# The use of bone marrow-derived mononuclear cells ameliorates airway inflammation in horses with recurrent airway obstruction

Horses stabled indoors live in a pro-allergenic environment and are exposed to molds, mites, and bacterial endotoxins from hay and bedding. This exposure exacerbates recurrent airway obstruction (RAO), an asthma-like disease. Affected horses suffer from recurrence of respiratory signs, requiring constant medical intervention. Horses with RAO have significant airway inflammation, characterized by an influx of neutrophils, mucus accumulation, increased respiratory effort at rest, coughing, and exercise intolerance. The persistence of the inflammatory state in equine asthma leads to pulmonary remodeling, further increasing respiratory difficulties.

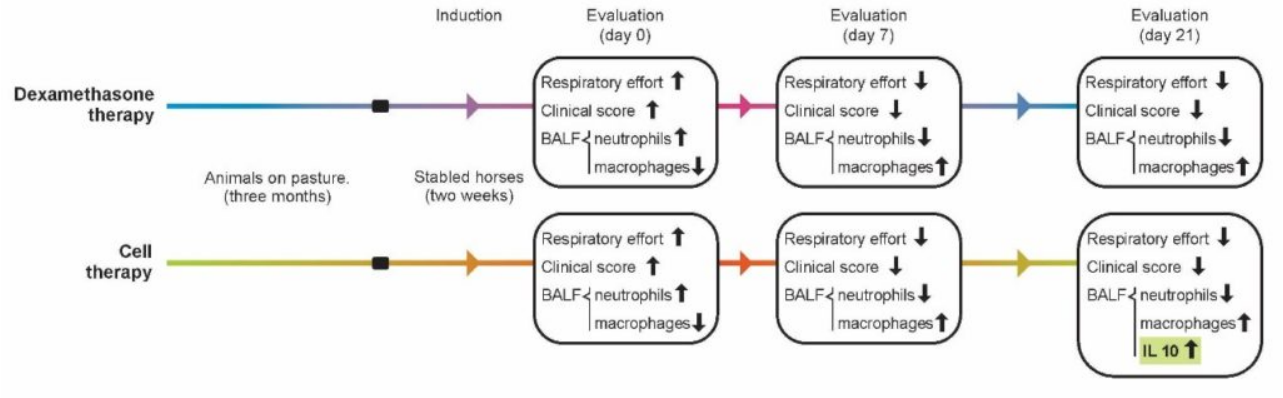


Fig. 1. Timeline of study with clinical and endoscopic evaluation at 7 and 21 days after dexamethasone or cell therapy in horses with recurrent airway obstruction. Diagnosis of RAO was confirmed by evaluation on day zero.

The clinical signs of RAO can be classified into a clinical score, adapted from the work of Tesarowski et al. (1996). Reactive airway obstruction compromises athletic ability and may lead to the inability to exercise or perform. The quality of life and welfare of the horse are also affected by RAO. In addition to the economic issues, RAO is considered equivalent to the human asthma, making the horse an ideal animal model for asthma studies.

There is no cure for RAO or human asthma. Medications (corticosteroids and bronchodilators) used to control the clinical signs may have adverse effects. There is a need for new therapies for RAO and human asthma, and cell therapy is a promising option.

The use of autologous bone marrow-derived mononuclear cells (BMMCs) showed promising results in a mouse model of asthma. Based on these studies, we evaluated the effect of

intratracheal instillation of BMMCs in horses with RAO. We compared therapy with BMMCs to conventional therapy with dexamethasone. We used BMMCs, rather than mesenchymal stem cells used in other models of asthma, due to lower cost, a simpler protocol, shorter processing time, and greater effectiveness.

Similar to conventional therapy, we found that respiratory effort and the clinical score were significantly decreased (p less than 0.05) in horses treated with cell therapy. The number of neutrophils significantly decreased (p less than 0.005), accompanied by an increase of alveolar macrophages (p less than 0.005), the resident cells of a healthy lung (Fig. 1).

Cell therapy in horses with RAO increased levels of interleukin-10 (IL-10; p less than 0.05), one of the chemical mediators responsible for the anti-inflammatory response. Conventional treatment for RAO did not increase levels of IL-10. While conventional therapy results in regression of the inflammatory process, cell therapy may protect or repair airway tissue, and may improve tolerance to allergens (Fig. 2).

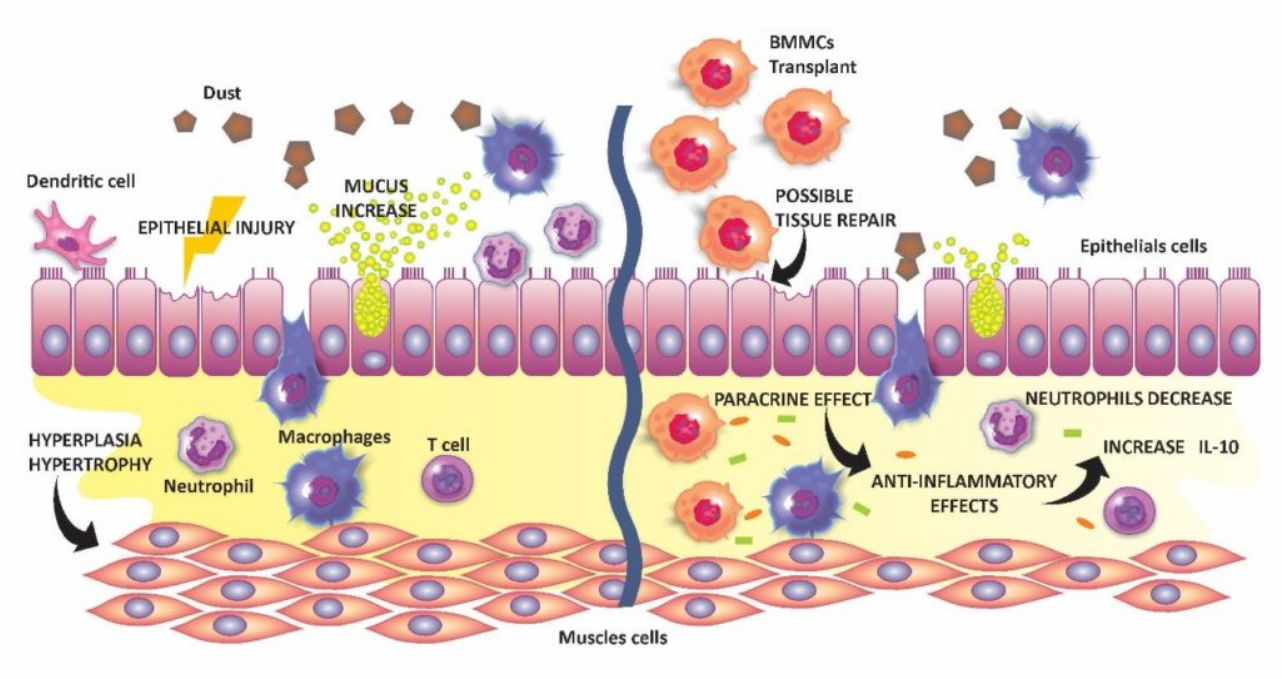


Fig. 2. Illustration of the asthma inflammatory process (left) and the influence of cell therapy on airway epithelium responses (right).

We used the horse as an animal model that naturally develops asthma. Our study is the first to demonstrate that the cell therapy is safe, reduces airway inflammation, and provides an improved immunomodulatory potential when compared to conventional therapy.

***Fernanda CM Barussi***[1], ***Fernanda Z Bastos***[1], ***Lidiane MB Leite*** [2], ***Felipe YI Fragoso*** [2], ***Alexandra C Senegaglia***[2], ***Paulo RS Brofman*** [2], ***Anita Nishiyama***[3], ***Cláudia T Pimpão***[1], ***Pedro V Michelotto Jr***.[1]

[1]*Department of Animal Science, Pontifícia Universidade Católica do Paraná, Rua Imaculada Conceição, 1155, Prado Velho, Curitiba, Paraná, Brazil*

[2]*School of Medicine, Experimental Laboratory for Cell Culture, Pontifícia Universidade Católica do Paraná, Rua Imaculada Conceição, 1155, Prado Velho, Curitiba, Paraná, Brazil*

[3]*Department of Physiology, Universidade Federal do Paraná, Av. Coronel Francisco Heráclito dos Santos, Jardim das Americas, Curitiba, Paraná, Brazil*

## Publication

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