

Horses as a Material Asset in Antivenom Production: What is Their Limit?

Historically, horses have been manipulated as ‘soulless machines’ whose useful characteristics may be expanded. In 1833, the Journal of the Franklin Institute described the expression ‘horse power’ as technically applicable “to any apparatus by means of which a horse is made to exert his power in propelling machinery.”¹ In the late 19th century, a new use emerged and equine bodies were subjected to scientific appropriation as a material asset for modern immunology. Since then, equine blood has functioned as an essential raw material in the antivenom industry. Even so, or for this very reason, just as horses have been trapped in a nest of vampires, their dramatic and unequivocal contribution as blood suppliers has been left to oblivion. Equine use in the serotherapy industry remains the horse’s most disregarded role, a systematic exploitation of animal bodies and suffering that has been carefully erased from history. Today, the absence of specific criteria to detect equine injuries resulting from continuous injections of venoms and subsequent bloodletting continues to be a major problem in the antivenom industry. What are the limits of a horse’s body? The answer to this question contributes to discussion on the connections between ethics, human–equine interactions and experimental techniques by examining antivenom production in Brazil, as well as related international challenges. With no intentions of exhausting the topic, this paper presents considerations that justify a greater commitment to the fate of horses serving the antivenom industry.

The Invisible Source of Raw Material

For 130 years, the conditions that serum-producing horses face has been a systematically neglected topic. These animals have been subjected to repetitive use in scientific experimentation, without adequate guidelines for managing the multiple impacts that the hyperimmunisation process has on their bodies. Although some improvements have been made, the current method of using horses to produce plasma follows the traditional model for producing anti-diphtheria serum, initiated in Europe in 1894.²

It consists of successive injections of toxins with adjuvants followed by bleeding to obtain hyperimmunised plasma for the production of antivenins, anti-rabies, antitoxin, and antitetanus serums. It was not until 2016 that the World Health Organisation Guidelines for the Production, Control and Regulation of Snake Venom Immunoglobulins recommended that the antivenom industry adopt ethical practices regarding the animals it uses.³ According to WHO Guidelines, monitoring of animals used to produce antivenom must include post-mortem examination, necropsy and histopathology, allowing a careful analysis of causes of death which must, in turn, be made available for external review.

This commitment to transparency regarding the condition of seroproducing horses has not been assumed by the antivenom industry. Until now, animal welfare directives for horses used in the industrial production of hyperimmunised plasma have not established specific guidelines regarding production procedures. When they do exist, such guidelines are defined by the industry itself, comprising an obvious

conflict of interests.⁴ Official standards regarding the limit of blood that can be extracted, frequency of collection, and criteria to be observed to define when an individual should be removed from the program have not yet been established.⁵

The broad impact of this lack of official standards are quite significant. In 2021, according to the Research and Market report, the global antivenom market was valued at USD 1.08 billion in 2023 and is anticipated to project impressive growth in the forecast period, and is expected to reach USD 1,585.01 billion, in 2026. In such a workplace, millions of horses and other equids have been used as a source of raw material for serum as well as in experimental activities. This data does not cover other types of equine serum, such as anti-rabies, anti-diphtheria, anti-botulism, and anti-tetanus varieties. Neglecting to monitor the condition of horses used to produce antivenom is a silent ingredient of endemic crises involving snakebite. Since 2017, the World Health Organisation has added the latter to its list of neglected tropical diseases, mainly affecting rural populations in Africa, Asia and Latin America. The highly complex and inefficient production system of the worldwide antivenom industry remains a current challenge mostly within the poor countries of these regions.³

In Brazil, the equine serum industry faces a series of problems that have not been resolved over the last 130 years. In 2016, the Ministry of Health issued a note explaining that the distribution situation of anti-rabies and anti-venom serums had been faulty “due to constant rescheduling of deliveries caused by workers’ strikes, theft of animals, and problems in the supply of raw materials”.

It is worth highlighting that Brazilian hyperimmune serum was first subjected to specific regulation in 2017, through Resolution 187. The resolution, approved by the National Health Surveillance Agency, aims to guarantee the quality, safety and effectiveness of antivenoms and other equine serums. Since its implementation, the production of antivenoms has been suspended by three of the four public producers of horse serum. Currently, only the Butantã Institute continues to supply the public health system, significantly compromising the national supply of antivenoms and other sera. According to the aforementioned Resolution, registering a new hyperimmune serum requires a technical report with specifications on the side effects, adverse reactions, restrictions or precautions to be considered, as well as precautions and warnings, and product development history including pre-clinical and clinical trials, among others. Specific information must also be included on all stages of manufacturing, including the equine immunisation plan and the site where the source material or toxin injections, bleeding procedures, and rest period will take place.

In 2023, for the first time, complaints of animal welfare regulations violations were accepted by a court. Then, the Supreme Court of Delhi, India, upheld a legal complaint filed by the People for the Ethical Treatment of Animals (PETA) to protest the atrocious and illicit conditions to which horses used in the commercial production of antivenoms were subjected. The court’s decision ordered responsible regulatory authorities



Image 1. A docile horse in service for our benefit: 'Serum straight from the horse,' German caricature showing von Behring extracting the serum with a tap. Source: Wellcome Images, UK, n.d. Available at <https://wellcomecollection.org/works/qxr83zuz>.

to conduct rigorous and continuous inspections to assess the welfare of these horses, as well as the immediate enforcement of punitive measures for violations of India's existing national welfare laws and regulations. It also mandated that the results of such inspections be transparent, ensuring public visibility.

Significantly, the court set a precedent by opining that "we can also not be oblivious to the dawn of cutting-edge, non-animal-centric techniques for antibody generation. Such advancements suggest a trajectory that these [serum] manufacturers might, and arguably should, consider in truth." Further emphasising that "the responsibility is on the (federal government's) regulatory authorities to not just delve cursorily into these contemporary methodologies but to diligently adopt them, thereby diminishing reliance on equines."

The evidence that supported this first legal decision in defense of horses used as a source of raw material for the antivenom industry can be found in the current antivenom production system that reproduces the method implemented 130 years ago. Successive regimes for injecting toxins and adjuvants, followed by the extraction of large volumes of blood, have severe and often fatal consequences for equines. Localised ulcers and abscesses on the spots where venom is injected, as well as thrombophlebitis from repeated venous punctures in the external jugular vein are the most obvious. Less visible, are the known systemic pathologies resulting from repeated injections of toxins, including chronic anemia, inflammation of the lymph nodes and inevitably, irreversible deterioration of the liver (amyloidosis) and kidney (amyloidosis), commonly

leading to organ rupture and agonising peracute death.^{4,6,7} Abdelkader et al identified advanced liver amyloidosis in the majority of the horses regularly immunised with live cultures of the endotoxin-releasing bacteria *Escherichia coli* or *Pasteurella multocida*, over periods varying from 2 weeks to 10 years.⁸

Docile Workers: the 'Limited' Perception of Horses' Sensitivity to Pain

For John Locke, one of the early theorists of contemporary liberalism, humans acquire property rights over animals through their labour, reducing them to mere tools or assets. It is only recently that scholars have started to focus on the ethical claims of animal workers as part of interspecies justice.⁹ Horses and other species of the Equidae family, such as donkeys and mules, are the largest, and most exploited, group of non-human workers in capitalist and colonial development.

These species present a very specific feature of hiding or masking signals of and emotional reactions to pain. Hence, due to the absence of vocalisation or other perceptible reactions, consolidated beliefs assume that these species do not feel pain. This in fact is fallacious. Horses, as well as all ungulates, developed an evolutionary adaptation built as a defensive reaction against predators that is based on their physiological processes of pain reception. Any harmful response to an injury or pain may signal a potential victim. Therefore, emotional reactions to pain or other signs are not easy to pick up on.¹⁰ To undo this conflation of what is felt and how it is manifested, several studies have been conducted on horses to develop methods to identify and evaluate their

subtle signs and emotional responses to pain, as well as aspects of their physiological processes of pain reception.^{11,12} Until recently, most experimental animal injury studies have been conducted on primates and other mammals, such as cats, and dogs, but most often applying models based on work with rodents. This has hindered the comparison of certain behavioural, as well as cellular, biochemical and molecular mechanisms which were only based on experimental animal models.¹³

The history of modern serotherapy presents a long-standing tradition of intense instrumentalisation, exploitation, and degradation of horses in which equines figure not only as sources of hyperimmunised plasma but as objects of experimental activities. Unlike other forms of horse use, the system for exploiting the equine organism for the production of antivenoms and other types of serum is based on invasive techniques for modifying and exploiting equine physiology. Under these conditions, clear evidence of the painful effects of such interventions emerges. Scientific literature is replete with findings that identify the countless damages that have been inflicted on these horses. It is noteworthy that, until now, horses, and mules as well, have been described as docile and easy to manage “objects” of antivenom production.

The Question Remains: Why is it so Difficult to Set Limits on the Use of Seroproducing Horses?

There is sufficient evidence that leads us to conclude that there is an urgent need to establish regulatory guidelines for the continued use of serum-producing horses as well as other equids. The greatest pressure falls on these horses in terms of ensuring (never reached) self-sufficient and efficient antivenom production at the national level, guaranteeing product quality in terms of producing a satisfactory level of antibodies. Concomitantly, equids are submitted to experiments that are carried out to test new serums, such as anti-covid and antizika serums, among others that have received wide media coverage. In this case, as experimental animals, horses are used repeatedly, normalising abusive practices as standards in the use of animals for scientific purposes, as established in Brazil and abroad.

The antivenom industry has a history of chronic neglect of good practices in animal welfare in which the entire range of specific interventions involving protocols of horse hyperimmunisation is neglected. To justify the lack of transparency regarding hyperimmunisation procedures, their protocol is often considered as ‘production confidentiality’, even though the standards that are currently in effect have, in essence, not moved beyond those developed in the last decade of the 19th century, when serotherapy was born inside stables.

In the end, horses have fascinated us not only because of their physical potential, in a technological sense, but due to the moral character of the aims and activities in which they are embedded. From a moral point of view, since the social context of their use is beneficial to us, it is deemed morally fit.¹⁴ How long such an argument will be enough to validate the uncountable injuries inflicted on horses by the antivenom industry, in the present?

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