic syndrome (EMS) (Hodovance, Ralston, & Pelczer, 2007, p.534). Although mice and rats have been employed in metabolic experiments, neither of these animal models produce a naturally occurring disorder. EMS, like NIDDM afflicts both adolescents and matured animals, which makes the horse an even more appealing candidate for future scrutiny of the metabolic pathways and pathogenesis involved with this disorder (Hodovance, Ralston, & Pelczer, 2007, p.533). Research done by Hodonvance, Ralston, and Pelczer, with the horse model, aimed to review NMR-based metabonomics as a tool for studying NIDDM and insulin resistance. NMR-based metabonomics makes possible the classification of metabolites formerly unidentified as being part of the metabolic response (2007, p.537). Because the condition in the horse mirrors the disease in the humans, researchers were able to metabonomically analyze equine plasma samples with NMR spectra to investigate typical and atypical metabolic responses to a various dextrose dosages, and be comfortable assuming that the same results would occur in NIDDM (Hodovance, Ralston, & Pelczer, 2007, p.536). The research concluded that NMR-based metabonomics is indeed an essential instrument in metabolic measurements, and the equine model serves as the best reproduction of adult-onset diabetes (Hodovance, Ralston, & Pelczer, 2007, p.537). The horse helped researchers conclude that as measurements become more advanced with the invention of more sensitive technology, significant contributions to further comprehension of the underlying biology of this disease can be anticipated.

Equus caballus is a species precious to our health, our economy, and our further understanding of detrimental diseases. This animal's impressive size does not come as a disadvantage, rather a teaching implement for young researchers that need to learn techniques such as obtaining blood samples (Lou& Davis, 2001). Not only does the equine species permit handling and experimentation, but they develop many of the same diseases that humans acquire, which relieves researchers of the hassle of genetically and surgically altering animals to emulate the human condition and yet still have to decipher which results would not realistically occur in humans. Hopefully, the human race can eventually look beyond the monetary benefit this animal provides, and appreciate what this animal has sacrificed in terms of medical discovery.

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