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The amazing career of the respiratory system in equine exercise research

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Introduction

The major function of the lung is „gas exchange". Oxygen (O_2) diffuses from open air into the blood and is transported to the cells, CO_2, the product of aerobic metabolism in the reverse direction. The lung and the airways play a role in a lot of other functions too. To mention only two: thermoregulation and acid-base balance.

Until about 30 years ago the clinical examination of the eminently important lung was limited to auscultation and percussion. For the visual examination of the larynx a stiff endoscope was used and sedatives ..... Now we know how inaccurate this examination was. At that time the opinion was, that the respiratory system couldn't be a limiting factor for maximal performance in healthy horses and „chronic coughing" was just a symptom of an allergic disease, which was a real problem in only a minority of the horses.

1964 *Spörri* and *Zerobin* described the possibility to perform lung function tests in horses. They measured tidal volume and airflow by means of a pneumotachograph *(Fleisch,* 1925) on a mask and the intrapleural pressure directly by punction. From that time on lung function tests were developed in many laboratories and clinics. *Gillespie* (1966) found, that intrapleural pressure values measured in the esophagus didn't differ from those measured directly by pleural punction. Now it was possible to perform lung function test during exercise on a treadmill.

At the same time the flexible endoscope was introduced in veterinary medicine. The fiberendoscope and the videoendoscope make visual inspection of the respiratory tract as far as the bronchi possible, and enable us bronchoalveolar lavage for cytologic, virologic or bacteriologic examination. Scintigraphy shows how ventilation and perfusion are distributed *(O'Callaghan,* 1991) all over the lung, even regional ventilation-perfusion matching can be analysed *(Clerx,* 1988).
In about 30 years the clinical examination of the lung has been changed from „a very difficult and hardly interpretable auscultation" into a reliable morphological and functional examination, both at rest and during exercise. A lot of diseases and problems, subclinical at rest but causing poor performance, have been demonstrated and can be diagnosed. Nevertheless, the horse's lung still has functional peculiarities, which are not unterstood.

Gas exchange

A lot of processes in which the respiratory and cardiovascular system cooperate, are involved in the gas exchange, i.e.

- ventilation and mechanics of breathing
- perfusion and ventilation: perfusion ratio in lung regions
- diffusion
- transport of O_2 to the tissues and CO_2 to the lung
- control of breathing.

For internal medicine, i.e. in patients, the examination of ventilation and the mechanics of breathing and the control of arterial bloodgases have been routine in many clinics for about 30 years. Up till now, other parameters are more investigated in exercise physiology.
The examination of the parameters mentioned above in clinics together with the endoscopy make it possible to diagnose important diseases like C.O.P.D. in early stages of the disease and make us understand how these diseases can cause poor performance (*Sasse,* 1971).

Ventilation and mechanics of breathing

The gas exchange takes place in the alveoli. Only a part of the inspired air reaches these alveoli, the rest remains in the (physiologic) dead space. During exercise the gas exchange requirement increases, the alveolar ventilation must increase too.
To meet exercise requirements tidal volume, or the respiratory frequency or both can be changed. The higher the tidal volume, the higher the percentage of alveolar ventilation.
During exercise the respiratory minute volume can be twenty times higher than it is at rest! In galopping horses respiratory frequence and locomotion are coupled (*Attenburrow,* 1982).

The total alveolar ventilation is not the only very important parameter. Lung regions are not uniformly ventilated, because intrapleural pressure changes are not uniform all over the thorax, due to gravidity. In dorsal parts of the thorax intrapleural pressure is more negative, the alveoli are more extended there than in other regions of the lung and accordingly ineffectively ventilated.
Local inequalities in airway resistance, especially in the small airways, cause a non-uniform ventilation of the alveoli. Regions with lower airway resistance are being ventilated better. At rest this phenomenon is not important in healthy horses, but the

problem increases in patients with increased airway resistance, especially when respiratory frequency is high.
In healthy horses non-uniform ventilation can be compensated at rest by matched perfusion (*Amis* et al., 1984). In healthy horses lung regions have a ventilation/perfusion ratio of 0.8. At this ratio gas exchange is optimal. The gradient of ventilation is matched by the gradient of perfusion. Even during exercise there ist only a small mismatch of ventilation and perfusion in the horse's lung.
In patients with airway obstruction exercise enhances mismatching. The impairment of alveolar ventilation increases. Gas ex-change is not longer optimal. The PaO_2-values (arterial oxygen partial pressure) decrease. In more advanced cases of airway resistance a decrease of PaO_2 can be demonstrated at rest already.

To guarantee alveolar ventilation, the respiratory muscles must perform work to overcome a lot of forces. For internal medicine, for horses with diseases of the respiratory system, the most important forces to overcome are the elasticity of the lung and viscous resistance, most of all the airway resistance. To do so, respiratory muscles change intrapleural pressure, which is in healthy horses at rest during inspiration negative and less negative during exspiration. The maximum change of intrapleural pressure (max. D.Ppl) in healthy horses at rest is about 4–5 cm H_2O (0.45 kPa), with a tidal volume of 5–6 liters. During exercise this max. D.Ppl increases up to the twentyfold. This max. D.Ppl will increase in many respiratory diseases too, especially when airway resistance increases, like in horses with C.O.P.D.. I once measured a max. D. Ppl of 106 cm H_2O (10 kPa) in a diseased horse at rest.
Simultaneous recording of airflow, tidal volume and intrapleural pressure enables the clinician to calculate airflow resistance, dynamic compliance and parameters like the work of breathing.
This work of breathing, calculated from the area of a volume-pressure diagramme (*Donleben*, 1959), increases more than hundredfold during exercise. In patients with airway obstruction even much more. There is a level, above which respiratory muscles consume the complete extra 0_2-uptake (*Bayly* et al. 1989). During strenuous exercise healthy horses demonstrate hypoxemia and hypercapnia. This phenomenon is unknown in other species.
In healthy horses nasal airway resistance is very important (*Art* et al., 1988). In patients laryngeal resistance and the resistance in the smaller airways become more interesting, because diseases in these regions are rather common.
The measurement of PaO_2 in horses only gives us an overall impression of the respiration and tissue O_2-supply. At rest the Euler-Liljestrand Reflex (alveolocapillary reflex) may correct uneven ventilation/perfusion ratios. In cases of anemia or increased packed cell volume PaO_2-values do not correlate with the O_2-content of the blood, and above a value of 70 mmHg the oxyhemoglobincurve is flat, about 96–97 % of the Hemoglobin being saturated with oxygen.
Normal PaO_2-values (> 90 mmHg at sea level) are altitude dependent (*Littlejohn*, 1978).

Respiratory function and disease

Clinicians, specialists for internal medicine, are interested in disease. Respiratory diseases in horses were well known and seemed to be no diagnostic problem. But in the past 30 years lung function tests, flexible endoscopes and the possibility to examine horses during exercise learned us, that even subclinical stages of respiratory diseases at rest can cause poor performance.
The amazing increasing interest in the respiratory system is demonstrated not only by research topics, but even so by the increasing variety and frequency of respiratory diseases in horses with poor performance.
Three examples:
- pharyngeal and laryngeal disorders
- chronic obstructive pulmonary disease (C.O.P.D.)
- exercise induced pulmonary hemorrhage (E.I.P.H.)

Pharyngeal and laryngeal disorders will be discussed elsewhere.

Chronic obstructive pulmonary disease (C.O.P.D.)

In almost all cases of C.O.P.D. a chronic bronchitis can be demonstrated, reason why the disease is called chronic obstructive bronchitis (C.O.B.) in Germany.
In advanced stages of the disease the diagnosis is easy. These horses show a mixed dyspnea with flaring nostrils, and an abdominal type of expiration. Coughing and nasal discharge not always complete clinical signs. The horses are incapable of any form of exercise.
Bronchospasm, mucosal edema and mucous plugging can be demonstrated.
During the first stages of the disease diagnosis often is impossible without the help of modern techniques. The main problem is the obstruction of smaller airways, causing an increase of the work of breathing and a non-uniform ventilation.

Especially during exercise these problems can be demonstrated by lung function tests and PaO_2-values. Sometimes endoscopy may show us the presence of mucus in the bronchi and bronchoalveolar lavage can be a help, too.
Two phenomena have been demonstrated to maintain the disease: hyperreactivity (*Klein* and *Deegen* 1986) and a decrease of mucociliary clearance (*Turgut* and *Sasse* 1989, *Dixon* 1992). The hyperreactivity is caused by direct stimulation of irritant receptors lying under the tight junctions. As a sequela of viral or bacterial bronchitis these tight junctions are „open", so that the receptors can be stimulated by dust particles very easy. This phenomenon previously was thought to be an allergy.

Prevention and therapy

In C.O.P.D. therapy without environmental control makes no sense. With bronchodilators, bronchomotorics, mucolytics and anti-inflammatory agents we can help to alleviate the signs of airway disease. Antibiotic therapy seldom is necessary. But the hyperreactivity remains. Every exposure to airborne pollutants can induce airway obstruction. And every degree of airway obstruction can be the cause of loss of performance.
Mucociliary clearance can be increased by bronchomotorics, but liquefaction of viscous mucus may increase the ciliary activity too.

In Germany the so-called Hyperinfusion- and Hydrotherapy are very popular and succesfully applied in horses with mucus plugging. On three days 0,9 % NaCl is administered intravenousl resp. peroral at a dose of 6,8l/100 kg bodyweight, together with bronchomotorics, e.g. Clenbuterol.
The intravenous administration takes 2fi–3 hours. The peroral administration takes place before the horses are fed and halfway through the horse is lead by the hand for about 10 minutes.
The results of the intravenous therapy are a few percents better, the method however is expensive and accidents have been described. The peroral method is cheaper and without any risk. Endoscopic control after one week ist decisive, whether this therapy must be repeated or not. Lungfunction tests may prove the result of therapy in horses suffering from C.O.P.D..

Exercise induced pulmonary hemorrhage (E.I.P.H.)

As late as 1974 *Cook* has written: „Epistaxis in the racehorse has received little study". The increase in research of the respiratory system cannot be demonstrated better!
E.I.P.H. nowadays is defined as the presence of blood in the tracheobronchial tree. And even *Cook* already knew: „blood from a lung hemorrhage is not foamy....". Most of the clinical signs are nonspecific. Only in a few horses epistaxis is seen during or after exercise, when the horse lowers its head. Other symptoms are abnormal respiratory sounds, swallowing and dyspnea. Some horses show poor performance, others do not.

The easiest way to prove E.I.P.H. in a horse is the detection of blood in bronchi or trachea by endoscopic examination 1–2 hours after exercise. Cytologic examination of the bronchoalveolar lavage reveals hemosiderophages. In this way it has been demonstrated, that a large number of horses suffer from E.I.P.H. Only 1 or 2 per cent show an epistaxis, however. The reported incidences: standard breeds 30 %, Quarter Horse 60 %, Thoroughbred 70 %. After repeated examination percentages as high as 95 % have been reported. It seems, that E.I.P.H. is inevitable in strenuous exercise in horses (*Clark*, 1985).
The cause of E.I.P.H. still is unknown. At necropsy the primary site of hemorrhage turns out to be in the caudo-dorsal region of the horse`s lung. In this part of the thorax intrapleural pressure is more negative than in others. The alveoli are dilated and week. Ventilation is non-uniform, pressure differences increase in parts of the alveoli, so ruptures may be easier than in other regions of the lung. Another possibility is, that the poor perfusion of the dorsal lung regions enables the bronchial circulation, because of its higher pressure, to enter into the pulmonary circulation via anastomoses.
C.O.P.D. has been suggested as a primary lesion in E.I.P.H. too. There are horses with E.I.P.H. with normal lung function tests, however, and E.I.P.H. is diagnosed all over the world, also in regions where C.O.P.D. is unknown. A lot of other possible causes for E.I.P.H. are being investigated, for example the neovascularisation in the dorsal regions following inflammations.
Coagulation defects have not been demonstrated.
A therapy for E.I.P.H. is unknown. Many regimens have been advocated. Efficacy never has been demonstrated, not even for bronchodilators or furosemide. Furosemide does improve racing time both in healthy horses and horses with E.I.P.H.
The respiratory system of the horse still has its secrets, but modern times have brought an amazing increase of knowledge.

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