UNIVERSIDADE DE LISBOA

Faculdade de Medicina Veterinária

EQUINE EXERCISE ELECTROCARDIOGRAM: STANDARDIZED LUNGEING TEST

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CONSTITUIÇÃO DO JÚRI

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Abstract

Cardiovascular lesions are common in horses, but these lesion are often minor and well tolerated by the horses. However, some cardiovascular lesions can become clinically significant, manifesting as poor performance or even exercise intolerance, arrhythmia, weakness, systemic infection, congestive heart failure, or sudden death. (Bonagura & Reef, 2004)

Arrhythmias may cause uncertainty to the equine practitioner especially when diagnosed in resting animals. They must be distinguished as being normal due to variations in autonomic tone ('physiological' arrhythmias), or as being caused by cardiac abnormalities. Although rest examination is critical to diagnose many clinical problems, exercise tests can help assess dynamic cardiac problems. Exercise testing can be conducted in a treadmill laboratory or in the field. There are advantages and disadvantages for both types of exercise test. However, both protocols might be difficult to implement, and their availability can be limited.

This study is focused on evaluating a protocol for standardized lungeing exercise test which was included in the protocol for cardiac examination, used to evaluate cardiac arrhythmias. Lungeing usually is part of most horse's training, and they can be walked, trotted, and galloped, and induce high levels of exertion, so performing it as an exercise test doesn't need sophisticated instruments nor specialized people, allowing it to be implemented with less limitations, as long as an arena and the wireless ECG recording equipment (telemetry or Holter monitor) are available.

Therefore, this study includes a sample of 10 diverse cases of clinically apparent healthy horses and horses with cardiac disease, in which a standardized lungeing exercise test was performed as part of a protocol for cardiac examination. The protocol for standardized lungeing test consisted of 5 minutes walking, 10 minutes trotting, 4 minutes galloping, 1 minute fast galloping, and 5 minutes walking.

Keywords: arrhythmias, cardiac examination, equine, electrocardiogram, exercise test

Resumo

As lesões cardiovasculares são comuns em cavalos, mas estas lesões são muitas vezes pouco significativas, e bem toleradas. No entanto, algumas lesões cardiovasculares podem tornar-se clinicamente significativas, manifestando-se em diminuição da performance ou mesmo intolerância ao exercício, arritmias, fraqueza, infeção sistémica, insuficiência cardíaca congestiva ou morte súbita. (Bonagura & Reef, 2004)

As arritmias representam incerteza para os clínicos de equinos, especialmente quando diagnosticadas em animais em repouso. Devem ser distinguidas como sendo normais devido a variações no tónus vagal (arritmia 'fisiológica'), ou como sendo causadas por lesões cardíacas. Embora o exame em repouso seja fundamental para diagnosticar muitos problemas clínicos, os testes de exercício ajudam a avaliar problemas cardíacos dinâmicos. A prova de esforço pode ser realizada em passadeira elétrica ou no campo. Existem vantagens e desvantagens para ambos os tipos de prova de esforço. No entanto, ambos os protocolos podem ser difíceis de implementar, e sua disponibilidade pode ser limitada.

Este estudo tem como objetivo estudar um protocolo de eletrocardiograma de esforço durante o trabalho à guia padronizado e inserido num protocolo de exame cardíaco, para a avaliação das arritmias cardíacas. O trabalho à guia geralmente faz parte do treino da maioria dos cavalos, sendo que estes podem ser conduzido a passo, trote, e galope, e originar elevados níveis de esforço. A sua realização enquanto prova de esforço, não torna necessária a utilização de instrumentos sofisticados e pessoas especializadas, dando a possibilidade de ser implementado com menores limitações, sempre que um picadeiro e um equipamento de ECG sem fios (Holter ou telemetria) estejam disponíveis.

Este estudo inclui uma amostra de 10 casos clínicos diferentes, que incluem cavalos aparentemente clinicamente saudáveis e cavalos com doença cardíaca, aos quais foi realizado eletrocardiograma de esforço durante o trabalho à guia padronizado e inserido num protocolo de exame cardíaco. Este protocolo consistiu em 5 minutos de passo 10 minutos de trote, 4 minutos de galope, 1 minuto de galope rápido, e 5 minutos de passo.

Palavras-chave: arritmias, exame cardíaco, equino, eletrocardiograma, prova de esforço

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List of abbreviations and symbols

ACVIM - American College of Veterinary Internal Medicine

AF – Atrial Fibrillation

APD - Atrial Premature Complexes

ARP - Absolute Refractory Period

AT – Atrial Trachycardia

aVF - Augmented vector foot

aVL - Augmented vector left

aVR - Augmented vector right

AV block – Atrioventricular Block

AV node – Atrioventricular Node

AV valves – Atrioventricular Vales

bpm – Beats per minute

Ca - Calcium

CHF - Congestive Heart Failure

cTn I - Serum Cardiac Troponin I

CV - Cardiovascular

ECEIM - European College of Equine Internal Medicine

ECG - Electrocardiogram

HR – Heart Rate

iCa – Ionised Calcium

IRAF - Immediate Recurrence of Atrial Fibrillation

IU – International units

K - Potassium

LA – Left Atrium

LV – Left Ventricle

LVD – Left Ventricular Dysfunction

Lone AF – Lone Atrial Fibrillation

MEA - Mean Electrical Axis

mEq - Milliequivalents

Mg - Magnesium

mmHg - Millimeter Of Mercury

MR – Mitral Regurgitation

Na - Sodium

PAF - Paroxysmal Atrial Fibrillation

PaO2 - Arterial Oxygen Tension

PHT - Pulmonary Hypertension

po – per os

RA – Right atrium

RBC – Red Blood Cell Count

RV – Right Ventricle

RRP - Relatively Refractory Period

SA - Sinoatrial

S1 – First heart sound

S2 – Second heart sound

S3 – Third heart sound

S4 – Forth heart sound

SCD - Sudden Cardiac Death

SNS – Sympathetic Nervous System

SVPD - Supraventricular premature depolarizations

TVEC - Transvenous Electrical Cardioversion

VA – Ventricular Arrhythmias

VF – ventricular Fibrillation

VT – Ventricular Tachycardia

VO2max - Maximal Oxygen Consumption

Brief description of the traineeship

My official curricular traineeship consisted of a 12 week Equine Programme at the Faculty of Veterinary Medicine of the University of Gent, completing a total of 511 hours distributed by the different departments of their Large Animal's Veterinary Hospital: Internal Medicine, Diagnostic Imaging, Surgery, Pathology, Obstetrics, Hospitalisation, and Reception; under the supervision of Professor Ann Martens.

In the department of Internal Medicine, I spent 4 weeks performing the following activities:

- Daily care of the hospitalised patients including administration of medication, discussions of the clinical cases etc.;
- Help with the complementary exams of patients including abdominal, thoracic and cardiac ultrasound, endoscopy of the upper respiratory tract, rectal examination etc.;
- Interpretation of blood analysis results;
- During one week, I performed the evening, night and weekend duties, and helped with the examination and treatment of emergency cases (mainly colics).

For another 2 weeks I was in the department of Medical Imaging department, the activities were:

- Provide help in taking the radiographs in and performing the ultrasonographic examinations;
- Interpret radiographic and ultrasonographic images under guidance of assistants, residents, and professors.

In the department of Surgery, in the following week, the activities were:

- Assist in the different soft tissue and orthopaedic procedures performed at the surgical department. Alternatively scrubbed-in with my colleagues with the surgeon, and provided help during the surgical procedures, or simply watched the surgeries, for which it was suggested to have done previous theoretical preparation;
- Surgical procedures on ruminants were also performed during this week.

One other week was spent in the department of Pathology:

- Necropsies were performed by the students and trainees under the guidance of the assistants and professors.

In the department of Obstetrics, for the following week, the activities were:

- Semen collections in stallions;
- Rectal ultrasound of mares for insemination/ pregnancy.

Two weeks were the spent with the patients, in the called 'Hospitalisation':

- Care of the hospitalised patients from the surgical department included administration of medication, changing bandages, flushing wounds and sinuses;
- Feeding, handling and daily care of the horses (including clinical examination);
- One of these 2 weeks, I was involved in the care of the patients during the evenings, nights and at the weekend. At the same time, I also assisted and scrubed-in to surgeries of emergency cases (mainly wounds and colics).

'Reception' was the designation given to the department responsible for the examination of the orthopaedic patients. I spent 1 week in this department, and my activities were the following:

- Involvement in writing the anamnesis of the lameness cases and performing the clinical examination. This included observation of the lameness, performing the hoof- and flexion tests, and assisting in the diagnostic anaesthesias;
- Interpretation of radiographs and ultrasound from the orthopaedic patients, also performed under the guidance of the assistants and professors.

In conclusion, it was a very intense but extremely enriching experience.

A. Literature Review

1. Introduction

The horse is an extraordinary athlete, due to the evolution of horses as grazing animals on the ancient prairies of North America. To survive in these open lands the horses needed to develop speed to escape predators, and endurance required to travel long distances in search of food and water (Hinchcliff, 2014).

Domesticated horses were selected and bred for certain particularities depending on the intended use. Nowadays there are many hundreds of breeds of horses, for example, large heavy breeds of horses were bred for draft work, such as pulling ploughs, sledges or carts, or military work, such as the chargers that carried heavily armoured knights during ancient battles (Hinchcliff, 2014).

Lighter horses were bred for speed and endurance, and were used for transportation, herding and sport. There are the Thoroughbred racehorses that can run at high speed (18 m/s, 64 km/h) over distances of 800 to 5000 meters, Standardbred horses trot or pace at high speed for distances up to 3600 m, and Arabians trot or canter at speeds of up to 29 km/h for up to 160 km in a single day during endurance events (and over longer distances during multi-day races). In contrast, draft horses pull huge weights (1000 kg or more) short distances in pulling competitions. Warmbloods perform elegant, and demanding, dressage routines, and ponies pull lightly laden jinkers or buggies (Hinchcliff, 2014).

Horses are most commonly used as athletes, rather than for professional purposes or for pleasure riding (Durando, 2010), and a series of characteristics, both physiological and anatomical, act in concert to enhance the horse with extraordinary athletic capacity. Therefore, the athletic capacity of horses is due to many physiological adaptations, and in some cases these adaptations are not affected by training. An example of this, is the lung size. Whereas other adaptations change in response to training, for example, blood volume. The superior athletic ability of horses results from their high maximal aerobic capacity, large intramuscular stores of energy substrates and in particular glycogen, high mitochondrial volume in muscle, the ability to increase oxygen carrying capacity of blood at the onset of exercise through splenic contraction, efficiency of gait, and efficient thermoregulation (Hinchcliff, 2014).

The cardiovascular system is a transport system consisting of a muscular pump, the heart, and a network of blood vessels that contain blood. Its principal function is transport of water, oxygen, carbon dioxide, fuels for energy production, electrolytes, hormones, and metabolic products. The cardiovascular system of the horse is specifically designed for exceptional transport of oxygen from the lungs to body tissues. Horses have a high maximal oxygen consumption (VO_2max) relative to body weight when compared with most other mammals. The superior oxygen transport of the horse is attributed to its specialized spleen, which is able to add an extra volume of red blood cells (RBC) to the circulation when it contracts after the stimuli of fear, excitement or exercise. This infusion of erythrocytes increases the oxygen-transport capacity of arterial blood and enables horses to greatly increase VO_2max during exercise. The stroke volume of blood pumped with each cardiac contraction is over 1 liter (L) in trained horses, and maximal rates of blood flow during exercise are likely to be up to approximately 400 liters per minute (L/min) in the most exceptional athletes. The structure and function of the equine cardiovascular system are, therefore, fundamental to the superior athletic performance of the horse (Hodgson, 2014).

The size of the heart is the most important determinant of maximum stroke volume, cardiac output, hence aerobic capacity and exercise performance. This relationship has been documented in humans by examination of the electrocardiogram (ECG), ultrasound, radiographs, and post-mortem examination of heart size. As noted by Poole & Erickson (2014), Paavo Nurmi, multiple Olympic champion distance runner, had a heart mass nearly three times larger than the size presumed for his body size. At post-mortem, the heart of the seven-time Boston Marathon winner, Clarence DeMar, who died of a non-myocardial cancer, was substantially larger than normal, and his coronary arteries were threefold larger than found in non-athletic equals. In horses, heart mass approximates 0.9–1% of body mass, which is greater than the other non-athletic species, and may exceed 1.1% of body mass in trained horses, possibly reaching ~2% in elite horses.

The heaviest horse heart actually weighed was Sham's heart, who was consistently runner-up to Secretariat, and it weighed 18 lb (8.2 kg). Secretariat was a Triple Crown winner and holds the track record at Belmont Park (2 min 24.4 s for 1.5 miles on turf). Secretariat's heart was never weighed, but Dr. Thomas Swerczek who weighed Sham's heart, calculated that Secretariat's heart weighed 22 lb (10 kg), considering it to be in perfect condition. If that mass is correct, it predicts that Secretariat may have achieved a

cardiac output in excess of 500 L/min and VO_2max over 120 L/min (Poole & Erickson, 2014).

Cardiovascular lesions are common in horses. Although these lesion are often minor, and well tolerated by the horses, some cardiovascular lesion can become clinically significant, manifesting as exercise intolerance, arrhythmia, weakness, systemic infection, congestive heart failure, or sudden death. The effect of the cardiovascular lesion on a performance horse that depends so much on circulatory function, can be difficult to quantify without a thorough examination (Bonagura & Reef, 2004).

In essence, any condition that reduces a horse's cardiac output will reduce performance. Causes of poor performance related to the heart include arrhythmias, systolic or diastolic dysfunction, valvular regurgitation, and intracardiac shunts. Severe regurgitation, large shunts, or sustained arrhythmias such as atrial fibrillation or ventricular tachycardia have an obvious impact on performance (Durando, 2003).

In the context of examinations for purchase, or in horses being investigated for poor performance, a murmur in an otherwise apparently healthy horse, may have uncertain significance (Marr, 2010). If echocardiography is a tool available to the clinician, the source of the murmur can be easy to identify. The difficulties arise when the clinician needs to know if the source is pathological, or perhaps the horse can be considered clinically healthy, advising or guiding the owner, rider or buyer. It is important to understand if, for example a valvular regurgitation, can lead to a cardiac arrhythmia during exercise and be potentially fatal (Buhl, 2010).

In general terms, arrhythmias can develop as a result of damage to: a few localized cells which act as a focus of abnormal depolarization; specialized cells within the conduction pathway; and also a damage to most myocytes. Whatever the form of damage (cell death, fibrosis, ischaemia, hypoxia), there may be changes in the membrane properties which determine the electrophysiology of the cells. The significance of these effects depends on which cells are affected, and any drugs or electrolyte abnormalities that might be present at the same time. In addition, the autonomic nervous system may have an effect on normal and abnormal rhythms (van Loon & Patterson, 2010).

Although, arrhythmias are for the most part benign in nature (McGurrin, 2011), they represent doubt to the equine practitioner especially when detected in resting animals. In horses, some arrhythmias are normal because of the high vagal (parasympathetic) tone. Therefore, the arrhythmias must also be distinguished as being due to normal variation in

autonomic tone ("physiological" arrhythmias), or as arrhythmias which occur because of valvular, myocardial or systemic disease. (Verheyen et al., 2010).

2. Introduction to cardiac physiology

2.1 Electrical Properties of the Heart

Orderly electrical activation of the heart is accomplished by the sequential propagation of action potentials along the anatomically defined structures. Within the sinoatrial (SA) node, the atrioventricular (AV) node and the specialized conduction fibres of the His Purkinje system, a spontaneous action potential without the need of an external stimulus (automaticity) can be generated, due to an inherent property of the myocytes. The cells of the SA node normally have the fastest rate of spontaneous action potential generation, consequently, the SA node is the site of impulse formation in the normal heart (Rastagi, 2007; Bright & Marr, 2010; Gilmour, 2015).

From the SA node, the impulse spreads over the atria to the AV node producing electrical potentials that inscribe a P wave on the surface electrocardiogram (ECG). The P wave reflects atrial depolarization and precedes the QRS complex (Miller et al., 1999). P waves are typically positive in a base-apex ECG recording, since spread of the cardiac impulse through the atria is in an overall direction that is dorsal to ventral (Bright & Marr, 2010). The P–R interval, measured from the beginning of the P wave to the beginning of the QRS complex, represents the time required for the wave of excitation to travel from the SA node to the ramifications of the His–Purkinje system (Bright & Marr, 2010; Gilmour & Moïse, 2015).

Because it is greatly innervated by the parasympathic and sympathetic nervous systems that provide stimuli to alter the heart rate, the degree of AV conduction delay is influenced by the autonomic tone, as the vagal tone reduces and sympathetic tone increases the rate of conduction. Therefore, in horses with dysrhythmias, such as atrial fibrillation, autonomic tone is an important determinant of heart rate. After relatively slow conduction through the AV node, the cardiac impulse is rapidly conducted over the bundle of His and Purkinje system to the terminal Purkinje fibres and the working ventricular myocytes (Bright & Marr, 2010).

The His–Purkinje system penetrates more deeply in horses, ruminants, swine and birds (Gilmour & Moïse, 2015), and is widely distributed throughout the right and left ventricular myocardium, penetrating the entire thickness of the ventricular walls (Bright & Marr, 2010). The vast distribution of the Purkinje system is physiologically important because the conduction velocity within the ventricular myocytes is approximately 6 times slower than conduction velocity of the Purkinje cells. Thus, the time duration and sequence of ventricular activation and, ultimately, the surface ECG is affected (Bright & Marr, 2010).

The earliest phase of ventricular activation in horses consists of depolarization of a small apical region of the interventricular septum. This early depolarization is often in an overall left to right and ventral direction. The electrical potentials generated from this early phase of ventricular activation may produce the initial portion of the QRS complex (*Q wave*) on the surface of the ECG (Bright & Marr, 2010; Stephenson, 2013). However, there is significant variation in the direction of the early phase of ventricular activation, and in some horses the vectors of local electrical activity effectively cancel each other, thereby eliminating any deflection on the surface ECG. Thus the duration of QRS complexes in normal horses may vary from 0.08 to 1.4 seconds (≤0,14, foal: 0,05 - 0,08) (Bright & Marr, 2010).

Immediately after early ventricular activation, the major masses of both ventricles and the middle portion of the septum are depolarized (Bright & Marr, 2010), and the extremely fast conduction of the cardiac action potential, from cell-to-cell, through the latter portion of the AV bundle, the bundle branches, and the Purkinje system, results in a nearly synchronous contraction of all the fibres in both ventricles (Stephenson, 2013). Since this depolarization occurs without a spread of the impulse in any specific direction, it’s contribution isn’t considered in the genesis of the QRS complex on the ECG (Bright & Marr, 2010).

The final phase of equine ventricular activation consists of depolarization of the basilar third of the septum, which occurs in an apical to basilar direction. This final phase of activation is responsible for the generation of most of the QRS complex and normally produces a negative deflection in a base-apex recording (Bright & Marr, 2010). The duration of the QRS complex represents the spread of impulses throughout ventricular muscle, and is a measure of the intraventricular conduction time (Gilmour & Moïse, 2015).

2.2 The Cardiac Cycle

An understanding of the cardiac cycle is essential to understand the healthy heart, and for an acknowledgment of how various diseases disturb its normal function (Bright & Marr, 2010). The cardiac cycle describes and relates temporally the mechanical, electrical and acoustical events that occurs in the heart and great vessels. It is the sequence of events occurring in the heart during every contraction (systole) and relaxation (diastole) (Bright & Marr, 2010; Hodgson, 2014; Riedesel, 2015).

Systole consists of the *isovolumic contraction* phase and ventricular ejection. Diastole consists of the *isovolumic relaxation* phase, the rapid filling phase, diastasis and atrial contraction. It is helpful to recall that mechanical events are stimulated by electrical depolarization, and, thus, the mechanical events occur slightly after the electrical events on the cardiac cycle diagram (Bright & Marr, 2010; Stephenson, 2013). The right and left ventricular cycles are almost identical except for the peak pressures. The right ventricle usually only achieves peak systolic pressures of 20–40 mmHg, while the left ventricle develops pressures of 100–160 mmHg in the resting animal (Riedesel, 2015).

The cyclic nature of cardiac activity depends on normal conduction of electrical impulses from the sinoatrial (SA) node, through the atrial and ventricular myocardium. The diffuse distribution of Purkinje fibres through the left ventricular wall, enables rapid depolarization and development of muscular tension. Right ventricular contraction slightly precedes left ventricular contraction (Hodgson, 2014).

2.3 Systole

Ventricular contraction (ventricular systole) is initiated by ventricular depolarization, which is indicated by the QRS complex, and mechanical systole begins slightly later with the contraction and closure of the AV valves (Bright & Marr, 2010; Stephenson, 2013). Blood is not immediately ejected from the left ventricle into the aorta at the beginning of systole, because the aortic valve remains closed until the left ventricular pressure exceeds the aortic pressure. Therefore, ventricular volume remains the same during this first phase of systole, which is therefore named *isovolumetric contraction* (Stephenson, 2013). During the *isovolumic contraction* phase of systole, the intraventricular pressure increases rapidly, and when pressure in the left ventricle exceeds pressure in the aorta, the aortic

valve opens and the blood begins to flow into the aorta. The opening of the aortic valve marks the end of *isovolumic contraction* and the beginning of *ejection*. The interval between the onset of the QRS complex and the onset of ejection is the pre-ejection period. The pre-ejection period includes both electromechanical delay and isovolumic contraction. During most of the ejection phase of systole, the left ventricular pressure is above the aortic pressure (Hamlin, 1999; Bright & Marr, 2010; Stephenson, 2013).

Left ventricular pressure begins to decrease during systole, and at the end of ejection, aortic pressure exceeds ventricular pressure briefly. Aortic blood flow velocity reaches a peak during the first third of ejection and then decreases. A short backflow of blood from the aorta into the left ventricle closes the aortic valve. The closure of the aortic valve marks the end of ventricular systole, and the beginning of ventricular diastole. The interval between opening and closure of the aortic valve is the left ventricular ejection time. Toward the end of systole the ventricular muscle repolarizes producing the T wave on the ECG (Hamlin, 1999; Bright & Marr, 2010; Stephenson, 2013).

2.4 Diastole

The ventricular diastole begins with the aortic valve closure. The left ventricular pressure, which has been declining due to relaxation of the myocytes, and continues to decline rapidly during early diastole, but ventricular volume remains constant due to the cardiac valves being closed (Bright & Marr, 2010). Therefore, this initial phase of diastole is *isovolumic relaxation,* and the rate of intraventricular pressure decline during this phase of the cardiac cycle, is determined by the rate of active relaxation of the myofibers (Bright & Marr, 2010; Stephenson, 2013; Riedesel, 2015). When left ventricular pressure drops below left atrial pressure, the mitral valve leaflets open and ventricular filling begins (Bright & Marr, 2010)..

Opening of the mitral valve marks the onset of the rapid filling phase of diastole, which filling occurs passively due to a difference in pressure between the ventricle and atrium that results largely from myocyte relaxation. The velocity of left ventricular inflow, and the volume of blood transferred from the atrium to the ventricle during this phase, are largely determined by the increasing pressure gradient created by the continuous decline in tension in the ventricular myocytes at this time (Bright & Marr, 2010).

As left ventricular pressure decline slows and ventricular fillings progresses, the atrioventricular pressure difference approaches zero, and ventricular volume reaches a

plateau (Bright & Marr, 2010). This phase of diastole is known as diastasis, and minimal changes in intraventricular pressure and volume are occurring at this time. The duration of diastasis varies inversely with the heart rate, and at resting heart rates in horses the diastasis is the longest phase of diastole. Atrial systole is the final phase of ventricular diastole. This phase begins slightly after P wave of the ECG. Atrial contraction recreates an atrioventricular pressure gradient that increases ventricular filling (Bright & Marr, 2010; Stephenson, 2013).

In healthy resting horses, atrial systole has minimal effects on ventricular filling and cardiac performance. However, absence of atrial contraction or loss of atrioventricular synchrony during exercise, has a considerable adverse effect on ventricular filling and cardiac output (Bright & Marr, 2010).

2.5 Normal Heart Sounds

During the cardiac cycle four heart sounds are generated as a result of rapid acceleration or deceleration of blood (Bright & Marr, 2010). In healthy horse two to four sounds can be heard. The recognition and understanding of these sounds provides information regarding timing of murmurs, and presence or absence of atrial contraction (Bright & Marr, 2010; McGurrin, 2011).

Normally the first (S1) and second (S2) heart sounds are the loudest and are audible in all healthy animals. S1 is audible at the onset of mechanical systole and occurs in association with closure of the atrioventricular valves (Bright & Marr, 2010; Stephenson, 2013). In healthy horses S1 is the loudest in duration, and is louder in young, thin animals and in those with high sympathetic tone, tachycardia, systemic hypertension, or anaemia (Sisson & Ettinger, 1999). S2 is heard at the end of systole with the closure of the semilunar valves, and is a shorter, higher pitched sound. The third heart sound (S3) follows S2, and if audible, is associated with early ventricular filling (the rapid filling phase of diastole). The fourth heart sound (S4), if audible, is heard immediately prior to S1, and is associated with atrial contraction (late filling) (Bright & Marr, 2010; McGurrin, 2011; Stephenson, 2013; Riedesel, 2015).

Typically, the normal heart sounds occur nearly simultaneously on the left and right sides of the heart. However, there are some conditions that may cause enough asynchrony so that the first or second heart sounds are split into two components. An audible splitting of S1 is unusual in horses and generally not significant unless the split is mistaken for an

audible S4 in horses with atrial fibrillation. S2 is frequently split in horses, and inspiration usually increases the degree of splitting in normal animals (Bright & Marr, 2010).

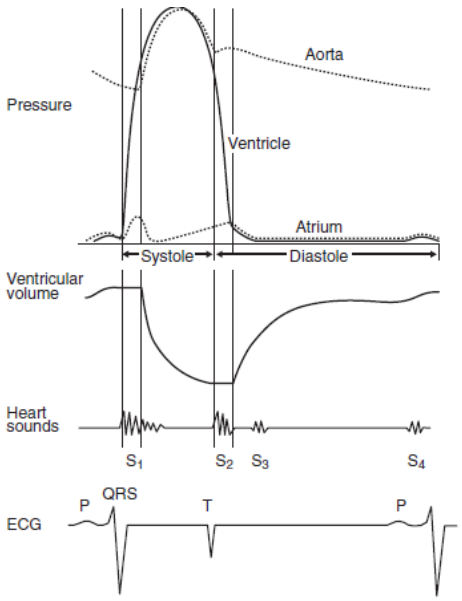
A murmur is a series of auditory vibrations occurring during a normally silent period of the cardiac cycle. The clinician should describe the timing, duration, quality or pitch, grade, point of maximal murmur intensity, and radiation of a murmur, as well as the effect of changing heart rate on the sounds (Bonagura & Reef, 2004; McGurrin, 2011; Blissitt, 2014).

One determines the timing relative to the heart sounds and categorizes murmurs as systolic, diastolic, or continuous. Skilled auscultators subdivide the timing of murmurs, because the timing and duration of the murmur often correlate with specific flow disturbances (Bonagura & Reef, 2004).

In general, the clinically significant murmurs are loud and long-lasting. However, the intensity of the murmur is related not only to the volume of regurgitant blood, but also to the driving pressure and the conformation of the horse. Hence grading of severity by auscultation alone is often not sufficient. Further classification of severity and determination of the exact diagnosis and prognosis require additional diagnostic tests (Buhl, 2015).

The most commonly detected murmurs associated with structural heart disease are those generated by TR, MR, aortic regurgitation, and VSD (Bonagura & Reef, 2004).

Fig 1 - Typical cardiac cycle diagram representing important electrical, mechanical and acoustical events occurring on the left side of the heart using a common time axis (Adapted from: Bright & Marr, 2010)



2.6 Electrophysiology and arrhythmogenesis

The normal electrical excitation, through the specialized conduction pathway that is part of the heart, is fundamental for the coordination of the myocardial contraction and relaxation. Many systemic homeostatic mechanisms have the capacity to alter heart rate in order to maintain an appropriate cardiac output, and may also affect the cardiac rhythm (van Loon & Patterson, 2010).

Recording the depolarization and repolarization of the excitable cells of the heart, is essential for understanding its electrophysiological properties. Even though the understanding of arrhythmogenesis is far from complete, the knowledge of the electrophysiology of cardiac cells is fundamental to an appreciation of the factors which lead to abnormal cardiac rhythm (van Loon & Patterson, 2010).

2.7 Recording electrical events in cells

The depolarization process can be detected at different levels by intracellular electrodes, intracardiac electrodes, and by electrodes placed on the body surface (van Loon & Patterson, 2010).

The surface electrocardiogram (ECG) records the potential difference between selected points on the body surface. It allows to detect changes in the electrical field around the heart during depolarization and repolarization (van Loon & Patterson, 2010). The physics of how the heart produces voltages that are detectable at the body surface is extremely complex. However, it is possible to develop an intuitive model adequate for clinical applications (Stephenson, 2013).

2.8 Cellular physiology

All myocytes possess the properties of excitability, refractoriness and conductivity. Like nervous tissue, individual cardiac cells exhibit the all-or-none phenomenon – that is once threshold is reached they are completely activated by an action potential. The cells can therefore be described as excitable. Once the action potential is initiated, cells cannot be depolarized again until they have returned to the resting potential following repolarization. This property of refractoriness ensures that all cardiac cells have a period after activation during which no level of further stimulus will cause an action potential. This prevents heart muscle from developing a tetanic spasm (van Loon & Patterson,

2010). Properties of automaticity, excitability, conductivity, and refractoriness are important in arrhythmia genesis and therapy (Miller et al., 1999).

Atrial and ventricular myocytes form two syncytia within which excitation passes from cell-to-cell through intercalated discs, conducting the stimulus for depolarization to their neighbours. Other tissues within the heart have specialized conductivity properties so that they conduct the impulse along a network either slowly (atrioventricular node) or rapidly (e.g. Purkinje fibres). While the atrial and ventricular myocytes have contractile function, the cells of the specialized conducting network have no contractile protein (Miller et al., 1999). Other cardiac tissues, including cells in the atria, mitral and tricuspid valves, distal atrioventricular (AV) node and AV junctional tissues, and the His-Purkinje system, are capable of automaticity. Normally, these latent pacemaker cells reach threshold later than do the SA node cells, and thus are discharged before they automatically depolarize. (Miller et al., 1999; van Loon & Patterson, 2010).

The electrophysiological features of myocytes result from specific properties of the cardiac cell membrane. Like all living cells, the inside of cardiac cells have a negative electrical charge compared to the outside, due to an accumulation of negatively charged ions. This voltage difference across the cell membrane is called the transmembrane potential, which is about −80 to −90 mV. All cells have a very high intracellular concentration of potassium and low levels of sodium and calcium, and for most cells this situation remains unaltered. However, excitable cells like cardiac cells have tiny pores or channels in the cell membrane. Upon appropriate stimulation, these channels open and close in a predefined way to allow specific ions to move across the cell membrane. This movement of ions results in changes in the transmembrane potential, from −90 mV to about +20 mV (depolarization), and finally back to −90 mV (repolarization) (van Loon & Patterson, 2010).

A graphical representation of these changes in transmembrane potential is known as the action potential (a cardiac action potential is created when the cell is depolarized to the threshold voltage for opening the voltage-gated Na+ channels). The currents, and the morphology of the action potential, vary in different tissues and determine the different properties of each specialized cell. Also, changes in extracellular ion concentrations, diseases and drugs may influence the action potential of the cells (van Loon & Patterson, 2010; Stephenson, 2013).

The action potential can be divided into five phases (0–4), but it is practical to consider the action potential in terms of three general phases: depolarization, repolarization and resting phase (van Loon & Patterson, 2010).

2.8.1 The cardiac electrical field

During the depolarization and repolarization processes, different currents are flowing across the cell membrane at various points, and a potential difference will be present between one part of the cell and another. When the current is flowing, an external electrical field is set up around the cell, which can be described as acting as a dipole (van Loon & Patterson, 2010).

However, when the cell is depolarized, or repolarized at a resting potential, no electrical field is formed around the cell because no current is flowing, despite the potential difference between the inside and outside of the cell. Each myocyte forms its own electrical field, but the electrical effects summate to produce an electrical field around the whole heart which (van Loon & Patterson, 2010), in simplified terms, can then be regarded as a single dipole, which is a pair of electrical charges (a positive charge and a negative charge) separated by a distance (van Loon & Patterson, 2010; Stephenson, 2013).

2.8.2 Depolarization

The Phase 0 represents the depolarization process, and onsets once a cell has reached a certain potential (the threshold potential), spontaneously in the case of pacemaker cells or as a result of depolarization of adjacent cells in the case of conduction pathway and myocardial cells. The upstroke of the cardiac action potential in atrial and ventricular muscle and His-Purkinje fibres is the result of a sudden increase in membrane conductance to Na+, resulting in rapid movement of extracellular-to-intracellular sodium ions through fast sodium channels (voltage-gated Na^+ channels). The rate at which the depolarization occurs (slope of phase 0) is a determinant of the conduction velocity for the propagated action potential (Miller et al., 1999; van Loon & Patterson, 2010; Stephenson, 2013).

In the conducting pacemaker tissues of the sinoatrial (SA) and AV nodes, the resting potential of the cell membrane is less negative (around –60 mV) than in non-pacemaker cells. This results in a decreased rate of phase 0 depolarization and relatively slow

conduction in pacemaker tissues. In these cells, the contribution of the fast inward current usually carried by sodium is small, and the relatively slow depolarization process is largely due to movement of calcium ions (van Loon & Patterson, 2010; Stephenson, 2013). As a result, these tissues are relatively sensitive to changes in calcium concentration (van Loon & Patterson, 2010).

2.8.3 Repolarization

Once a cell is depolarized, it cannot be depolarized again until the cell has first recovered, by restoring the initial ion gradients and thus by regaining its polarized state. This recovery process is called the repolarization process and corresponds to phases 1–3 of the action potential (van Loon & Patterson, 2010).

Because during these phases the cell cannot be excited again, this period is called the refractory period and corresponds to the width of the action potential. Consequently, cardiac myocytes do not undergo contraction (i.e. tonic contraction) (van Loon & Patterson, 2010). The repolarization phase starts with the early rapid repolarization phase (phase 1) which shows as a relatively small but sharp drop in potential towards 0 mV, partly owing to inactivation of sodium current or activation of an outward potassium current (van Loon & Patterson, 2010; Stephenson, 2013).

This phase is immediately followed by the plateau phase (phase 2) which may last several hundred of milliseconds, about 200 msec. During this period, membrane conductance to all ions falls to rather low values, with a complex interaction of ion movements involving sodium, potassium, magnesium and chloride, and an inward L-type calcium current (slow Ca^{2+} channels). These channels, especially the latter, interrupt the repolarization process and prolong the action potential (van Loon & Patterson, 2010; Stephenson, 2013).

Therefore, the cardiac muscle cells become partially relaxed before the earliest possible subsequent contraction can begin. This means, that each cardiac action potential produces a contraction that is distinctly separated from the preceding contraction. Because of its long refractory period, cardiac muscle cannot sustain a continuous contraction. Therefore, the heart has a guaranteed period of relaxation (and refilling) between heartbeats (Stephenson, 2013). As such, the action potential duration, and therefore the refractory period, is predominantly determined by the balance between the inward and outward currents during the plateau phase, which have a very important role in the generation of some arrhythmias (van Loon & Patterson, 2010).

After the plateau phase, the final rapid repolarization (phase 3) takes place due to a series of potassium currents. In order to maintain the concentration gradients, sodium is pumped out of the cell in exchange for potassium, resulting in a return to its stable, negative resting potential (phase 4) (van Loon & Patterson, 2010; Stephenson, 2013).

During this final recovery process, the cardiac myocyte gradually regains excitability. This means that the cell is not excitable during phase 1, phase 2 and the beginning of phase 3, regardless of the magnitude of the stimulating impulse (van Loon & Patterson, 2010). This period is called the absolute refractory period (ARP). As the cell repolarizes, it becomes excitable. However, there is a period of time during which the cell can only be excited by a large current (the amplitude of such an action potential is lower than normal because only a fraction of the Na+ channels have returned to the resting state and are available for activation). This period is known as the relatively refractory period (RRP) (van Loon & Patterson, 2010; Gilmour, 2015).

2.8.4 Resting phase or diastolic depolarization

Normally, membrane potential of atrial and ventricular muscle cells remains steady at around -90 mV (-80 mV, according to Stephenson (2013)) throughout diastole (phase 4). Although, in certain specialized conducting cells, or due to leakage of ions across the cell membrane, the resting membrane potential does not remain constant in diastole but gradually depolarizes. This spontaneous depolarization is called a pacemaker potential, and may reach threshold potential (around -60 mV) by itself and produce an action potential (automaticity) (van Loon & Patterson, 2010; Stephenson, 2013).

The rate of this change in potential is mainly determined by a time-related change in membrane potassium or sodium permeability. It is influenced by autonomic tone, electrolytes, drugs and diseases. The steeper the slope of phase 4, the faster the rate of automaticity. Phase 4 is more abrupt in SA nodal cells. However, the AV node and the junctional tissue also have automaticity, as mentioned before, and will take over as pacemaker if the SA node fails to depolarize. In some disease states, Purkinje tissue may also act as a pacemaker, and abnormal automaticity may occur in other cells (Miller et al., 1999; van Loon & Patterson, 2010).

As mentioned before, compared to the action potential of a ventricular or Purkinje fibre cells, the sinoatrial and atrioventricular nodal cells have a slow depolarization phase (phase 0). This slower depolarization phase occurs because of a lack of rapid sodium

channels responsible for the rapid depolarization phase. The sinoatrial and atrioventricular nodes are mainly dependent on the slow calcium channel for depolarization. Because of the slower rate of depolarization, the sinoatrial and atrioventricular nodes conduct electrical pulses slowly. For the atrioventricular node this slow conduction is reflected on the surface ECG as the PR interval (van Loon & Patterson, 2010; Stephenson, 2013).

2.9 Innervation of the heart

The cardiovascular system is under the control of both neuronal and humoral components of the autonomic nervous system, acting both on the heart and on the peripheral vasculature. Cardiovascular physiologic responses to pharmacologic and physiologic disturbs are related to selective distribution of autonomic fibres. These actions are associated with parasympathetic and sympathetic nerves (Miller et al., 1999; van Loon & Patterson, 2010).

Acetylcholine activates *muscarinic cholinergic receptors* on the cell membranes of pacemaker cells, which slows the ion channel changes that are responsible for the pacemaker cell's spontaneous depolarization. Because the pacemaker cells take longer to reach threshold in the presence of acetylcholine, there is a longer interval between heartbeats. Therefore, heart rate is decreased below its spontaneous level. Therefore, parasympathetic neurons release acetylcholine at the SA node cells, and thus parasympathetic activity decreases the heart rate (Stephenson, 2013).

Sympathetic neurons release norepinephrine at the SA node cells, and thus sympathetic nerve activity increases the heart rate. Epinephrine (or norepinephrine), which is released from the adrenal glands and circulates in the bloodstream, has the same effect. This results in an increased automaticity, an increased conduction velocity, and a shortened refractory period. Therefore, cells recover quicker, allowing a higher rate of stimulation, and resulting in increased myocardial contractility (van Loon & Patterson, 2010; Stephenson, 2013).

The subcellular effect of these hormones is largely due to effects on contractile proteins; however, they also affect transmembrane potentials, and alter cardiac rhythm in some circumstances (van Loon & Patterson, 2010).

2.10 The conduction process

The conduction process follows a pathway in the normal heart, leading to a coordinated contraction of atrial and then ventricular muscle. An impulse spreads from the SA node, across the atria, to the AV node. The electrical activity associated with depolarization of this muscle mass results in a sufficiently large electrical field for it to be detected on a body surface ECG as a P wave (van Loon & Patterson, 2010; Stephenson, 2013; Gilmour, 2015).

The precise location of impulse formation within the SA node and the pattern of depolarization across the atria, can be influenced by heart rate and autonomic tone, which can result in a different configuration of P waves (wandering pacemaker, normal finding in horses [McGurrin, 2011]) even though the SA node remains the source of the impulse (van Loon & Patterson, 2010).

When the impulse reaches the AV junction it finds a barrier to further spread. The specialized cells of the AV node conduct the impulse slowly. Because only a small number of cells are depolarized, no deflection is seen on the surface ECG. This period is represented by the P–R interval (van Loon & Patterson, 2010). Conduction through the AV node is profoundly affected by vagal tone in the horse (Bright & Marr, 2010; van Loon & Patterson, 2010). Even in normal animals, conduction is often sufficiently slowed or reduced in amplitude to result in a marked reduction in the normal rate of conduction (first degree AV block), or complete abolition of further spread of the impulse (second degree AV block) (van Loon & Patterson, 2010).

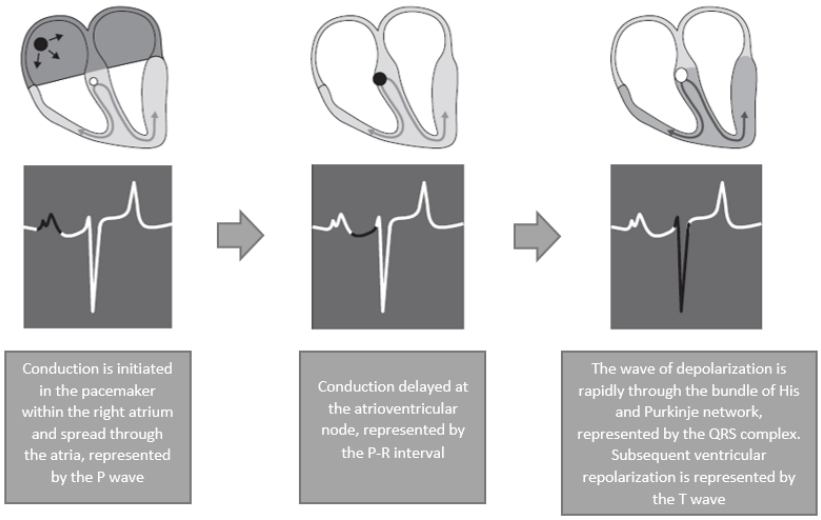
An important feature of the AV node is its long refractory period, which helps protect the ventricles from being stimulated to contract at rates that are too rapid for efficient pumping. This protective function of the AV node is critical to an animal's survival when atrial action potentials are extremely frequent (atrial flutter/ fibrillation) (Stephenson, 2013).

When the impulse passes through the AV node it is rapidly conducted through the bundle of His and the Purkinje network to the ventricular myocardium. Depolarization of the ventricles is rapid and results in a coordinated contraction. Depolarization of the Purkinje network is not detected on the body surface ECG; however, depolarization of the myocardium results in substantial electrical forces, the net result of which produces the QRS complex on the surface ECG (van Loon & Patterson, 2010).

Each cell within the heart repolarizes after depolarization. The sum of the repolarization processes within the heart can be detected at the body surface in the same way as the depolarization (van Loon & Patterson, 2010). Ventricular repolarization is seen as the T wave (van Loon & Patterson, 2010; Stephenson, 2013; Gilmour, 2015). The change in electrical field caused by atrial repolarization may or may not be seen (atrial T wave or Ta wave) (van Loon & Patterson, 2010).

Identification of the characteristic waveforms allows a clinician to detect when depolarization and repolarization of the atria and ventricles has occurred. The timing of the waves, the relation between the different waves, and the morphology and duration of the complexes and intervals allows for the deduction of the origin and of the conduction pathway of the impulse (van Loon & Patterson, 2010; Stephenson, 2013).

Fig 2 - Diagram representation of the cardiac conduction system and the relationship between the spread of conduction and the surface ECG (Adapted from: van Loon & Patterson, 2010)



2.11 The surface ECG

The changes in the electrical field around the heart can be detected by a galvanometer attached to the body surface, which records the potential difference between two electrodes. The link between a positive and negative electrode is called a bipolar lead. An ECG records the potential difference between electrodes placed at various points on the body surface, which reflects the sum of all the electrical fields which are present at any one time (van Loon & Patterson, 2010).

The ECG is a moving record of the deflections generated by the electrocardiograph stylus calibrated in voltage (vertical axis) and time (horizontal axis). Electrocardiographic electrodes (leads) sample cardiac potentials at the body surface. These are measured by the electrocardiograph (galvanometer) and recorded (Miller et al., 1999).

The points at which the ECG electrodes are placed are chosen to represent electrical changes in the heart; however, a number of other factors also affect the potential difference between different areas of the body. The position of the heart within the body, the course of the spread of activation within the heart, the shape of the thorax, the conductivity of tissues between the heart and the electrodes, and the exact location of the body surface electrodes all affect the body surface ECG (van Loon & Patterson, 2010).

2.12 The concept of cardiac vector

The surface ECG reflects the combined effects of all the electrical activity of the heart. The sum of the electromotive forces has a direction and magnitude, which is termed the cardiac vector (van Loon & Patterson, 2010; Gilmour, 2015).

The ECG samples these vectors as they project onto a two-dimensional surface, represented in the frontal plane by Einthoven's triangle. Any given ECG lead, by recording the difference in potential between two sites on the torso, captures the magnitude of a given vector, but not its direction. Consequently, the measurements provided by ECG leads are scalar quantities, rather than vector. However, the cardiac vector, represented by the mean electrical axis, can be reconstructed using recordings from at least three ECG leads (Gilmour, 2015).

The ECG voltmeter will have a positive deflection if the net direction of overall activity (vector) if it points towards the positive electrode of a bipolar lead, and a negative potential if it is away from it. The voltage recorded will be largest when the vector is directly towards the positive electrode. If the direction of the maximum potential difference is at an angle to the lead axis, the deflection will be smaller. If the electrodes are positioned perpendicular to the vector of electromotive force, no potential difference will be detected. The amplitude of the deflection indicates the magnitude of the vector and is proportional to the mass of myocardial tissue which is depolarized (van Loon & Patterson, 2010).

2.13 ECG lead systems

The aim of the lead systems is to clearly record each of the waveforms and complexes so that the conduction process can be evaluated, and also to gain some information about the direction and magnitude of the cardiac vector (van Loon & Patterson, 2010).

Einthoven's triangle is a lead system that looks at the combined electrical activity which reaches the body surface in the frontal plane, in which the heart is assumed to sit in the centre of a triangle formed by the two forelimbs and the left hindlimb (van Loon & Patterson, 2010; Stephenson, 2013). This system, which is commonly used in small animals and humans, can also be used in horses, and provides useful information about cardiac rhythm and conduction (van Loon & Patterson, 2010).

Other systems have also been designed to accommodate the fact that, in horses, the heart does not sit in the centre of a triangle formed by the limbs. These systems assess the cardiac vector in three dimensions, by measuring the electrical field in three semi-orthogonal planes (van Loon & Patterson, 2010).

Standard bipolar leads are recorded this way: lead I is between the left arm electrode (–) and the right arm electrode (+); lead II is between the right arm electrode (–) and the left foot electrode (+) and lead III is between the left arm electrode (–) and the left foot electrode (+)van Loon & Patterson, 2010). For the augmented unipolar leads, the positive exploring electrode (right arm for aVR; left arm for aVL and left leg for aVF) is compared with the remaining two electrodes (–) (van Loon & Patterson, 2010; Stephenson, 2013).

The base-apex lead is most frequently used for recording rhythm strips. To record a base-apex lead the left arm electrode (+) is positioned at the cardiac apex, and the right arm electrode (-) is placed two thirds of the way down the right jugular groove or at the top of the right scapular spine. The third electrode is placed at any site remote from the heart (Durando, 2003; van Loon & Patterson, 2010; McGurrin, 2011). Lead 1 is selected to record the ECG. For the Y lead the right arm electrode (–) is attached over the manubrium sterni and the left arm electrode (+) over the xiphoid process of the sternum. The third electrode is placed at any site remote from the heart (van Loon & Patterson, 2010; McGurrin, 2011). Alternatively, the positive electrode can be positioned at the right side of the withers, and the negative electrode at the ventral middle (McGurrin, 2011). Lead I is selected to record the ECG. Consistency in lead placement facilitates interpretation

(McGurrin, 2015). Durations of the ECG components in normal horses can then be consulted.

The ventricular depolarization process is different in horses compared with human beings and small animals. In human beings and small animals, the Purkinje network carries the impulse to the subendocardial myocardium, and depolarization then spreads out from the ends of the fibres, through the myocardium, to the subepicardial layers in a series of wavefronts (van Loon & Patterson, 2010). In human beings and small animals, the duration of the QRS complex may be prolonged when the left ventricle is enlarged, because the wavefront takes longer to spread throughout the myocardium. The amplitude of the R wave in lead II may also be increased as a result of the increased muscle mass (van Loon & Patterson, 2010, McGurrin, 2011, McGurrin, 2015).

In the horse, the depolarization process differs from that described above because of the very widespread distribution of the Purkinje network (Bright & Marr, 2010; van Loon & Patterson, 2010; Gilmour & Moïse, 2015). The fibres extend throughout the myocardium, and ventricular activation takes place from multiple sites. The electromotive forces therefore tend to cancel each other out and, consequently, no wavefronts are formed (van Loon & Patterson, 2010).

Because the surface ECG represents the sum of the electromotive forces within the heart, the overall effect of the depolarization of most of the left and right ventricles on the ECG is minimal. Most electrical activity seen at the body surface results from depolarization of the basal interventricular septum and part of the left ventricular free-wall. A wavefront spreading towards the heart base is responsible for this last part of ventricular activation, so the cardiac vector is directed dorsally and cranially with respect to the body surface (van Loon & Patterson, 2010).

Frontal plane MEA, or the cardiac vector in the orthogonal systems are therefore of very limited value in horses. In addition, the duration of the QRS complex does not depend on the spread of a wavefront across the ventricles, and is therefore not necessarily related to their size (van Loon & Patterson, 2010). Equine ECGs still give useful information about heart rate and rhythm, but provide very little or no information about the relative or absolute sizes of the ventricles (McGurrin, 2011).

3. Ambulatory and exercise ECG

As mentioned before, some arrhythmias are not present at the time of electrocardiography, despite being obvious during physical examination, or may be suggested by a clinical history of intermittent reduction in cardiac output and not identified clinically. There are several reasons why the arrhythmia may not be detected at the time of recording a patient-side ECG, and may be related to changes in autonomic tone such that they only occur during exercise or during rest. In these situations 24-hour ambulatory ECG monitoring and telemetry can be very useful in order to document cardiac rate and rhythm at the times when clinical signs have been reported, such that a dysrhythmia may be reproduced (Durando, 2010; Bowen, 2014).

Therefore, an ambulatory ECG can be recorded for a brief period, or for a longer period while monitoring for less frequent dysrhythmias, and an exercise ECG can be recorded to assess the importance of certain dysrhythmias found at rest or exercise-induced, especially in horses with poor performance (Durando, 2010; Verheyen et al., 2010).

3.1 Equipment

The basic equipment consists of electrodes, a recording device and a way to display the trace. Self-adhesive electrodes are well tolerated by the horses, and significantly improve recording quality. Specific equine self-adhesive electrodes should be used as they contain more gel to improve skin contact and stronger glue to remain in place, even during exercise. Clipping of the hair coat is generally not necessary and even undesirable since it causes the electrodes to fall off more easily, especially with sweating. Extra gel can be used when the hair coat is very long, or extra glue in case of excessive sweating (Verheyen et al., 2010).

There is no universally accepted lead system for the use in large animals. Usually, a single-lead recording is sufficient (Verheyen et al., 2010; McGurrin, 2011; McGurrin, 2015). However, the advantage of a multiple lead system is that each lead detects the potential difference between its 2 electrodes from a unique angle, which might help to differentiate between a normal or abnormal complex. In addition, when one electrode falls off in a multiple-lead system, the recording can still continue from the remaining

electrodes. Whichever method is used, the procedure should be standardized so that ECGs can be compared (Verheyen et al., 2010).

Systems with 4 electrodes are most commonly used. In such a system, the black electrode serves as a reference electrode for the electrocardiogram, and can be positioned anywhere on the body surface of the horse. The remaining 3 electrodes are used to construct 3 leads: lead I between the red (right arm, -) and the yellow (left arm, +) electrode, lead II between the red (-) and the green (left foot, +) electrode, and lead III between the yellow (-) and the green (+) electrode. Although, these color conventions can vary depending on the country of origin. Modern devices will automatically record from all 3 leads at the same time, offering the advantages of a multiple-lead recording. Older devices might require a manual switch between each lead (Verheyen et al., 2010, Young & van Loon, 2014; McGurrin, 2015).

Any ECG device can be used for ambulatory recording, but a small battery-powered device fixed to the horse's back allows to make recordings during exercise. The signal can then be digitally stored or wireless transmitted (telemetry) through radio-frequency or Bluetooth. Telemetry allows for beat-to-beat real-time monitoring and thus represents an advantage above other systems, allowing to assess the quality of the recording (while Holter devices cannot do this). When a device has sufficient storage capacity, long-term (24-hour ambulatory ECG monitoring, usually with Holter monitor) monitoring becomes possible (Verheyen et al., 2010; Durando, 2010; McGurrin, 2011; McGurrin, 2015).

The recorded signals can be imported into computer software for the automatic analysis of normal and abnormal rhythms. The software detects R waves and screens for sudden irregularities in the R-R interval. Complex algorithms for the analysis of the QRS morphology exist in more advanced software packages designed for human or small animal cardiology. Although, these algorithms usually fail to interpret the horse's ECG correctly, partly because of the large P and T wave on the equine ECG. Many systems indicate 'bradycardia' at the heart rates higher than the normal heart rate of a horse. Therefore, the visual screening of the horse's ECG remains necessary (Verheyen et al., 2010; McGurrin, 2015).

Exercise or stress can cause changes in the P and T waves with no clinical meaning. With a systematic approach while evaluation the ECG recordings, the artefacts can easily be interpreted as so (Verheyen et al., 2010).

In a protocol used in a study by Verheyen et al. (2013), the recording started as soon as the monitoring system was fitted, including a 15 min recording at rest. In this protocol the horses walked for 7 minutes, trotted for 10 minutes, cantered for 4 minutes, and galloped for 1 minute. The recovery period was of 7 minute.

This study focuses on evaluating the relevance of the use of standardized lungeing exercise protocols in the evaluation the cardiac performance of apparently clinically healthy horses, and horses with cardiac disease.

3.2 Exercise ECG recording

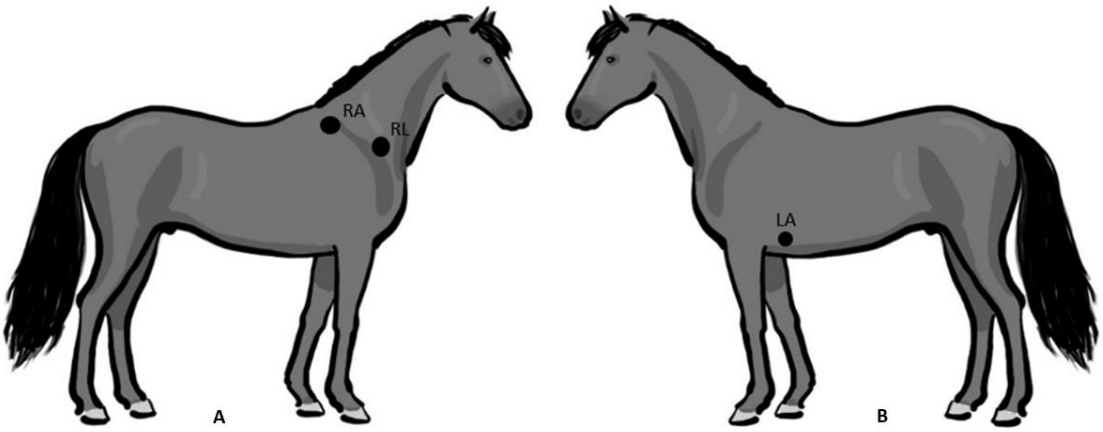
The base-apex system is unsuited for recordings during exercise, since electrodes are then more prone to creating movement artefacts and falling off, and can interfere with the freedom of movement of horse and rider (Verheyen et al., 2010). The negative (red) electrode is placed on the left shoulder blade, near the withers. When saddled, this position is just in front of the left saddle flap. The positive (green) electrode is placed just behind the saddle girth on the left, on a position where the leg of the rider doesn't interfere with it. The remaining yellow electrode can be placed just above or underneath the green one, creating an extra lead. A good position for the reference (black) electrode is just underneath the red one. This way, the rider can easily reattach any electrode, and the electrodes are unlikely to be affected by the saddle or girth slipping backwards during fast exercise (Verheyen et al., 2010; McGurrin, 2015).

The left-to-right component of the MEA is missing, but the deflections on the ECG are still clearly visible, although the atrial deflection (P wave) will be slightly lower in amplitude. The negative (red) and reference (black) electrodes can also be placed underneath the left saddle flap, which offers extra protection against dislodging. To prevent electrodes from dislodging, e.g. during intensive exercise or during lungeing exercise, one can use an elastic girth around the horse's thorax and place the electrodes underneath the girth (Verheyen et al., 2010).

In this vertical modification of the base-apex system, the cranio-caudal orientation of the MEA is lost. Therefore, the P wave will be lower in amplitude than the one of a true base-apex configuration, but large QRS deflections will still be present. The negative (red) electrode is positioned on the right side of the withers, and the positive (green) electrode behind the left elbow joint, on the apex beat area. The remaining (yellow) electrode is placed about 10 cm above the green one. The reference electrode can be positioned

anywhere under the girth (Verheyen et al., 2010; McGurrin, 2015). The girth can be used during lunging exercise but also during ridden exercise or in trotters, where it is placed just cranial and partially underneath the saddle or harness (Verheyen et al., 2010).

Fig 3 - Sites for lead placement for obtaining a base-apex electrocardiogram in the horse. The black circles represent the sites of attachment for the electrodes. (A) Position of the electrodes on the right side of the horse for obtaining a base-apex ECG using the electrodes from lead I. RA: right arm; RL: right leg. (B) Position of the electrode placement on the left side of the horse for obtaining a base-apex ECG using the electrodes from lead I. LA: left arm. (Adapted from: van Loon & Patterson, 2010)



4. Identification and assessment of dysrhythmias

The horse's heart rate should be obtained (normal, slow or fast) and the rhythm characterized (regular, regularly irregular or irregularly irregular) in order to determine if a cardiac dysrhythmia is present. The normal heart rate of an adult horse is of 28–44 bpm at rest with a regular (sinus) rhythm, and in foals is 80 bpm (average in the neonate is 70 bpm). The heart sounds should be identified and their timing and intensity described. It is particularly pertinent to attempt to distinguish all four heart sounds in horses with dysrhythmias, as their presence or absence may alert the clinician to the specific dysrhythmias (Reef & Marr, 2010).

The arterial pulses should be palpated simultaneously with auscultation of the heart, to determine if the arterial pulses are synchronous with every heartbeat. The jugular vein, saphenous vein, and other peripheral veins should be evaluated for distention and

pulsation. Auscultation of both lung fields should be performed at rest and, if possible, with the horse breathing into a rebreathing bag (Reef & Marr, 2010).

The normal components of the surface ECG are:

- P wave: generated by atrial depolarization (≤0.16)
- PR segment: representing the duration of atrioventricular (AV) conduction (≤0.5; pony: ≤0.24; foal: 0.11-0.18)
- QRS complex: produced by ventricular depolarization (≤0.14; foal: 0.05-0.08)
- ST segment: representing the duration of the ventricular refractory period (≤0.58; foal: 0.19-0.36)

The surface ECG provides a "road map" of electrical events within the heart and allows the origin of any abnormalities to be identified (Reef & Marr, 2010). Diagnosis of arrhythmias has been greatly enhanced by improvements in technology, which allow ECG recordings to be taken readily in resting and exercising horses (Reef & Marr, 2010; McGurrin, 2011).

A variety of options for lead placement are available. However, a base-apex lead is often the only lead needed (with some variation in the exact electrode positioning) to accurately diagnose the rhythm disturbance present, because this lead produces large, easy to read complexes and is usually well tolerated by the horse. It is conventional to display the base-apex lead with negative QRS complexes; however, some clinicians, prefer to invert the leads to produce positive QRS complexes (Reef & Marr, 2010; McGurrin, 2011, Young & van Loon, 2014).

4.1 Classification of dysrhythmias

It is useful to categorize cardiac dysrhythmias by their site of origin (supraventricular or ventricular) and by their rate (bradydysrhythmias or tachydysrhythmias) as these factors determine their clinical significance and most appropriate management. In horses, most bradydysrhythmias are physiological and associated with high vagal (parasympathetic) tone, while most tachydysrhythmias are abnormal (Reef & Marr, 2010).

Profound bradydysrhythmias and rapid tachydysrhythmias, particularly those of ventricular origin, are the rhythm disturbances most likely to need immediate treatment to control the ventricular rate and relieve the clinical signs of cardiovascular collapse (Reef & Marr, 2010). Syncope is particularly important, as opposed to other species, since

it has the potencial do harm the riders and the people handling the affected horses (Reef & Marr, 2010, McGurrin, 2011).

4.2 Bradydysrhythmias

Bradydysrhythmias are usually detected in healthy horses and are associated with high parasympathetic tone. They can be described as delays in atrioventricular conduction and are the most common conduction disorders (Young & van Loon, 2014).

Second degree atrioventricular (AV) block is the most predominant bradydysrhythmia detected in resting horses. Sinus arrhythmia, sinus bradycardia, sinoatrial (SA) block and SA arrest also occur in normal horses with high vagal tone. These normal dysrhythmias are present at rest and should disappear with a decrease in parasympathetic tone and/or an increase in sympathetic tone such as occurs with excitement or exercise (Reef & Marr, 2010). Despite this, on rare occasions, all of these normal rhythms can also result from cardiac disease, when the dysrhythmia causes serious decrease of to performance and presents important risks to the rider and horse (Bonagura & Reef, 2004; Reef & Marr, 2010; Young & van Loon, 2014).

Second degree AV block

Second degree AV block is the most common dysrhythmia detected in normal horses. Second degree AV block is detected in over 40% of healthy horses during 24-hour continuous electrocardiographic monitoring (Reef & Marr, 2010). The condition is associated with high vagal tone. This results in decreased conduction at the level of the AV node. Whereas first degree AV block is defined as delayed conduction at the AV node that is not blocked (Reef & Marr, 2010, McGurrin, 2011).

These horses have a slow to normal heart rate (usually 20– 40 bpm). The first (S1) and second (S2) heart sounds are regularly spaced. During severe second degree AV block, one or more isolated fourth (atrial) heart sounds, S4, will be audible during the long diastolic pauses. In most normal horses only one period of second degree AV block occurs before the next conducted impulse, but occasionally two blocks occur (double) in sequence which should still be regarded as a normal physiological variant, providing that the dysrhythmia disappears with exercise, excitement, or the administration of a vagolytic drug such as atropine or glycopyrrolate (Bonagura & Reef, 2004, Reef & Marr, 2010; McGurrin, 2011; Young & van Loon, 2014).

The ECG reveals a slow to normal heart rate with a regular R–R interval and a normal QRS complex. Each QRS complex is preceded by a P wave with a normal to near normal PR interval but there are occasional P waves not followed by a QRS complex. The P–P interval is regular or may vary slightly (Reef & Marr, 2010; McGurrin, 2011).

Advanced Second degree AV block

Advanced Second degree AV block (multiple cycles at a time) is rare in horses, and is a pathological form of conduction block at the AV node that can be caused by electrolyte imbalances, digitalis toxicity and AV nodal disease, which can be inflammatory or degenerative (Reef & Marr, 2010, McGurrin, 2011). Horses with advanced second degree AV block usually have severe exercise intolerance and may collapse. A complete cardiovascular examination, biochemistry screen and complete blood count should be performed on all horses presenting with advanced second degree AV block to attempt to determine the underlying cause of the dysrhythmia (Reef & Marr, 2010).

Affected horses have a slow heart rate (usually 8–24 bpm). On auscultation S1 and S2 is regularly spaced with an audible S4 preceding each S1. S4 is heard in the diastolic pauses with one, or more, S4 for each period of second degree AV block (Reef & Marr, 2010).

The ECG reveals a slow heart rate with a regular R–R interval between episodes of AV block and normally configured QRS complexes. The QRS complexes are each preceded by a P wave at a normal to near normal P–R interval, which is the evidence of AV conduction. The P–R interval may be slightly prolonged as a first degree AV block may also be present (Mobitz type I). The P–P interval is regular and the atrial rate is rapid with numerous (two or more) P waves not followed by QRS complexes (Mobitz type II) (Reef & Marr, 2010; McGurrin, 2011).

Appropriate treatment should be instituted as soon as possible, based upon the probable aetiology of the dysrhythmia to hopefully prevent the progression of the conduction block to Complete (third degree) AV block, if this is considered to be a possibility (Reef & Marr, 2010).

Complete (third degree) AV block

Complete (third degree) AV block is rare in athletic horses, but when present it always affects performance and carries a guarded prognosis, since no atrial action potential is conducted to the ventricles (Young & van Loon, 2014; Stephenson, 2013).

Usually this is associated with inflammatory or degenerative changes in the AV node, but it may occur with electrolyte imbalances or other metabolic abnormalities such as is seen with foals with uroperitoneum, particularly when anaesthetized (Reef & Marr, 2010; Young & van Loon, 2014).

Complete heart block has also been observed as a congenital defect and associated with mediastinal lymphoma and rattlesnake poisoning. Horses with third degree AV block will typically have severe exercise intolerance and frequent syncope. The resting heart rate (ventricular rate) is very slow but regular with a more rapid, independent atrial rate (Reef & Marr, 2010).

The heart rate does not increase appropriately with a decrease in vagal tone or an increase in sympathetic tone. The S1 and S2 are usually loud and regularly spaced with more rapid independent S4 (usually ≤60/minute), which are also regularly spaced. Occasional "bruit de cannon" sounds, caused by the summation of S4 with another heart sound are detected. An irregular rhythm may be detected in some horses with concurrent paroxysms of ventricular tachycardia (Reef & Marr, 2010).

The ECG usually reveals regular P waves that are not followed by QRS complexes (i.e. there is no evidence of AV conduction), and QRS complexes that are widened and bizarre in their appearance occur (Reef & Marr, 2010, McGurrin, 2011), because they are originating from an idionodal or idioventricular pacemaker. These are known as escape complexes because they represent the ventricles attempt to escape in the absence of AV conduction. If there is other ventricular ectopy present, there will be more than one QRS configuration, and the R–R interval may vary (Reef & Marr, 2010).

The P–R intervals will be of varying lengths with no consistent relationship between the P waves and the QRS complexes. The atrial rate is usually very rapid with a regular P–P interval and there are many more P waves than QRS complexes (Reef & Marr, 2010, McGurrin, 2011).

Treatment of complete heart block in horses should be initiated as soon as the diagnosis is made, but is not usually attempted. Pharmacological treatment is of limited value. The use of sympathomimetics has been reported, however caution should be taken due to risk of ventricular tachyarrhythmias. Corticoids may be useful to treat inflammation, but caution is indicated if active viral infection is suspected. If the underlying cause of the complete heart block cannot be corrected or removed, the definitive treatment for third degree AV block is a pacemaker (Reef & Marr, 2010; McGurrin, 2011, Jesty, 2014).

Sinus bradycardia, sinus arrhythmia, SA block and SA arrest

Sinus bradycardia, sinus arrhythmia, SA block and SA arrest occur in normal fit horses and are associated with high vagal tone, but are less common than second degree AV block. These dysrhythmias can occur in combinations: sinus arrhythmia is usually also present in horses with sinus bradycardia, and SA block can occur in conjunction with second degree AV block (Reef & Marr, 2010; McGurrin, 2011). On resting ambulatory ECG, many normal horses will display a variety of physiological bradydysrhythmias throughout a 24-hour period (Reef & Marr, 2010).

Auscultation reveals regular S1 and S2 with a pause in the rhythm (SA block or arrest), or rhythmic variation of diastolic intervals (sinus bradycardia and sinus arrhythmia) with heart rates of 20–30 bpm. An S4 precedes each S1 and there are no isolated S4 in the diastolic pauses representing the period of SA block. The atrial and ventricular rates are slow or low normal, and normal QRS complexes are detected associated with the preceeding P waves, evidence of AV conduction. The P–P and R–R intervals are regularly irregular with sinus arrhythmia (Reef & Marr, 2010; Jesty 2014).

SA blocks are characterized by pauses of less than, or equal, to two P–P intervals, whereas sinus arrest is present if SA activity ceases for longer than two P–P intervals. These rhythms are normal manifestations of high vagal tone and disappear with exercise or the administration of a vagolytic drug or sympathomimetic drugs, for example, atropine or glycopyrrolate. No treatment is required for the benign form, and for the advanced block, pacemaker implantation is the only option (Reef & Marr, 2010; McGurrin, 2011, Jesty 2014).

Sick sinus syndrome

Prolonged periods of SA arrest, profound sinus bradycardia or high-grade SA block may be indicative of sinus node disease, denominated sick sinus syndrome. Ventricular escape rhythms may occur during prolonged pauses (Reef & Marr, 2010, Jensen et al., 2014). In humans, sick sinus syndrome is described as a cardiac conduction disorder characterized by symptomatic dysfunction of the sinoatrial node. On the ECG, it usually shows as sinus bradycardia, sinus arrest, or sinoatrial block, and is sometimes accompanied by supraventricular tachyarrhythmias (‘*tachy-brady’ syndrome*). Typical symptoms, include

syncope, dizziness, palpitations, exertional dyspnoea, easy fatigability from chronotropic incompetence, heart failure, and angina (Jensen et al., 2014).

Sinus node disease is rare in horses, periods of profound sinus bradycardia and tachycardia have not been reported in horses. However, inflammatory and degenerative changes must be considered possible aetiologies. Affected horses may have a history of collapse or weakness. These horses should be carefully evaluated with exercise electrocardiography, and the response of the horse to vagolytic and sympathomimetic drugs determined (Reef & Marr, 2010; Jesty, 2014).

It may be possible to increase the heart rate and abolish the dysrhythmia during exercise tests, although the maximal heart rate may be reduced and the dysrhythmia may recur shortly after cessation of exertion. Corticosteroids should be initiated for horses with life-threatening abnormalities of sinus rhythm, in the hope that pacemaker implantation will not be necessary. Definitive treatment of sick sinus syndrome is pacemaker implantation (Reef & Marr, 2010; Jesty 2014).

4.3 Tachydysrhythmias

Tachydysrhythmias result from abnormal pacemaker activity (Stephenson, 2013), and can be defined as either supraventricular or ventricular. Various forms exist including premature depolarizations, tachycardia, fibrillation and pre-excitations syndromes (Reef & Marr, 2010).

Isolated supraventricular (SVPD) and ventricular (VPD) tachydysrhythmias are found in low numbers in horses without heart disease, particularly in prolonged resting ECG recordings, but these "normal" dysrhythmias are less common than second degree AV block and other bradydysrhythmias (Reef & Marr, 2010; McGurrin, 2011).

Persistent and frequent tachydysrhythmias are more commonly associated with cardiac and non-cardiac pathology (Reef & Marr, 2010).

Supraventricular premature depolarizations and tachycardia

Supraventricular premature depolarizations (SVPD) or atrial premature complexes (APD) are usually a single event (McGurrin, 2011). This tachycardia originates in the atria before SA nodal discharge. There is often an underlying regular rhythm and the SVPD (or APD) may or may not be conducted to the ventricles. On auscultation, beats occurring earlier than normal are detected (Reef & Marr, 2010).

Electrocardiography reveals a normally configured QRS–T complex, occurring prematurely. A bizarre P wave may be visible or may be hidden in the preceding T wave. Supraventricular or atrial tachycardia is defined as more than four SVPD occurring in sequence. Horses with frequent SVPD or supraventricular tachycardia are often able to maintain a normal ventricular response rate as some of the SVPD are blocked at the level of the AV node (Reef & Marr, 2010; McGurrin, 2011).

According to Bonagura and Reef (2004), atrial premature complexes are more likely to be clinically significant in the following circumstances: if they are frequent at rest; are associated with nonsustained or sustained runs of atrial tachycardia; are related to poor performance (while other causes are excluded); precipitate paroxysmal atrial flutter or fibrillation; or develop along with other signs of cardiac disease.

Documentation of atrial arrhythmias during exercise may be critical for determining if paroxysmal atrial tachycardia or fibrillation is likely to be the cause of poor performance (Bonagura & Reef, 2004; Durando, 2010).

However, frequent SVPD and atrial tachycardia may be indicative of myocardial disease, or occur in association with atrial enlargement due to AV valvular disease or congenital heart disease (Reef & Marr, 2010).

Atrial tachycardia is a sustained ectopic and abnormal atrial tachyarrhythmia that occurs infrequently. Atrial tachycardia may be sustained or non-sustained (paroxysmal), and is precipitated by an atrial premature complex. The atrial rate is rapid and regular. Although, many of the ectopic P waves are physiologically blocked in the atrioventricular node, an irregular ventricular rate often occurs (Bonagura & Reef, 2004).

Atrial rates of 120 to 300 bpm (100-200 bpm, according to McGurrin [2011]) are typical in horses with sustained Atrial Tachycardia. At lower atrial rates, 2:1 atrioventricular conduction may yield a regular, relentless heart rate. At the higher atrial rates, the rhythm may be indistinguishable from atrial flutter (Bonagura & Reef, 2004; Reef & Marr, 2010; McGurrin, 2011).

Usually no treatment is required (McGurrin, 2011). If an obvious predisposing cause is identified, treatment should be directed at that. In some horses, SVPD resolve following a period of rest and therapy with corticosteroids. Specific antidysrhythmic therapy is rarely necessary provided that the ventricular rate is not affected by the SVPD (Reef & Marr, 2010). In case it is affected, the goal of therapy is to slow the ventricular rate. This can be accomplished by slowing the ventricular response to the atrial depolarizations (i.e.,

by slowing conduction through the AV node) or by breaking the underlying rhythm. For this purpose, calcium channel blockers, beta-blockers, and digoxin can be used (Jesty, 2014).

Horses with persistent SVPD, but no performance limitations, and minimal identifiable underlying cardiac disease, can continue to be used for ridden activities, as it is unlikely that these horses will collapse or represent a danger to a rider. However, numerous SVPD are a risk factor for the development of atrial fibrillation and thus, the potential for future performance-limiting problems must be considered, particularly during pre-purchase examination (Reef & Marr, 2010).

Atrial fibrillation

AF is the commonest cardiovascular cause of poor performance (Reef et al., 1995). As expected, exercise intolerance is most common in high-performance horses (racehorses, advanced combined training horses, polo ponies, and some jumpers) and less common in show hunters and in pleasure, dressage, and endurance horses. Exercise-induced pulmonary hemorrhage, respiratory distress, CHF, ataxia or collapse, and myopathy have been reported associated with atrial fibrillation. Nevertheless, the arrhythmia often is detected as an incidental finding (Bonagura & Reef, 2004, Reef & Marr, 2010; Young & van Loon, 2014).

According to Reef & Marr (2010), in the majority of the horses that develop AF during racing, the dysrhythmia is paroxysmal. Any gender predispositions seems to be unlikely, but AF is more prevalent in racehorses older than 4 years of age, compared to 2-year-olds. AF is common in large draft breeds, but Standardbreds have been overrepresented compared to hospital populations in some studies (Reef & Marr, 2010). Nevertheless, the initiating event is unknown in horses (McGurrin, 2011).

In atrial fibrillation, waves of excitation circle continuously around the atria causing independent contraction of individual muscle fibres rather than a synchronous contraction of the atria. As a consequence, atrial contribution to ventricular filling is lost, causing a decrease in stroke volume, especially during exercise. In addition, sympathetic tone prevails during exercise, reducing the blocking function of the AV node. This causes many of the atrial fibrillatory impulses to be conducted to the ventricles, resulting in a disproportionate tachycardia (Blissitt, 1999; Verheyen et al., 2013).

Shortening of the effective refractory period, atrial inhomogeneity, and SVPDs, set the stage for the development of AF. Due to their high resting vagal tone (leads to variability in action potential duration in the atrial tissue), and large atrial mass (allows multiple pathways within the atria), normal horses are predisposed to the development of AF in the absence of structural heart disease (Reef et al., 1995; Reef & Marr, 2010; McGurrin, 2011; Reef et al. 2014).

Most horses with AF have little or no underlying cardiac disease and in this situation, the term "lone AF" is applied (Reef & Marr, 2010: Reef et al. 2014). Transient potassium depletion, such as can occur with the administration of furosemide or with the loss of large amounts of potassium in the sweat of exercising horses, is also thought to be a predisposing factor in the development of AF (Reef et al., 1995; Reef & Marr, 2010).

The presenting complaints for horses with AF include: poor performance in horses engaged in athletic activities, tachypnoea, dyspnoea, exercise-induced pulmonary haemorrhage, myopathy and colic. According to McGurrin (2011), these findings in horses with AF are related to underlying cardiac disease rather than to the AF. Therefore, in these situations the arrhythmia should be considered a consequence of underlying heart failure.

Horses with lone AF usually have normal resting heart rates (<44 bpm), except animals with extensive heart failure. Although, the rhythm is irregularly irregular, and no S4 is produced. The intensity of the peripheral arterial pulses is also irregularly irregular. Pulse deficits may be present, particularly in horses with two conducted beats occurring in rapid succession. Increased resting heart rates (>50 bpm) and loud cardiac murmurs and signs consistent with congestive heart failure should alert the clinician to the possibility that significant underlying heart disease is present (Reef & Marr, 2010; McGurrin, 2011, Jesty 2014).

The ECG reveals irregularly irregular R–R intervals, no P waves and normal appearing QRS-T complexes. Rapid baseline fibrillation "f" waves are usually present, which may be small (fine) or large (coarse) (Reef & Marr, 2010; McGurrin, 2011, Jesty 2014).

AF may be paroxysmal (PAF), and spontaneous conversion to normal sinus rhythm may occur in otherwise normal horses. Spontaneous conversion usually occurs within 24–48 hours of the onset of AF. Most often occurs during strenuous exercise and the horse will often pull up abruptly, displaying signs of distress. In these cases, it is extremely helpful if the dysrhythmia can be documented to be AF at the time of the initial episode. However,

if this is not achieved, frequent SVPD documented on subsequent 24-hour ambulatory ECG provides supportive evidence that the episode of distress was due to PAF (Durando, 2010; Reef & Marr, 2010). Although, very similar clinical signs can be seen with exercise-associated ventricular dysrhythmias and this possibility should be explored with 24-hour ambulatory and exercise ECG, if it has not been possible to obtain an ECG at the time of the initial episode (Reef & Marr, 2010).

Although PAF can be a recurrent condition, this is not typically the case, but exercise ECG should be obtained while training, to ensure that there is no persistent exercise-associated arrhythmia (Reef & Marr, 2010). In humans, paroxysms gradually increase in duration, and AF often develops (McGurrin, 2011).

Horses with little or no underlying cardiac disease are candidates for conversion to sinus rhythm either with pharmacological or electrical cardioversion. Factors likely to influence the success of treatment include the presence of AV valvular regurgitation, atrial enlargement and primary myocardial disease (Reef et al., 1995; Reef & Marr, 2010). When AF is maintained for a prolonged period, electrical and structural remodelling occurs within the atria thus aggravating the condition and making it less responsive to cardioversion. As a result, higher doses of anti-arrhythmic drugs are required with an increased likelihood of unwanted side effects. The atria undergo electrical remodelling in response to AF and the likelihood of successful conversion decreases and recurrence rate increases with increased duration (Belloli & Zizzadoro, 2006). It can be difficult to determine the onset of the AF but the horse's caretakers should be questioned closely on the horse's performance history (Reef & Marr, 2010).

All available treatment options carry some risk, and in horses with no performance limitations, particularly those in which the AF has likely been present for a considerable period, owners should be counselled to consider the risks and benefits of treatment carefully. It may be more appropriate to evaluate such horse's exercising heart rates and rhythms and continue to use them for ridden activities, provided the exercise ECG reveals no further abnormalities (Reef & Marr, 2010). The prognosis for restoration and maintenance of sinus rhythm is considerably reduced in older horses, larger horses, when underlying disease is present, and when the duration of AF exceeds 4 months (Reef & Marr, 2010; McGurrin. 2011).

Quinidine remains the most widely used drug for treatment of AF due to its action of prolonging the effective refractory period. External cardioversion with biphasic

defibrillation waveform was reported successful, in one horse with AF durantion of 3 weeks, and concurrent antiarrhythmic medication. Transvenous electrical cardioversion appears to be the most viable alternative to treatment with quinidine sulphate at this time. Alternative, more modern anti-dysrhythmic drugs are under investigation (Reef & Marr, 2010; McGurrin, 2011).

Ventricular pre-excitation

Ventricular pre-excitation syndrome (Wolff-Parkinson-White syndrome) is very rare in horses. It is characterized by an accessory conduction pathway between the atria and the ventricles or bundle of His and surrounding tissue. There may be a δ wave, a slurring of the R wave due to abnormal ventricular activation (Reef & Marr, 2010; McGurrin, 2011). Pre-excitation syndrome may be an incidental ECG finding, or if rapid tachycardia develops, may present with clinical signs of weakness and distress. The accessory pathway may allow the establishment of a circus movement with antegrade movement from the atria to the ventricles through the pathway and retrograde movement from the ventricles to the atria through the bundle of His and AV node. It may also predispose to PAF (Reef & Marr, 2010; McGurrin, 2011). Nonetheless, this is a form of supraventricular tachycardia, but it appears electrocardiographically very similar to ventricular tachycardia, with broad QRS complexes (McGurrin, 2011).

Ventricular premature depolarizations

Ventricular premature depolarizations or premature ventricular depolarizations (VPD) originate within the ventricular myocardium, are common in horses, and variable in their clinical significance. Single ectopic complexes are likely to be clinically insignificant. Long trains or frequent occurrence of complexes may be associated with myocardial inflammation or disease (Reef & Marr, 2010; McGurrin, 2011).

Auscultation reveals a beat occurring earlier than normal, loud first heart sound and loud sounds produced when two heart sounds are occurring simultaneously (Reef & Marr, 2010; Jesty, 2014). There may be pulse deficits (Reef & Marr, 2010). On electrocardiography, VPD occur early, have often bizarre QRS–T complexes and are not preceded by P waves. The most common form is a wide QRS complex that is followed by a T wave orientated in the opposite direction (Reef & Marr, 2010; McGurrin, 2011).

If all the VPD have the same configuration, they are described as monomorphic, whereas VPD with more than one configuration are defined as polymorphic, and implies that they are originating from more than one site within the ventricles (Reef & Marr, 2010). Infrequent VPD can be detected at rest, during, and following exercise in normal horses (Ryan et al., 2005; Physick-Sheard & McGurrin, 2010; Buhl et al., 2010; Reef et al., 2014; Young & van Loon, 2014). Although, if they are frequent, polymorphic or occur frequently during exercise, they are considered to be abnormal (Reef & Marr, 2010).

Potential causes include myocardial inflammation, degeneration, necrosis or fibrosis, electrolyte abnormalities, hypoxia and endotoxaemia. VPD are common in horses with severe mitral insufficiency and heart failure. Because of the possibility of life-threatening ventricular tachycardia developing during exercise, horses with ventricular premature beats at rest should be retired from ridden work until thorough systemic and cardiovascular examinations can be performed (Reef & Marr, 2010; Young & van Loon, 2014).

Infrequent premature ventricular complexes, as with unusual supraventricular premature complexes, may be clinically insignificant and not require treatment. Rest is highly recommended for horses with frequent ventricular premature complexes. In the majority of horses with premature ventricular complexes, the arrhythmia seems to resolve spontaneously after 4 to 8 weeks of rest, and corticosteroid administration (Bonagura & Reef, 2004). Again, if an underlying cause can be identified, treatment has to be directed at it (Reef & Marr, 2010; McGurrin, 2011).

Ventricular tachycardia

Ventricular tachycardia is defined as four or more VPD occurring in sequence and it is often indicative of primary myocardial disease. However, the horse should be carefully examined for other systemic causes of ventricular tachycardia such as hypoxia, electrolyte imbalances or drug induced ventricular dysrhythmias (Reef & Marr, 2010; McGurrin, 2011).

During sustained ventricular tachycardia, a high (usually in excess of 100 bpm) regular rhythm will be noted by auscultation. At very high rates, aortic valve opening cannot occur for every ventricular depolarization, rendering the heart sounds and the rhythm irregular at auscultation. Horses with sustained ventricular tachycardia (150 bpm or more) eventually develop biventricular heart failure, and will often develop jugular pulsations,

ventral oedema and even ascites within 1–3 days. Syncope may occur, and has been reported in horses with monomorphic ventricular tachycardia and a heart rate equal to, or greater, than 150 bpm (Reef & Marr, 2010; Young & van Loon, 2014; McGurrin, 2011). Auscultation reveals a rapid rhythm that can be fairly regular if monomorphic ventricular tachycardia is present, and irregular with polymorphic ventricular tachycardia. Heart sounds are often loud and vary in intensity. Loud booming heart sounds (bruit of cannon) can be detected in some horses associated with the simultaneous production of two heart sounds during periods of AV dissociation. The ventricular rate in horses with ventricular tachycardia is usually increased (>60 bpm) with a slower independent atrial rate. Jugular pulsations occur in association with the AV dissociation (Reef & Marr, 2010; Jesty 2014). The ECG is important in determining the frequency and severity of the ventricular dysrhythmias detected. The configuration of the QRS complex and T wave is abnormal, and the QRS complex is unrelated to the preceding P wave. The P–P interval is regular but the P waves are often buried in QRS and T complexes (AV dissociation) (Reef & Marr, 2010; McGurrin, 2011; Jesty 2014).

Monomorphic ventricular tachycardia occurs when the ectopic focus originates from one place in the ventricle, creating only one abnormal QRS and T wave configuration and usually the R–R interval is regular. Polymorphic ventricular tachycardia occurs when the VPD originate from more than one focus in the ventricle, creating abnormal QRS and T complexes of different orientations (Reef & Marr, 2010).

Polymorphic VPD are associated with increased electrical inhomogeneity and instability and an increased risk of a fatal ventricular rhythm developing. The R-on-T phenomenon, which is a QRS complex occurring within the preceding T wave, also indicates marked electrical inhomogeneity and instability, and increases the chance for ventricular fibrillation to develop (Reef & Marr, 2010). Ventricular tachycardia may be life threatening if: R-on-T phenomenon is detected; the arrhythmia is rapid (such as >180 to 200 beats/min); multiform ventricular tachycardia is detectable; or polymorphic tachycardia with *torsades de pointes* is present. The horse may require immediate treatment for cardiovascular collapse. If pulmonary oedema is present, it represents an emergency. Intravenously administered lidocaine or quinidine usually is chosen for emergencies, although administration of either drug has been associated with side effects, including sudden death (Bonagura & Reef, 2004, Reef & Marr, 2010; McGurrin, 2011; Jesty, 2014).

The echocardiogram in horses with monomorphic ventricular tachycardia is usually normal, but there can be wall motion abnormalities associated with the rhythm disturbance. Severe myocardial dysfunction is usually detected in horses with polymorphic ventricular tachycardia, indicating possible myocardial disease. The aortic root should be carefully examined in horses with colic, and monomorphic ventricular tachycardia, particularly older stallions, as these horses may have intracardiac aortic root rupture (Reef & Marr, 2010).

Correction of any underlying conditions, such as electrolyte imbalances, is of great importance. If pulmonary oedema is present, treatment should include the administration of nasal oxygen and furosemide. Administration of intravenous lidocaine may be corrective. Excitement and seizure activity have been associated with lidocaine administration, therefore, caution should be taken. The selection of an appropriate antidysrhythmic treatment (quinidine, procainamide, magnesium sulfate, and propafenone have been used) for a horse with ventricular tachycardia depends upon the severity of the dysrhythmia, the associated clinical signs, the suspected aetiology and the availability of appropriate antiarrhythmic drugs (Reef & Marr, 2010; McGurrin, 2011; Jesty 2014).

Ventricular fibrillation

Ventricular fibrillation is a fatal arrhythmia that can be encountered in various situations. The causes of ventricular fibrillation are many and variable. Precedes death by a few seconds. Peripheral pulse and heart sounds are absent (van Loon, 2010; McGurrin, 2011). During ventricular fibrillation there are no longer coordinated contractions of the ventricles. It is almost invariably a terminal event despite treatment. The ECG undulations of the baseline with no identifiable QRS complexes or T waves. Although, P waves can still be present, but they do not precede QRS complexes (Verheyen et al., 2010; McGurrin, 2011).

Therapeutic options are limited, and there's often inadequate time to respond, unless the horse is under general anaesthesia, and it is immediately recognized. Electrical defibrillation may be attempted, however success is uncommon. Biphasic defibrillation is the indicated treatment, if attempted (McGurrin, 2011)

Tabela 1 - Arrhythmias, electrocardiogram findings, and observations in horses. (Adapted from: McGurrin, 2015)

Rhythm	P wave	QRS complex	Other findings
Sinus rhythm	Normal; each associated with a QRS complex	Normal	
Sinus arrhythmia	Normal; each associated with a QRS complex	Normal	Associated with vagal tone; less common than in other species. Usually during recovery from exercise.
Second degree AV block	Normal; some not associated with a QRS complex	Normal	Associated with vagal tone. Depolarization blocked at the AV node. Rare advanced form can cause clinical signs.
Third degree AV block	Normal; not associated with a QRS complex	Normal	Complete disassociation of atrial and ventricular depolarization. Low ventricular rate. Pathologic rhythm. Rare.
Atrial premature depolarizations	Altered morphology	Normal	Ectopic foci (atria). Warrants investigation, especially if frequent.
Atrial fibrillation	Absent	Normal	Irregularly irregular rhythm. flutter waves associated with atrial activity. Performance limited. Investigate for underlying disease.
Atrial tachycardia	Altered morphology	Normal	Run of >4 atrial premature complexes. Rare. Investigate for underlying disease. Performance limited.
Ventricular premature depolarizations	Not associated with a P wave	Altered morphology, generally wider.	Ectopic focus within ventricle. Significance varies.
Ventricular tachycardia	Not associated with a P wave	Altered morphology	Run of >4 ventricular premature complexes. May be monophormic or polymorphic. Emergency if heart rate >100. Clinical signs variable; always needs to be investigated.

B. Case studies

1. Objectives

The purpose of this study is to prove the reliability of the standardized lungeing test, inserted as exercise test in a cardiac examination protocol, to study the impact of specific cardiac arrhythmias on the health and performance.

2. Material and Methods

2.1 Sample

A selected sample of 10 diverse cases of cardiac arrhythmias, with different characteristics and outcomes, treated in the Department of Internal Medicine of the Large Animal Hospital in the University of Gent during the years of 2013, 2014, and 2015.

2.2 ECG recording equipment

Continuous monitoring of the ECG was performed with telemetry equipment, using electrodes positioned in a modified base-apex configuration, and attached to a transmitter, which sent wireless signals to a receiver set up in a computer with a specific software. The data was analysed after the appointment, and the diagnosis and treatment was informed to the owner afterwards.

2.3 Standardized lungeing test protocol

The protocol of the standardized lungeing test consisted of: 5 minutes walking, 10 minutes trotting, 4 minutes galloping, 1 minute fast galloping, and 5 minutes walking. Slight adaptations may have been done during some of the appointments.

3. Clinical Cases

3.1 Case I

Clinical History

A 5 year old gelding with 580 kg, doing high level dressage, came on the 28.11.2013 for heart examination. He had an endocarditis in December 2010, and came for re-evaluation.

Clinical Examination

On general examination the mucosae were rose, and the peripheral circulation was normal. The heart auscultation on the left side revealed an irregular rhythm, and a holo-systolic murmur (3/6 degree). On the right side, there was an irregular rhythm, and a pansystolic murmur (3/6 degree and light vibration). The auscultation of the lungs and abdomen was normal. Lumbar reflex was positive.

Diagnostic and Laboratory Studies

The blood test showed normal values of white blood cell count, electrolytes, and cardiac troponins. The ECG at rest revealed sinus rhythm with numerous monomorphic premature ventricular complexes (VPDs). During exercise ECG numerous monomorphic VPDs were found. In a total of 1h10m recording there were 546 VPDs counted. The Ambulatory ECG (total recording time: 2 hours) showed 2 VPDs during the time the gelding was standing quiet in the stable (the VPSs occurred when the heart rate slightly increased). After the resting time, the horse was taken to the arena and lunged. Increased heart frequency originated premature ventricular complexes (8 VPDs while trotting).

On the echocardiography (pictures and measurements), the B-mode didn't show any injuries on the heart muscle, but a thickening of the tricuspid valve (approximately the same as in 2010) was seen. There was an abnormal movement pattern during the closing of the tricuspid valves. All diameters are within the normal range. The Colour Flow Doppler revealed severe regurgitation on the tricuspid valve, and the mitral valve showed a light insufficiency.

The echocardiographic parameters have remained very similar compared to 2010. Diameters of the heart were within the normal reference values. An old fin-like injury on the tricuspid valves was present as in the last pictures. There was severe regurgitation of the tricuspid valve, and slight regurgitation of the mitral valve.

There was a very pronounced ventricular ectopy, which was strongly correlated with stress. It was important that this ectopy reduced the horse's riding safety. Premature ventricular complexes during work can constitute a risk for sudden collapse or dangerous ventricular tachyarrhythmia. There was a drastic difference in ventricular ectopy when the horse was calm, and in a familiar environment.

Treatment and Conclusion

It was recommended to check the body temperature occasionally to see if there was no fever, and full box rest for two weeks. The horse could be hand walked three times a day. After two weeks of rest, he could be lunged, doing very light work, avoiding high HR, and without getting tired.

The medication prescribed consisted in 600 mg of prednisolone *po*., once a day, preferably in the morning, for 10 days. On the following 10 days, 600 mg of prednisolone every 2 days. To finish the treatment, 300mg of prednisolone every 2 days, for 10 days.

Approximately one week after the end of the medication, a control ECG would have to be made. It was recommended to do so under the same conditions at the faculty. In this way, the effect of the treatment could be evaluated. Subsequently, and depending on the results, the gelding would have to be examined with ECG to check whether, and at what dose, supplements should be provided which could adequately reduce the stress to suppress the ectopy. Repeated follow-ups would be required for this purpose.

3.2. Case II

Clinical History

An 11-year-old gelding, 505 kg, 165 cm, came on 18.09.2015 for a heart examination. The horse was normally used for riding at high level. He was 6 times per week intensively trained. In August during a competition, an irregular heart rhythm was found, and the horse was brought out of the race. The horse was then studied at the University of Utrecht, and the echocardiographic examination didn't present abnormalities.

The electrocardiogram at rest showed premature ventricular complexes which were less numerous while working. In Ghent, the gelding was kept at rest and treated with corticosteroids, Vitamin E and C. This treatment was then kept for approximately one week.

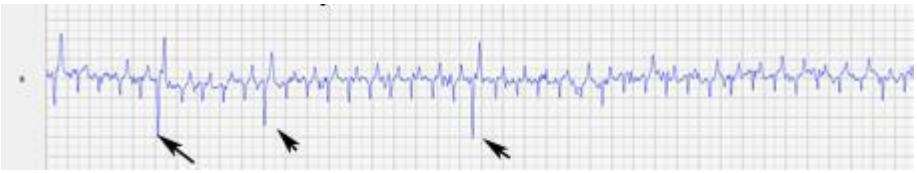
Clinical Examination

On general examination the gelding was presented in good general condition, rose mucosae, and normal peripheral circulation. The heart auscultation on both right and left side revealed regular rhythm, and no murmurs. Normal lung and abdomen auscultation.

Diagnostic and Laboratory Studies

The ions and cTn I values were normal. The ECG at rest and exercise had a total recording time of 1h43min. The Electrocardiogram at rest showed a normal sinus rhythm, and on the exercise ECG during lungeing test (5min walk, 10min trot, 4min gallop, 1min fast gallop, 5min walk), there were numerous premature ventricular complexes (VPDs). During exercise the horse exhibited 110 monomorphic ventricular extrasystols.

Fig 4 - Exercise ECG recording, the black arrows represent 3 of the ventricular premature depolarizations recorded



The echocardiography showed a very slight regurgitation of the mitral valve (no clinical significance). All diameters were just within the normal reference values. During rest the horse had a normal sinus rhythm. Although, during labour the gelding showed numerous monomorphic VPD. The irregular HR during exercise was caused by those numerous monomorphic ventricular extrasystols.

Treatment and Conclusion

The horse exhibited a pronounced ventricular ectopy which appeared to be correlated mostly with stress or work. It is important that this ectopy decreases to safely ride with the horse. Premature ventricular complexes at work can constitute a risk for sudden collapse or dangerous ventricular tachyarrhythmia.

Given the problem has long been presented, and there was still no resolution despite treatment, it was considered likely that the susceptibility for extrasystols would continue. As long as the VPDs remained, the horse should not be ridden or used for work. The horse could be in the pasture and walked by hand. Also quiet lungeing (walking and trotting), may have optionally been carried out (whenever there was no danger) to maintain fitness. In the following months, the gelding should have been auscultated repeatedly (at rest and after mild exertion) to see whether the arrhythmia was established.

Since the occurrence of the arrhythmia (at least at the moment) appeared to be related with stress and exertion, various "calming" supplements (approved for the sport) could be tried to see if it could help suppress it. It was advised to supplement the horse for about two weeks or so, and then do an ECG at rest and during an exercise test on the lunge. However, the effect of such supplements on cardiac function is not scientifically proven. The following natural sedative products could have been tried: Mood Control (25ml per day in the diet), Relax and Easy (40g per day), and Prokalm. Also administration of hawthorn extract ('cardioprotective').

Also, some vitamin supplements were recommended: Electrolytes pasta 3 or 4 times per week (according to manufacturer's recommendation); Vitamin E: 5000 IU in the feeding, once a day for 2 additional months, and Vitamin B1: 5 gr, once a day for one month.

As long as irregular heartbeats were present, on the following months, detected by auscultation at rest and immediately after exercise, it wasn't worth to make additional examinations.

If no irregularities were found, an ECG at rest and during exercise could be done, to decide whether it was possible to use the horse as a riding horse again. Once the arrhythmia gradually disappeared during mild exertion, the work should be gradually rebuilt, but periodic checks during the real work should be performed, to ensure that there were no arrhythmias during heavier exercise. It was expected that if this happened, the horse could work normally again, but that would take some time to ensure.

3.3 Case III

Clinical History

A holsteiner gelding, 565 kg, born on 07.07.2007, was presented at the department on 29.09.2014. The rider complained about a decreased performance since 4 week ago. On the pre-purchase examination (2 years ago) no abnormalities were found, nor by the veterinarian during routine examinations. Although 3 week earlier, when doing a blood test, the auscultation revealed an arrhythmia. The veterinarian diagnosed 'lone atrial fibrillation'.

Clinical Examination

On general examination the gelding presented good general condition, normal respiration and lung auscultation, cardiac auscultation revealed an irregularly irregular rhythm, and no pathological murmur. No other remarkable findings.

Diagnostic and Laboratory studies

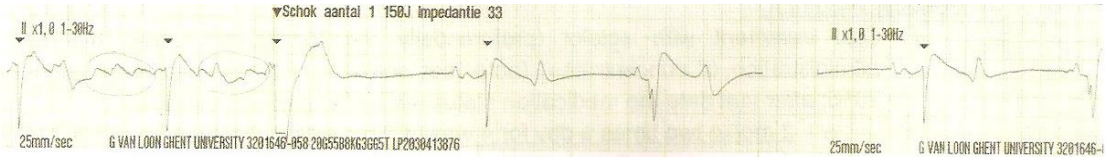
The ECG at rest confirmed the atrial fibrillation. The echocardiography didn't show any predisposing underlying heart disease, and the left atrial size was normal.

The ECG during lungeing exercise, showed R-on-T-like phenomenon. Also ventricular ectopic beats were found. The mean maximal heart rate during the lungeing test (gallop) was 290/min.

Lameness of the right forelimb was found, but according to the owner the horse often showed an abnormal gait during exercise, which had been examined previously with no further findings.

The horse was then treated for the atrial fibrillation, and a transvenous electrical cardioversion on the 2nd of October was performed. With the first shock sinus rhythm was successfully restored.

Fig 5 - Transvenous electrical cardioversion ECG recording of Case III: with the first shock sinus rhythm was successfully restored.



Immediately after conversion, multiple atrial premature beats were still found which decreased with medical treatment.

Over the following days, he was closely monitored and on the 6th and 7th of October an echocardiogram and 24-hour ECG recording (in the absence of anti-arrhythmic treatment) were performed. The atrial function and diameters were measured 1 week after the

cardioversion, and the atrial contractile function was assessed once more. The peak velocity of contraction measured by tissue Doppler imaging was low, but just within the reference values. On the 24-hour recording ECG, 80 APDs, 160 VPDs were recorded with the following morphologies: 1rS; 105RS. Most atrial premature beats were seen during stress situations. Some APDs were shortly coupled which represents a risk for AF recurrence. The horse returned home on the 9th of October.

Treatment and Conclusion

The 'Lone atrial fibrillation' was successfully treated by transvenous electrical cardioversion (TVEC), but post-conversion examination still revealed a high prevalence of atrial and ventricular premature beats.

The medical treatment consisted of: oral treatment with sotalol (note that sotalol was a FEI 'banned medication' until the 1st of January 2015, after that, it has been considered 'controlled medication'), 2 mg/kg twice a day for 4 weeks. Subsequently, 1 mg/kg twice a day for 2 days, after which the treatment was terminated.

About one week after termination of this medical treatment the horse should have been re-evaluated with a 24h- recording ECG (including a mild exercise test) to check whether the atrial and ventricular premature beats were gone when the horse was no longer on sotalol.

The gelding should have been rested for 10 days, only hand walked. After that the horse should have been rested but could walk once or twice a day for 10 to 15 minutes, or be brought into the field or paddock gradually.

By the beginning of November, mild lungeing exercise (trot) could have been started. In total, the horse shouldn't have been ridden until the ECG re-assessment at rest and during lungeing exercise. If the ECG results were normal, ridding could be gradually resumed.

As atrial fibrillation recurrence rate is about 30-35%, the gelding should be frequently checked in the future, for example, every 2-3 weeks and immediately before competitions. This could be done at home by palpation of the apex beat area or by auscultation (or ECG if possible). If recurrence was suspected, an ECG recording should have been performed before continuing training or competition. Training with a heart rate monitor is sometimes helpful to find recurrence of atrial fibrillation, for example, when suddenly the heart rate appears to be much higher for the same level of exercise.

The gait that was observed should have been checked to be re-assured there it didn't represent lameness.

3.4 Case IV

Clinical History

A 16 years and 2 months old mare, 610 kg, was presented at the clinic on the 2nd of May 2015 in shock.

Clinical Examination

The mare presented ulcers on the lips and in the mouth, and was in a depressive state. The temperature was 39.1 ºC, heart frequency was 76 bpm, very congestive and yellow mucosae, and negative lumbar reflex. On cardiac auscultation the rhythm was irregular, but there was no murmur. The ECG revealed multiple VPD, with 3 different morphologies. On echocardiography there were multiple areas of density on the myocardium of the left ventricle. Lung auscultation revealed enhanced breathing.

Diagnostic and Laboratory Studies

In the blood test, the values of Na, K, and Ca were normal, and the other results are presented on the following table:

Table 2 – Blood analysis of Case IV's first appointment

HCT (ref: 35-45%)	50%
BE (ref: -5/+5)	0.2 mEq/l
GB (ref: >11)	19.9 x 109
Urea (ref: 3.6-8.9 mmol/l)	<2.5 mmol/l
AST (ref: < 600 U/l)	>734 U/l
GGT (ref: <80 U/l)	166 U/l
Bile Acid (ref: <4 µmol/l)	80.7 µmol/l
Ammoniac (ref: 13-108 µg/dl)	19 µg/dl
cTn I (<0.03ng/ml)	0.06 ng/dl
Digoxine	<10ng/ml

Treatment

The horse received infusion (hypertonic solution followed by infusions with glucose), and antibiotic for 5 days. Also, received omeprazole to protect the stomach during 14 days. Small increasing quantities of mash and haylage were fed. Although, during the first days the appetite wasn't good, it improved gradually.

The ulcers of the mouth started to heal, and the wounds in the pasterns were treated. The horse received Ecuchol for liver treatment. To avoid laminitis, the horse had 'ice packs' on the limbs for 4 days.

The liver enzymes were re-evaluated on the 6th of May (GGT: 90 U/L; AST: 734 U/l), and on the 18th of May the mare was allowed to live the clinic.

It was advised to keep her resting, and the pasture should be avoided, especially because of the toxins and UV-rays exposition (photosensibilisation). The liver enzymes would have to be controlled 6 weeks after. A control of the pasture was essential, to eliminate the toxic plants and the rusty objects.

Smalls quantities of food *per day* was recommended, like 500g of fibreforce 4 times a day, to help the digestion by the liver, and 60 ml of Ecuchol *per day* for 1 month. Wound care of the pasterns with chlorhexidine and dermazyne was advised. After 6-8 weeks the liver enzymes would have to be controlled (AST, GGT, AF, bile acids). After 3-4 months of rest, the heart should be re-examined (ECG at rest and during exercise).

6th of August

Clinical History

On the 6th of August the mare returned to the clinic to be re-examined, and determine if she was safe to ride.

Clinical Examination

On the clinical examination the mucosae were rose, and the peripheral circulation was normal. Heart auscultation at rest revealed an irregular rhythm but no murmur, and lung auscultation was normal. On the blood test the values of cTn I were normal (<0.03 ng/ml). The ion values were within the normal reference values, and the liver enzymes were normal as well.

The ECG at rest and exercise (standardized lungeing test) recorded during approximately 57 minutes, registered 102 VPDs, with 2 different morphologies.

Treatment and Conclusion

The great number of VPDs increase the risk of developing ventricular tachycardia, which can also induce ventricular fibrillation. Ventricular fibrillation is a life-threatening condition that can cause sudden death. Therefore, it wasn't at all advisable to ride the mare, or use her for reproduction.

Given the fact that the liver enzymes were normal, the mare could be progressively introduced back in the pasture.

3.5 Case V

Clinical History

A 14 year old gelding, 618 kg, 168 cm height, came on the 27th of September 2015 for a cardioversion (TVEC) of an atrial fibrillation.

The owner had had this horse for 1.5 months, and it was bought without a pre-purchase exam. The gelding was ridden every day, and had been very tired from training since 14 days before. The veterinarian in the field diagnosed atrial fibrillation.

Clinical Examination

On general examination the horse showed good general condition, normal temperature, rose mucosae, and normal peripheral circulation. The cardiac auscultation on the left side revealed an irregular rhythm, but no murmur. Although, on the right side, it revealed a systolic murmur (1/6 degree). The lung auscultation was normal.

Diagnostic and Laboratory Studies

The echocardiography showed that all the heart diameters measured were within the normal values, but there was moderated tricuspid valve insufficiency, and light insufficiency of the mitral and aortic valves. The length of the fibrillation cycle at the right atrium was 156.5 ms.

The ECG at rest confirmed the atrial fibrillation, and the exercise ECG with a standardized lungeing test, confirmed atrial fibrillation too. The average heart frequency on gallop was 237 bpm.

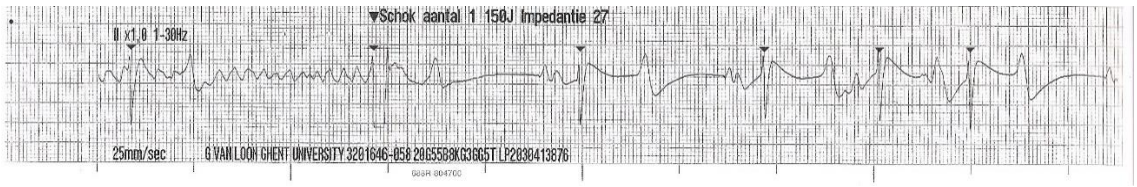
It was noted that the horse was stiff on trot, and lame on the right forelimb.

The murmur on the right is due to the moderate insufficiency of the tricuspid valve, but at the time, that murmur didn't represent a problem to the horse's performance.

Treatment

On the 1st of October an electrical cardioversion (TVEC) was performed under general anaesthesia. The sinus rhythm was restored after the very first shock, and the recovery was normal.

Fig 6 - Transvenous electrical cardioversion ECG recording of Case V: with the first shock sinus rhythm was successfully restored



On the following days, ECG and echocardiography were performed to control the treatment. The atrial contractile function was examined 24 hours and 5 days after the treatment. The contractile function of the left atrium was low on the following 24 hours, but improved 5 days after treatment.

The 24hour-recording ECG done on the 5th of October registered 19 APD's (slightly high). On the 6th of October the gelding was allowed to leave the clinic.

Because of the APDs, the horse received sotalol for 4 weeks with the following dosage: 8 pills (160 mg/pill) in the morning, and 8 pills in the evening. At the end of the treatment, for the last 2 days, he received 4 pills twice a day.

The horse should be rested for 1 week, hand walking only. Afterwards, he could start exercising at the pasture or paddock, but always in a quiet environment. In total, he should be rested for 6 weeks after cardioversion. If on the 15th of November the heart rhythm

was normal, he could start to do some light work, and after 2 weeks, it could be gradually increased.

The risk of recurrence after electrical cardioversion is 35%. Therefore, the heart rate should be controlled by palpation or auscultation once a month, and before a competition. If the rhythm is irregular, an ECG should be done to confirm the type of arrhythmia present.

3.6 Case VI

Clinical History

A 4 year old Arabian mare, 420kg, 151cm height, born on the 17th of January 2010, came on the 4th of August of 2014 for heart examination.

This mare worked 2 times per week. The owner participated with her several times in endurance competitions (20 km), and an irregular heartbeat was noticed (before and after the competitions). The mare had been examined because of a wound in the past, and on general examination, an irregular heartbeat had been found as well.

Clinical Examination

On general examination the mucosae were rose, and general peripheral circulation was normal. The auscultation of the heart at rest revealed and irregular rhythm, but no murmur. The auscultation of the lungs was normal. Blood test values were within normal values too.

Echocardiography was performed in order to obtain pictures and measurements. The B-mode revealed no injuries on the endocardium, myocardium and pericardium. All the diameters of the heart were within the reference values. Colour Flow Doppler showed no regurgitation on the tricuspid, pulmonic, aortic and mitral valves.

The ECG at rest revealed multiple APDs. An exercise ECG was performed with a standardized lungeing test in the arena (5 minutes walking, 10 minutes trotting, 5 minutes galloping, and 5 minutes walking). While walking, the horse still had APDs, but during trot and gallop the horse presented a regular heart rhythm.

The horse had frequent atrial premature depolarizations which were short-coupled (often occurred in the T-wave or immediately after the QRS complexes). The echocardiography

didn't reveal any regurgitations, no abnormal densities, and all the diameters measured were within reference values.

It was determined that the APDs occurred related with stressful situations (while waiting in the examination room, hearing other horses, walking to the arena). During trot and gallop (heart frequency > 125 bpm) in the arena, there were no APDs recorded, probably because they were 'overcome' by the fast sinus rhythm.

The presence of the APDs represent a risk factor for the development of Atrial Fibrillation. The APDs could be caused by a local inflammatory injury of the heart muscle, which can be treated with corticosteroids (preferably a type with low risk of developing laminitis). Some horses may take benefit, but in chronic cases, such as this one, there could be no improvement.

Treatment and Conclusion

On the 6th of August, it was advised that the horse should be rested for 4 months, and that the work would have to be performed very quietly and avoiding stressful situations.

The medication protocol was the following:

- 800 mg prednisolone *po*, once a day, in the morning, for 7 days;
- 600 mg prednisolone *po*, once a day, in the morning, for 7 days;
- Afterwards, 400 mg prednisolone *po*, once a day, in the morning, for 7 days;
- At the end of the treatment, 400 mg prednisolone *po*, once every 2 days, in the morning, for another 4 days;

The atrial premature complexes were present especially during stressful moment, and it was recommended to give these supplements:

- 10g magnesium oxide *po*, once a day,
- 5g vitamin E *po*, once a day,
- And a natural tranquilizer that tests negative for doping: 'Relax & Easy'

It was recommended to start the administration of supplements four weeks before a new examination.

13th of December

Clinical History

On the 13th of December of 2014 returned for re-examination.

Clinical Examination

During the ordinary work everything remained the same. The owner wanted to know if the mare could still participate in endurance competitions (20-80km).

During examination, the mare presented a good general condition, normal peripheral circulation, normal lung auscultation, a good but irregular pulse, and the heart auscultation revealed again an irregular rhythm, but no murmur. No further significant abnormalities.

Diagnostic and Laboratory studies

On the ultrasound the atrial myocardium was re-examined, but no visible changes were found. A 12-hour ECG was performed, and 432 APDs and 1 VPD were recorded.

Treatment

After the re-evaluation, it was determined that the problem encountered was chronic, and for that reason the treatment with corticosteroids was not effective. The number of APDs per day was too high. The problem was going to remain, and probably worsen. This high number of APDs increases greatly the risk of developing Atrial Fibrillation. However, AF is also related with big atrial chambers, and the values measured on echocardiography were normal. For that reason, even though there was a risk, it wasn't as high as otherwise. Nonetheless, it was advised that the mare should be monitored frequently with ECG.

The irregular heartbeat isn't life-threatening, but it reduces the performance, and the exertion may in some cases increase the susceptibility for AF. Therefore, a low level of work is possible, but the horse should not participate in endurance competitions.

3.7 Case VII

Clinical History

A gelding, 6 years old and 9 months, came on the 8th of March 2015 for cardioversion (TVEC). A dysrhythmia was found in October during a clinical examination in an appointment for vaccination on another clinic. The ECG revealed an atrial tachycardia (approximately 160/min) and slow conduction at the level of the AV node, and variable AV-blocks. Over a HR of 150 bpm, the HR was proportional to the effort required as in a normal horse. On the 20th of January the horse received a treatment based on quinidine,

which reduced the HR from 144 to 63 bpm. The treatment was kept until it showed signs of toxicity.

Clinical Examination

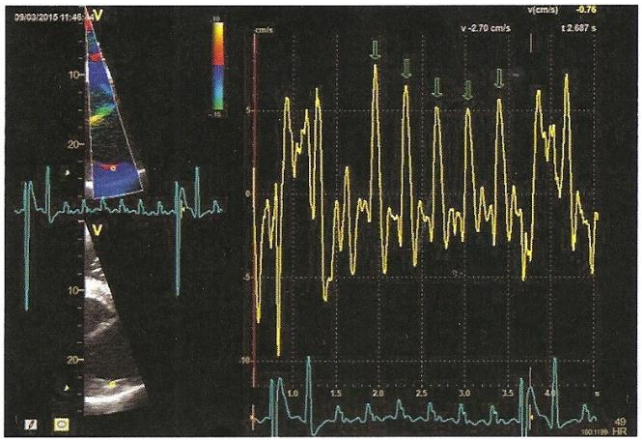
On general examination the gelding showed a good body condition, 492 kg, 173 cm height, rose mucosae, and normal temperature. Heart auscultation revealed an irregular rhythm, but no murmur, and the lung auscultation was normal.

Diagnostic and Laboratory studies

The ECG at rest confirmed the atrial tachycardia: +/- 166 bpm. The ventricular frequency was 36-50 bpm. The exercise ECG confirmed that over a heart rate of 150 bpm, HR was proportional to the effort required as in a normal horse.

The echocardiography confirmed what had already been found by the previous clinician, which was that there were no cardiac abnormalities. The contractile function of the left atrium (confirmed with tissue Doppler) during atrial tachycardia was within normal values.

Fig 7 - Myocardial contraction of the left atrium (4 chambers): maximum rate of contraction of the left atrium is shown by the arrows

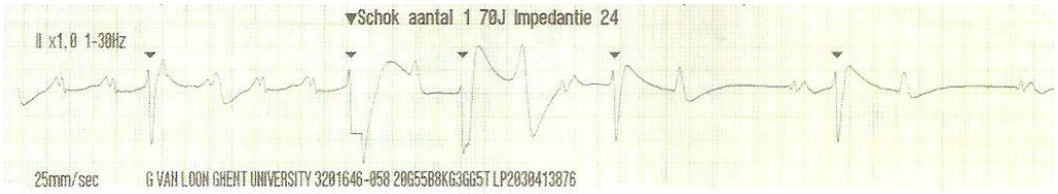


A very light aortic insufficiency was diagnosed (physiological), and the diameters of the heart measured were normal.

Treatment

After a pre-treatment with anti-arrhythmic therapy, the TVEC under general anaesthesia was performed on the 12th of March. The heart rhythm became normal after the first shock. The recovery had no complications.

Fig 8 - Transvenous electrical cardioversion electrocardiogram recording of Case VII: with the first shock sinus rhythm was successfully restored



The gelding received anti-arrhythmic medication *po* until the day he left the clinic. Following controls were performed, including a 24-hour recording ECG on the 16th of March (while the horse was receiving anti-arrhythmic medication). Only 1 APD was recorded, without other abnormalities.

On the 17th of March, he could leave the clinic.

At home the horse received 2 boxes of sotalol (98 pills of 160 mg) *po*, with the following indications:

- From the 22th of March to the 6th of April, 6 pills twice a day.
- On the 7th and the 8th of April, 3 pills twice a day.

It was advised that the gelding should have been rested till the 25th of April, but he could be walked by hand. Afterwards, he could walk in the paddock or at the pasture, but he could not be ridden.

After the period of rest, he could start work gradually. At the beginning, only light trot, and then increasing the periods of trot for 2 weeks. Afterwards, he could progressively restart the normal workload.

The estimated risk of recurrence for AT after TVEC is lower than for Atrial Fibrillation (which is 30%). Nonetheless, the heart rate should be controlled by palpation or auscultation once a month, and before and after a competition.

3.8 Case VIII

Clinical History

A 5 year old mare, 550kg, 1m59cm height, came on the 26.11.2015 for heart examination. The owner had this horse for one month at the time. No pre-purchase was done, the pictures of a previous exam were then used. During a general examination a light murmur

was noted. The horse was only doing light work normally (30 minutes 4 times a week, mostly walking).

Clinical Examination

On general examination the mucosae were rose, and the peripheral circulation was normal. Although the heart auscultation on the left side showed a regular rhythm, there was an early to mid-systolic murmur (3/6 degree) variable in intensity (depending on the heart rate). The lung auscultation was normal (vesicular murmur), and the abdomen auscultation was normal as well.

Diagnostic and Laboratory Studies

The ECG at rest showed normal sinus rhythm, a few second degree AV Blocks, and Sinus Arrhythmia. The exercise ECG with standardized lungeing test, showed normal sinus rhythm (sinus tachycardia).

The echocardiography was normal. All the diameters measured were within the normal reference values. There was a small density and a mild regurgitation on the aortic valve.

Treatment

The murmur that could be heard on the left side was a functional and physiological murmur. This murmur did not affect the performance. There was a mild regurgitation present on the aortic valve, but at the moment this regurgitation had no impact on the horse's performance. It was expected that it would remain for a long time, but this type of regurgitation is usually very slow in progression over the years.

Nonetheless, the horse is still young, and there is a light density visible on the aortic valve. This situation allows a slightly increased risk that over the time there could be a more audible murmur that might cause an impact on the horse's performance. There was, however, a small chance of this situation becoming clinically important given the horse's career. It was appropriate to carry out a control echocardiography and electrocardiogram 3 years from then, to determine whether there were changes over this period of time. The horse could work normally, and be ridden.

3.9 Case IX

Clinical History

A 6 years old mare, 573 kg, arrived on the 27.10.2015 for heart examination.

This mare was ridden twice a week for 60 minutes, and participated on jumping competitions (jumping 1m20cm). No problems were noted. Although, on the context of pre-purchase examination, an irregular heart rhythm was found.

Clinical Examination

On general examination the mucosae were rose, the peripheral circulation was normal but the rhythm was irregular. The heart auscultation on both right and left side was regularly irregular, without murmur, and an S4 sound was heard during the second degree AV Block. Lung and abdomen auscultations were normal.

Diagnostic and Laboratory Studies

The ECG at rest revealed sinus rhythm with a few second degree AV Blocks and double second degree AV Blocks. During the exercise ECG with standardized lungeing test, the AV-blocks disappeared when the horse started to move (sinus tachycardia). There was a normal sinus rhythm and chronotropic response during work. The highest heart rate (without block) was 47/min, and the highest heart rate during gallop was 172/min.

Fig 9 - ECG recording at rest, the black arrows represent the Second AV blocks

Echocardiography on B-mode didn't reveal any lesions on the endocardium, myocardium and pericardium. All the diameters of the heart were within the reference values. The Colour Flow Doppler only showed a light regurgitation on the mitral valve, which was considered physiological.

Treatment

The mare has a significantly decreased atrioventricular conduction at rest. The combination of both First degree AV Block and second degree AV Block (the later with double events), all of which stop during effort, seem to be caused by a high vagal tone. For this reason, given the fact that it immediately disappeared after stress or work, and there is a normal chronotropic response, it was considered physiological. No advice or risk was strongly indicated for the pre-purchase exam. This arrhythmia has no impact on the performance.

3.10 Case X

Clinical History

A 10 years old mare, 710 kg, came on the 9th of November 2015 for heart examination. This mare worked 4 to 5 times a week, and participated on jumping competitions. There was no performance decrease, but she was then more tired after work. She was prone to put on weight, and due to a tendon problem, she had been resting for 8 weeks. During general examination, the auscultation of the heart revealed an irregular rhythm (before and after work), and a murmur (after work).

Clinical Examination

On general examination the mare's body score was 7-8/9. The mucosae were rose, peripheral circulation was normal, but with irregular pulse. The heart auscultation on the left and right side showed an irregular rhythm, but no murmur. Lung and abdomen auscultation were normal.

Diagnostic and Laboratory Studies

The blood test revealed normal values of cTn I, normal ion values (Na, K, Mg, iCA). PaO2 at rest was 97.7mmHg, and PaO2 at work was 96%.

The ECG at rest showed sinus rhythm and atrial extrasystols especially after stressful moments. On the exercise ECG the mare showed normal sinus rhythm, even while there were other horses near the arena. After the work, the heart rhythm dropped, and the horse showed again a few APDs. The heart rate during trot was 95 bpm, and the heart rate

during gallop was 115 bpm. The highest heart rate was during fast gallop, which was 153 bpm.

The echocardiography showed no abnormalities, all the diameters measured were within normal values, no densities were found in the myocardium, pericardium, and endocardium. There was only a light regurgitation of the tricuspid valve, which was considered physiological.

The irregular rhythm was caused by the APDs, which were more frequent when the heart rate dropped after stressful work. There were no APDs during gallop and trot in the arena, presumably because they were 'supressed' by the fast sinus rhythm.

There was always risk for development of AF to be considered, but given the normal heart diameters measured, and the absence of other lesions, this risk was limited.

Treatment

The horse could be ridden normally. It was advisable to take the heart rate at least once a month, to control the possible development of AF. Training with a heart rate monitor could also be considered.

The owners were assured that there was no risk for the mare, at time, to be put under general anaesthesia, there was no increased risk compared to any other horse, and that she could be used as a breeding mare (since the irregular heart rhythm isn't inherited).

Table 3 – Summary of the cases

Patient (Cases)	Sex	Age (years)	Weight (kg)	Irregular HR	Poor Performance	Murmurs	Arrhythmias ECG at rest (Yes or No)	Arrhythmias exercise ECG (Yes or No)	Diagnose
I	gelding	5	580	Yes	No	Left side: holo-systolic murmur (3/6 grade) Right side: pansystolic murmur (3/6 grade and light vibration)	Yes	Yes	**Premature Ventricular Complexes**
II	gelding	11	505	Yes	Yes		No	Yes	**Premature Ventricular Complexes**
III	gelding	8	567	Yes	Yes		Yes	Yes	**Atrial fibrillation**
IV	mare	16	610	Yes	No		Yes	Yes	**Premature Ventricular Complexes**
V	gelding	14	618	Yes	Yes	Right side: systolic murmur (1/6 grade)	Yes	Yes	**Atrial Fibrillation**
VI	mare	4	420	Yes	No		Yes	Yes	**Supraventricular premature depolarizations**
VII	gelding	6	492	Yes	No		Yes	No	**Atrial Tachycardia**
VIII	mare	5	550	No	No	Left side: early to mid-systolic murmur (3/6 grade)	Yes	No	**Second Degree Atrioventricular Blocks, Sinus Arrhythmia**
IX	mare	6	573	Yes	No		Yes	No	**Second Degree Atrioventricular Blocks**
X	mare	10	710	Yes	Yes		Yes	No	**Supraventricular premature depolarizations**

4. Discussion

Cardiac arrhythmias are often identified in horses engaged in all levels of performance in equine sports, and often are of concern in the equine athlete, because of their potential effects on performance and the possibility that they may lead to sudden death. The challenge for the clinician is to determine the importance of any cardiovascular abnormality on present and future performance, on rider or driver and horse safety, and to consider any long-term effects on health and longevity (Durando, 2010; Slack et al., 2014; Reef et al., 2014).

This retrospective case study included 5 mares and 5 geldings, with ages between 4 and 16 years old, and the average age was 8.5 years. The average weight was 562.5 kg, and the median weight was 570 kg.

The motives for the appointment varied. The main ones were irregular heart rate, poor performance, and murmurs. Irregular HR was found in 90% of the cases; poor performance complains were present in 40% of the cases; murmurs were diagnosed in 30% of the cases.

Electrocardiography (ECG) is the test of choice for confirming the diagnosis of heart rhythm disturbances, and an exercise ECG is often indicated to determine if an arrhythmia has potential for impairing performance or might become a safety issue (Reef et al., 2014).

The main arrhythmias diagnosed were: Premature Ventricular Depolarizations: 30%; Supraventricular Premature Depolarizations: 20%; Atrial Fibrillation: 20%; Atrial Tachycardia: 10%; Second Degree AV-block: 20%.

In the context of the cases of this study in particular, the standardized lungeing test used in the protocol by the clinicians provided essential information while elaborating the final diagnose.

Arrhythmias on the ECG at rest were found in 90% of the cases. Only one case had no arrhythmia at rest, and it could only be diagnosed on the exercise ECG. On the exercise ECG 60% of the cases presented arrhythmias. The other 40%, which were cases without arrhythmias on the exercise ECG, represented cases with arrhythmias at rest. This difference in results demonstrate that the standardized lungeing test was important to diagnose the arrhythmias, and to access the severity or non-severity, according to the specific disease encountered.

4.1 Clinical Approach

A Consensus Statements of the American College of Veterinary Internal Medicine (ACVIM) and the European College of Equine Internal Medicine (ECEIM) provided the veterinary community with up-to-date information on the pathophysiology, diagnosis, and treatment of clinically important cardiac equine diseases, and in particular a guideline article named: Recommendations for Management of Equine Athletes with Cardiovascular Abnormalities. These recommendations for equine athletes presume clinical knowledge in equine auscultation, echocardiography, electrocardiography (ECG), exercise testing, and interpretation of laboratory testing, along with an understanding of the pathophysiology of equine heart disease. Most management decisions and risk assessments are based on these evaluations, along with the performance history, physical examination findings, athletic demands placed on the horse and owner expectations (Reef et al., 2014).

Therefore, a thorough history and physical examination will guide the rest of the examination and eliminate needless diagnostic tests (McSloy, 2011). Horses with a defined cardiac lesion need a schedule of follow-up examinations to redefine the prognosis, reassure the horse owner, and anticipate and manage medical complications (Reef et al., 2014).

Objective, negative prognostic factors in the setting of structural heart disease include progressive chamber remodelling (dilatation and altered chamber shape) and dysfunction, great vessel enlargement, as well as the development of pulmonary hypertension (PHT), congestive heart failure (CHF), and potentially dangerous arrhythmias (Reef et al., 2014).

When a murmur is detected, a detailed cardiac examination should follow. This will substantially increase the chances of determining the exact origin of the murmur and quantifying its significance (Malalana, 2015). A complete echocardiogram is the best diagnostic test of choice when evaluating a horse with a cardiac murmur, and is advised when (McSloy, 2011; Reef et al., 2014): auscultation or clinical findings are not consistent with a physiologic murmur (McGurrin, 2011; Reef et al., 2014); if the murmur is moderate to loud; or when a murmur is detected as part of a pre-purchase examination. Serial echocardiographic evaluations are more meaningful for prognosis, than findings from a single examination. Doppler findings, including the width of the vena contracta and the regurgitate jet area, are used to assess valvular regurgitation, but these variables,

are unreliable in isolation. For example, in the absence of cardiac chamber enlargement, it is unlikely that chronic, severe regurgitation is present, regardless of the Doppler findings. Furthermore, Doppler studies often reveal physiological valvular regurgitation that is silent on auscultation. The history, cardiac rhythm, and the results of auscultation should be known before interpreting the echocardiogram. (Reef et al., 2014).

The Panel specifically recommended an echocardiogram in the following situations: a previously diagnosed 'functional' murmur that is louder on serial examinations; a degree 3–6/6 left-sided murmur compatible with mitral regurgitation (MR) or aortic regurgitation (AR); a degree 4–6/6 right-sided systolic murmur compatible with tricuspid regurgitation (TR); suspected ventricular septal defect (VSD) or other congenital heart lesion; continuous or combined systolic-diastolic murmurs; clinically important arrhythmias, whether a murmur is present or not; suspected myocardial injury; or suspicion of CHF (Reef et al., 2014).

It's important to remember, that in the horse, echocardiography provides the only means of assessing chamber enlargement, and allows the clinician to identify structural anomalies and to assess the cardiovascular effects of these findings (McGurrin, 2015). Therefore, an echocardiographic study should address the following: morphologic lesions: motion abnormalities; cardiac chamber and great vessel size; cardiac valve function; blood flow disturbances; global and regional ventricular systolic function; estimates of hemodynamic variables including pressure gradients and volumetric flow; and ventricular diastolic function and filling pressures (accepting these two are challenging to measure in mature horses) (Reef et al., 2014). Such parameters were evaluated in the cases studied.

Exercise testing is also indicated during a pre-purchase examination when a non-functional heart murmur or sporadic arrhythmia is identified (Reef et al., 2014). Although, not exactly on pre-purchase exam, but not too long after, there is the example of Case V and IX.

Case I, V and VIII revealed murmurs on auscultation. Most murmurs are of minimal consequence to performance (Davidson, 2015). Although they can give the first clues to the clinician.

Case I presented a left holo-systolic murmur. Van Loon (2014) refered that mitral regurgitation usually results in a left sided systolic murmur, early to mid, holo- or pansystolic, plateau type murmur over the mitral valve area, radiation dorsally with an

intensity varying between 1/6 and 5/6 (Bonagura & Reef, 2004; van Loon, 2014; Malalana, 2015). The backflow of blood into the left atrium results in an increased atrial filling, and more blood flow during early LV filling often producing a louder S3 sound (Bonagura & Reef, 2004; van Loon, 2014). According to McSloy (2011), MR is most likely to cause clinical signs, since it causes an increased left atrial pressure and pulmonary hypertension, which lead to performance-related signs. If the intensity is 3/6 or more, the murmur has more chance to be clinically important, or to become so in the future. Echocardiography is of great importance to assess the severity of the regurgitation and whether there are secondary changes. Although, we know that MR just by itself does not affect performance, it is important to be aware that such situation increases the risk of AF development (van Loon, 2014; Reef et al., 2014; Malalana, 2015). But it was not the case of Case I, since the mitral valve was considered to have only a slight insufficiency. The right side pansystolic murmur (3/6 grade and light vibration), however, revealed a severe regurgitation on the tricuspid valve. Tricuspid regurgitation is very frequent in normal horses, probably given its complex apparatus (van Loon, 2014), particularly in high performance horses (Malalana, 2015). According to Young & van Loon (2014), the murmur of tricuspid regurgitation (TR) is a systolic murmur heard over the right side of the thorax. It is usually soft, band shaped, extends throughout systole and can incorporate S1 and S2. A regurgitation mild to moderate doesn't affect performance, but it may increase the risk of AF (van Loon, 2014; Young & van Loon, 2014).

Case V presented a right side systolic murmur (1/6 degree), that was related to the tricuspid valve as well, which was due to moderate insufficiency, but at the time, it was reported that the murmur didn't represent a problem to the horse's performance. However, AF was present and it was the horse's main problem, and it is going to mentioned later in the discussion.

Case VII revealed on the left side an early to mid-systolic murmur (3/6 degree) variable in intensity (depending on the heart rate), with a corresponding small density and a mild regurgitation on the aortic valve. Although, aortic regurgitation is often correlated with a decrescendo, left side diastolic murmur (van Loon, 2014), it can be auscultated from both sides of the chest as the diseases progresses (Malalana, 2015), confirming the importance of the cardiac ultrasound to confirm the suspicions detected by auscultation. According to Bonagura & Reef (2004), AR can be identified with cardiac auscultation, which reveals a holodiastolic murmur, with the point of maximal intensity over the aortic valve area and

good radiation to the right and toward the left cardiac apex. The murmur may vary greatly in intensity. Mild to moderate aortic regurgitation will have no effect on performance, because the ventricle is able to compensate for the limited volume overload, and during exercise the increase in heart rate shortens the diastolic time and thus the time of regurgitation (Bonagura & Reef, 2004; van Loon, 2014). It was considered appropriate to make a control echocardiography and electrocardiogram 3 years from then, to determine whether there were changes over this period of time. But in conclusion, the horse could work normally, and be ridden.

Exercise testing can help assessing the clinical significance of cardiac murmurs, because valvular regurgitations may predispose to development of cardiac arrhythmias during exercise. At present, there is no standard exercise test for horses, so the test chosen will vary depending on the horse examined, and whether it is necessary to find subtle cardiovascular diseases, or diagnose severe arrhythmias (Buhl, 2015). Exercise testing is an important component of CV assessment, and includes continuous recording of the ECG, that should be obtained with a device that has permanent storage and playback capabilities set on the horse, as described before.

An exercise test should not be performed when there is CHF, severe valvular regurgitation with secondary AF, PHT, severely reduced systolic function, or when a ventricular arrhythmia of dangerous complexity is present (Reef et al., 2014). That's why in Case IV, the mare wasn't submitted to an exercise test the first time she came for examination (on the 2nd of May 2015), because multiple ventricular extrasystols were present with 3 different morphologies. Even not knowing exactly what caused the myocardial injury (probably a hepatotoxic and cardiotoxic substance) in the horse from Case IV, a study by Solis et al (2015), concluded that horses with haemorrhage due to a variety of causes, experienced myocardial injury, which was characterized by increases in plasma cTn I, and also developed cardiac arrhythmias. Arrhythmias included APD, multifocal VPD, and ventricular ectopy that included runs of ectopic beats.

According to Schwarzwald et al. (2003) myocardial damage can lead to a disruption of the intracellular contractile proteins and to a release of cTn I into the extracellular compartment. Acute myocardial infarction, unstable angina, ischemia, myocarditis, myocardial contusion, myocardial toxicity, and severe congestive heart failure have been associated with high serum concentrations of cTn I in human patients.

Specific non-invasive cardiac assessments include the effects of exercise on auscultation (rate, rhythm, and murmurs); peak HR during exercise; HR and rhythm during the different phases of the exercise test and during recovery; and, optionally (wasn't reported in any of the cases studied) echocardiography before and after exercise (stress echocardiogram). Additional tests that might be indicated are analysis of gait, airway dynamics, arterial blood gas tensions, and other clinical laboratory tests, such as cTn I measurement (Reef et al., 2014; Buhl, 2015).

If an exercise test is indeed performed, present recommendations for interpretation of exercising ECGs are that the finding should be considered abnormal if there are more than two ectopic beats during peak exercise, five ectopic during the immediate recovery period, or pairs of ectopic beats at any time (Ryan et al., 2005; Buhl et al., 2013). However, recent research indicates that many variations in cardiac rhythm during and immediately after exercise, that have previously been considered abnormal, were common and usual in certain high-performance horses (Ryan et al., 2005; Jose-Cunilleras et al., 2006; Buhl et al., 2013; Durando, 2010; McGurrin, 2015). In a study by Jose-Cunilleras et al. (2006), premature depolarisations were commonly observed immediately during the recovery period from maximal exercise, which is the time that the fast heart rate drops due to parasympathetic reactivation and sympathetic withdrawal. In conclusion, clinical history is paramount to determine the significance of these exercise ECG findings (McGurrin, 2015).

The Second Degree Atrioventricular Block is observed in case VIII, and IX. This pathology is considered normal in equine athletes. The HR is in the low normal range and there are usually several conducted P waves before the AV Block. The P-P interval is regular or may vary slightly. Auscultation is characterized by an irregular rhythm with a repetitive pattern. Fourth (atrial) heart sounds (S4) that are not followed by first and second heart sounds may be audible in the regular pauses in some horses. Physical activity or increased sympathetic tone should cause the arrhythmia to disappear, the cases in which it doesn't are rare, but shouldn't be underestimated (Bonagura & Reef, 2004; Reef & Marr, 2010; Reef et al., 2014). A study by Buhl et al. (2013), about cardiac arrhythmias in clinically healthy show jumping horses, still reported second degree AV Block in a few horses of the study during exercise. However, it wasn't the case of none of these patients.

When second degree AV block results in more than 2 consecutively blocked P waves, the term ‘high grade’ is used and the rhythm is considered abnormal. If the horse with high-grade second degree AV-Block cannot be exercised, an atropine response test can be used. When there is a history of collapse, a continuous 24-hour Holter ECG with simultaneous video recording should be obtained (Reef et al., 2014). Therefore, in some cases, as in these reported cases in particular, an exercise ECG is needed to confirm the physiologic basis of the arrhythmia.

Atrial fibrillation (AF) is observed in cases III and V, and is the most common arrhythmia affecting performance (Reef et al., 1995; Reef et al., 2014; Decloedt, et al., 2015).

AF is usually recognized during auscultation and is characterized by an irregularly irregular rhythm that can sound like a combination of premature beats and long pauses. S4 is absent. Resting tachycardia suggests underlying heart disease, sympathetic nervous system (SNS) stimulation because of stress or pain, or in unusual cases, presence of an accessory atrioventricular conduction pathway. Some horses have AF with a patterned AV conduction sequence that must be distinguished from second degree AV block. Although AF often sounds more regular at higher HRs, the rhythm remains irregular and a careful auscultation will reveal (Bonagura & Reef, 2004; McGurrin, 2011; Reef et al., 2014).

With acute onset of AF, spontaneous conversion to normal sinus rhythm (NSR) can occur, usually within 24–48 hours. This is referred to as Paroxysmal AF (PAF) (Reef et al., 2014), and is an important cause of poor performance, that can be hard to document, and to do a detailed electrocardiographic examination in those horses in which an irregularly irregular rhythm is auscultated after fading or stopping in a race, unless an ECG is obtained in that moment (Durando, 2010).

AF in the absence of detectable underlying heart disease is called ‘lone AF’ (Reef & Marr, 2010: McGurrin, 2011; Verheyen et al., 2013; Reef et al 2014).

According to Physick-Sheard (2013), there appears to be no immediate danger in lone equine AF. The primary concerns are performance inconsistency and economic impact, rather than safety or mortality. Horses with lone AF may experience a significant reduction in performance, depending on their use, but at work they do not typically collapse, they simply tire faster. The majority respond to treatment and, in young

horses at least, they usually return to normal (Physick-Sheard, 2013; Reef et al., 2014).

This designation of 'lone atrial fibrillation' is used to describe the disease in Case III: 'The echocardiography didn't show any predisposing underlying heart disease, and the left atrial size was normal'. Although, microstructural lesions or channelopathies that predispose to AF might be present in some of these horses, but cannot be detected using routine diagnostic tests (Reef et al., 2014).

Recurrent or persistent AF can arise from structural heart diseases. Therefore, a complete examination should be performed to identify relevant murmurs, such as valvular regurgitation, and cardiac (atrial) enlargement as described above. A slight increase in LA size can result from AF, even in the absence of MR (McGurrin, 2011; Reef et al., 2014). For example, Case V presented with a murmur, however, it was heard on the right side: systolic murmur (grade 1/6).

The diagnosis is confirmed with an ECG, which is characterized by an irregularly irregular R-R interval with normal QRS morphology, the absence of P waves and the presence of "f" waves. Concurrent VPDs might be found. Atrial flutter represents a slow variation on AF. Flutter waves resemble saw-toothed P waves without an isoelectric shelf and have a regular atrial rate of about 170–275 bpm, while fibrillation waves are less organized and faster (275–500 bpm). AV conduction in atrial flutter is usually variable, resulting in a ventricular rate response that can be irregular, or regular during periods of increased sympathetic tone (Reef et al., 2014).

In horses with clinically important structural lesions, intermittent premature complexes, or lone AF that cannot be converted to sinus rhythm, exercise testing can determine if the HR is appropriate for the work performed, or if an arrhythmia deteriorates the performance over the course of the test (Reef et al., 2014). An exercising ECG should be performed if the owners decide against any treatment, even if the rhythm is an incidental finding and the horse's performance is believed to be unaffected (Young & van Loon, 2014). This procedure will ensure whether the horse is able to perform its duties comfortably within its reduced cardiac reserve, and will confirm that withdrawal of parasympathetic tone during exercise does not result in accelerated conduction of wavelets, excessive tachycardia, or other malignant cardiac rhythms that could increase the horse's risk of exercise-related injury, or predispose it to collapse and sudden death (Young & van Loon, 2014; Reef et al., 2014)

The suspected duration of AF should be determined when possible because it affects the prognosis for successful conversion and the likelihood of recurrence (Belloli & Zizzadoro, 2006; Reef & Marr, 2010; McGurrin, 2011; Reef et al., 2014, Young & van Loon, 2014). Additionally, atrial disease might be associated with recurrent premature atrial complexes (SVPD) that can act as triggers for recurrent AF after successful treatment. A sudden change in performance and results compared to previous veterinary examinations, provide the best estimate sign for the onset of the AF. When this information is lacking, it should be assumed that AF is long-standing. Significant LA enlargement reduces the likelihood of successful cardioversion and increases the risk for recurrence (Reef et al., 2014). For that reason, in both, Case III and IV, on the following days after TVEC, ECG and echocardiography were performed to control the treatment.

The level of intended activity influences the clinical decision as sustained AF is likely to limit high level athletic work, and occasionally impairs performance at mid to low levels of activity. Other horses with persistent AF are able to perform successfully when used for less intense athletic work. However, cardioversion of AF is recommended when the average maximal HR during exercise at an intensity that is at, or slightly, exceeding the horse's normal activities (greater than 220 bpm) (Reef et al., 2014).

Although uncommon, collapse during exercise has been reported with AF. Additionally, ventricular ectopy during exercise or during SNS stimulation indicates a possible risk for SCD (sudden cardiac death), particularly when short R-R intervals or R-on-T phenomenon are observed, as observed in case III. AF associated with exercise-induced VA (ventricular arrhythmias) resulting in SCD has been documented in at least one horse. For this reason, treatment for AF is also recommended when concurrent VA is observed (Verheyen et al., 2013; Reef et al., 2014).

Management strategies for AF include no treatment, pharmacologic cardioversion, and transvenous electrical cardioversion (TVEC). Horses with CHF and AF should be treated for CHF and are not candidates for cardioversion (Reef et al., 2014).

Cardioversion is generally not performed for the first 24–48 hours of a documented recent onset of AF, because spontaneous cardioversion might occur. Nevertheless, according to Young & van Loon (2014), horses should not be treated for the first 72–96 hours. However, after spontaneous cardioversion, an evaluation is still indicated, including measurement of serum K^+, and Mg^{++}, fractional excretion of K^+ (in racehorses), echocardiography, continuous 24-hour ECG, and optimally an exercising ECG test to

identify atrial triggers or other arrhythmias. These tests are also appropriate in a horse with NSR if paroxysmal AF is suspected from the clinical history. However, if AF persists beyond 48 hours, prompt treatment of AF is recommended to stop progressive atrial remodelling (Reef et al., 2014).

Cardioversion is desirable in all horses performing athletic work. Successful treatment allows a return to the previous level of performance, assuming an absence of clinically relevant underlying cardiac disease. Cardioversion of AF should only be performed in a controlled setting with continuous (ECG) monitoring, regardless of the treatment method. There are no prospective, randomized studies directly comparing the efficiency of quinidine to TVEC. Success rates of 65–90% have been reported for both. Young racehorses with lone AF probably have a better prognosis for successful cardioversion, independent of treatment modality (Reef et al., 2014). A study by De Clerq et al. (2006), presented amiodarone for the first time as an efficient and tolerable treatment for horses with chronic AF. Amiodarone is a class III anti-arrhythmic drug, used frequently in humans, which offers a completely different pharmacodynamic approach.

TVEC provides a therapeutic option for the management of AF in the horse, when drug therapy is not viable, and also as a first line therapeutic choice. The advantages of TVEC include the avoidance of drug related side effects and toxicity, success in long-standing AF, and decreased convalescence (McGurrin et al., 2005). TVEC involves a timed shock delivery on the R-wave. The procedure should be performed by experienced operators using specialized equipment, and it is performed at the Faculty of Veterinary Medicine of the University of Gent. TVEC can be used to treat lone AF, AF with mild LA enlargement, horses either intolerant or unresponsive to quinidine treatment, horses in which quinidine is contraindicated (as in case VI, in which it showed signs of toxicity), and horses with Atrial Tachycardia (as observed in case VII) (Reef et al., 2014; Young & van Loon, 2014). The risks of TVEC include the ones related with general anaesthesia or rarely, development of a fatal arrhythmia. Electrical cardioversion is painful, therefore it always needs general anaesthesia, which carries risks for morbidity and death (Young & van Loon, 2014). None of the cases presented any of this complications.

The immediate recurrence of AF (IRAF) within the first 24 hours after cardioversion, although infrequent, is more likely than with quinidine cardioversion. Pre-treatment with antiarrhythmic drugs before TVEC, or administration of an antiarrhythmic drug during and after anaesthesia might minimize the likelihood of IRAF (De Clercq et al., 2006;

Young & van Loon, 2014; Reef et al., 2014). In the long term, recurrence rates after TVEC and quinidine cardioversion are believed to be similar (Reef et al., 2014).

On the 24h- recording ECG of case III after TVEC, 80 atrial premature beats (APCs), and 160 ventricular premature beats (VPD) were observed. Most atrial premature beats were seen during stress situations. Some APCs were shortly coupled (risk for AF recurrence). Recurrent atrial arrhythmias can be found in some horses following successful cardioversion, both pharmacological and electrical, (such as atrial tachycardia) and these are well identified using a continuous 24-hour ECG (Patterson, 2002; Bowen, 2014; Reef et al., 2014).

However, the optimal timing of this examination, the influence of premature atrial complexes on long-term prognosis, and the best approach to management of recurrent atrial ectopy are unknown (Reef et al., 2014).

Although successful cardioversion results in immediate restoration of sinus rhythm, atrial contractile dysfunction can persist longer due to AF-induced atrial remodelling (Decloedt et al., 2013). A complete echocardiogram after cardioversion can evaluate LV and LA mechanical function and reassess heart size and valvular function. A study by Decloedt et al (2015), hypothesized that horses with more severe atrial contractile dysfunction at 24 hours after cardioversion, could be more likely to suffer recurrence. However, echocardiography 24 hours after cardioversion to assess atrial contractibility has the major limitation of the possible interference with the antiarrhythmic drugs.

LV function should return to normal within 3 days. Recovery of LA contractile function can occur within a few days or might take several weeks when AF has been long-lasting (Reef et al., 2014). In case III, the atrial function and diameters were measured 1 week after TVEC, and the peak velocity of contraction measured by Doppler imaging was low, but just within the reference values. Allowing full atrial reverse remodelling is advisable before returning to maximal exercise, in order to decrease AF recurrence (Decloedt et al., 2013). However, it will always depend on the chronicity of the arrhythmia (Young & van Loon, 2014)

Accurate quantification of atrial dysfunction can help in determining the rest period after cardioversion (Decloedt et al., 2013). Ideally, rest is enforced until atrial electrical and contractile function has normalized or nearly so. Horses with paroxysmal AF and short-duration lone AF can return to training within 1 week, unless LA abnormalities or post-

conversion arrhythmias are detected. Horses with long-standing AF might need a month or longer of rest (Reef et al., 2014).

In conclusion, recurrence of AF is therefore higher in horses with underlying cardiac disease, especially chronic valvular regurgitation with atrial enlargement. Persistent LA mechanical dysfunction is thought to indicate irreversible atrial remodelling and might also represent a poor prognostic sign (Reef et al., 2014).

Supraventricular premature depolarizations, Premature Atrial Complexes, or Atrial Premature Complexes (APD) are observed in case VI and X, they are characterized as being isolated cardiac contractions noted to follow too early in an otherwise normal rhythm during cardiac auscultation, or pulse palpation. The first heart sound of the premature beat usually has a normal or decreased intensity (Young & van Loon, 2014).

At times, APDs are difficult to differentiate from marked sinus arrhythmia. APD are an uncommon cause for poor performance. The greatest concern about APD lays on the potential to induce atrial flutter and AF (van Loon, 2011; Reef et al., 2014).

The ECG is needed for definitive diagnosis, and continuous ECG monitoring enables the clinician to more completely characterize the atrial ectopy. APDs are characterized by ectopic, premature atrial activation (P0), usually with changes in normal P-wave morphology. APDs can be conducted with a variable P0-R interval or blocked at the AV node. Also are easily missed when buried in the ST segment or T wave, especially at higher HR. The conducted QRS is generally normal in morphology, but ventricular conduction can be aberrant resulting in wider, taller or bizarre QRS complexes with secondary ST segment and T wave changes (Reef & Marr, 2010; McGurrin, 2011; Reef et al., 2014).

Case VI had multiple APDs on the ECG at rest. An exercise ECG was performed, and while walking the horse still had APDs, but during trot and gallop the horse presented a regular heart rhythm. However, the horse presented frequent atrial premature depolarizations (APDs) which were short-coupled, that often occurred in the T-wave or immediately after the QRS complexes. No other remarkable findings were reported. On its second appointment, a 12-hour ECG was performed, and 432 APDs and 1 VPD were recorded.

In case X, the ECG at rest showed sinus rhythm and atrial extrasystols especially after stressful moments. No remarkable abnormalities were found on the echocardiography.

On the exercise ECG the mare showed normal sinus rhythm, even while there were other horses near the arena. After the work, the heart frequency dropped, and the horse showed again some APDs. However, according to a study by Buhl et al. (2013), more than 50% of the horses develop SVPCs during racing or in the immediate recovery period, and this may not be necessarily associated with poor performance. Therefore, it doesn't need to be considered an abnormal finding by itself.
For case VI it was advised that the horse shouldn't compete. However, case X could be ridden normally. This happened because case VI represented a bigger risk for development of Atrial Fibrillation.

Premature Ventricular Complexes, Premature Ventricular Depolarizations or Ventricular Premature Depolarizations (VPD), were observed in cases I, II, and IV, and are usually detected during auscultation, characterized by premature beats interrupting an otherwise regular rhythm, usually followed by a compensatory pause (Reef et al., 2014). These arrhythmias are the result of abnormal electrical activity originating in the ventricles, which results in premature contractions. The significance of VPDs is debatable, and generally they are considered indicative of myocardial disease (Buhl et al., 2013; McGurrin, 2011).
Occasional VPDs, may be clinically insignificant, not requiring any treatment (Bonagura & Reef, 2004; Durando, 2003). Rest is recommended for horses with frequent ventricular premature complexes, and the arrhythmia seems to resolve spontaneously after 4 to 8 weeks of rest (Bonagura & Reef, 2004).
During sustained ventricular tachycardia, a fast (usually in excess of 100 bpm) regular rhythm will be noted by auscultation. Horses with sustained ventricular tachycardia for 150 bpm or more, eventually develop biventricular heart failure and will often develop jugular pulsations, ventral oedema and even ascites within 1–3 days (Young & van Loon, 2014).
The approach to the horse with ventricular arrhythmias should be ruling out the non-cardiac causes, correcting them (if such is possible), and then following if necessary with a complete cardiovascular examination, including electrocardiography and echocardiography (Bonagura & Reef, 2004).
VPD are characterized by premature ventricular activation without an associated P wave. The QRS complex is typically wide and bizarre and followed by a large T wave of

opposite polarity (Bonagura & Reef, 2004; Reef & Marr, 2010; McGurrin, 2011; Reef et al., 2014). Impulses arising from high in the ventricle (near the bundle of His) can be difficult to distinguish from a junctional (nodal) rhythm (Reef et al., 2014).

Defining the safety risks to the horse and to the rider or driver is paramount in cases of ventricular ectopy. The complexity of a ventricular arrhythmia is presumed to relate to the risk of hypotension and sudden cardiac death (SCD) because of the risk of development of ventricular fibrillation (VF). However, risk stratification for VA is imperfect. In the absence of clear evidence, the panel believed recommendations should be biased toward safety, as opposed to maintaining athletic activity (Reef et al., 2014).

A history of collapse raises great concern in a horse with VPD (Reef et al., 2014). Although, for none of the horses studied a history of collapse was reported. Similarly ventricular ectopy in association with important structural heart disease (and cardiomegaly) poses another long-term safety concern (as discussed above, exercise ECGs are generally recommended for those horses) (Reef et al., 2014).

Detection of systemic hypotension during a documented run of VT is another indication of a serious arrhythmia. Also, Verheyen et al. (2013) reported that ventricular ectopy occurs frequently in horses with AF. But in the absence of clinical signs, or serious structural heart disease, the risk of ventricular ectopy is usually defined by electrocardiographic characteristics, accepting its limitations. This assessment includes the morphology, timing, and rate of the ectopic activity (Reef et al., 2014).

The origin of the VPD dictates the morphology of the QRS complex. When the premature complex originates in the ventricular myocardium the QRS morphology appears most wide and bizarre. A junctional premature complex is a premature beat arising in the AV junction or His-Purkinje system. If the premature complex originates high in the Purkinje network it will be conducted using the normal pathway, and may not appear wide and bizarre., there is typically a small change in the R or S wave of the QRS complex (Allen et al., 2016).

According to Reef et al. (2014) the following are features of complex or potentially *malignant* VA: multiform or polymorphic QRS morphology; short coupling intervals (especially R-on-T timing); sustained VT; rapid ventricular rate (exceeding 120 bpm); and repetitive ectopic activity (couplets, VT). Polymorphic VT can be observed with diffuse myocardial disease or with drug toxicity (quinidine toxicosis) and induces both hemodynamic and electrical instability. Conversely, the well tolerated accelerated

idioventricular rhythm tends to be monomorphic, start with a relatively long coupling interval, and become established at relatively slow ventricular rates (50–80 bpm at rest). Occasional monomorphic VPD overdriven with exercise or only detected in the immediate post-exercise period are not usually a cause for poor performance. A wide range of Ventricular Arrhythmias (VA) occur during and immediately after intense exercise in normally performing horses. The importance of these arrhythmias and the risk of sudden cardiac death requires further investigation. VPD can also occur during exercise and are a cause of concern (Ryan et al., 2005; Jose-Cunilleras et al., 2006; Physick-Sheard & McGurrin, 2010; Buhl et al., 2013; Reef et al., 2014; Young & van Loon, 2014), which means that the exercise ECG is of great importance.

In case I, the ECG at rest revealed sinus rhythm with numerous monomorphic VPD. During exercise ECG numerous monomorphic VPD were found as well. After the resting time, the horse was taken to the arena and lunged (trot). Increased heart frequency originated premature ventricular complexes (8 VPD while trotting). Case II exhibited 110 monomorphic ventricular extrasystols during exercise. On case IV second appointment, the ECG at rest and exercise, recorded for approximately 57 minutes, registered 102 VPD with 2 different morphologies.

Their relationship with poor performance is also uncertain and requires further investigation (Reef et al., 2014), only case II presented poor performance complains.

Assessment of the overall clinical picture is important because VA can be associated with medical or surgical disorders, and often resolve with correction of the underlying problem. A clinical laboratory profile, including plasma or serum cardiac troponin I (cTn I) concentration should be obtained from affected horses (Reef et al., 2014). Also, an echocardiogram might be valuable in any horse with VA (Jesty, 2014), this test is specifically recommended for horses with VT or complex VA; when VA is recurrent or persistent; or when VA is identified in the clinical settings of poor performance, collapse, a clinically relevant cardiac murmur, or a moderately to severely increased cTn I (Reef et al., 2014).

Case I presented a murmur, and the echocardiography showed only a thickening of the tricuspid valve, and an abnormal movement pattern during the closing of the tricuspid valves. Case II echocardiography showed a very slight regurgitation of the mitral valve (no clinical significance). All diameters were just within the normal reference values. During rest he had a normal sinus rhythm. Although, during labour the gelding showed

numerous monomorphic VPD. In all these cases the principle of safety was applied, and for none of the horses it was advised to work normally.

On its first visit, case IV was in shock condition, and revealed multiple VPDs with 3 different morphologies on ECG at rest, and showed multiple areas of density on the myocardium of the left ventricle on the echocardiography.

In horses with sustained VT, the echocardiogram should be repeated once the horse has returned to NSR. A continuous 24-hour ECG should also be obtained to more completely evaluate the VA as they are often intermittent. Further workup of a horse with VPD or accelerated idioventricular rhythm, in the absence of underlying systemic disease, should include an exercising ECG. Horses with VT or complex VA should not be exercise tested (Reef et al., 2014).

The therapeutic aims are to treat the underlying disease process, restore normal electrolyte and acid–base status, return the heart to normal sinus rhythm if the ventricular rhythm disturbance is life threatening, and abolish abnormal ventricular automaticity (Jesty, 2014; Young & van Loon, 2014). It is a general rule that an arrhythmia should always be considered in the context of the horse's concurrent disease (Young & van Loon, 2014).

Premature depolarizations are usually associated with hypoxia, myocardial disease, electrolyte and metabolic disturbances, elevated sympathetic tone, fever and toxaemia. Therefore the first therapeutic goal is to treat the predisposing disorders rather than the arrhythmia itself. Treatment of a ventricular rhythm disturbance with antiarrhythmic agents is only warranted when there is obvious decrement to cardiac function as a result of the abnormal rhythm, or if the rhythm is likely to worsen into a more life-threatening arrhythmia (such as ventricular fibrillation) (Bonagura & Reef, 2014; Young & van Loon, 2014).

Case I and II could only be rested and work lightly before being rechecked to evaluate if the horses were safe to work again. But case IV presented too many VPDs, therefore a higher risk of developing VT and VF which is seriously life-threatening, and thus the mare wasn't safe to work anymore.

Atrial Tachycardia is present in case VII, and it may indicate underlying atrial myocardial disease. The underlying pathology is unknown, and is characterized by multiple APCs and AT with a rate often between 100 and 200 bpm. The QRS complexes are normal in appearance and are proceeded by a P wave. The P wave can have an abnormal

comformation, and can also be superimposed by the T wave (McGurrin, 2011). A thorough clinical examination and laboratory evaluation should be done in order to try to identify any underlying diseases. Atrial tachycardia is occasionally seen during quinidine conversion of AF (Patterson, 2002).
The echocardiography confirmed that there were no cardiac abnormalities. On the exercise ECG (with the standardized lungeing test: 5 minutes walking, 10 minutes trotting, and 5 minutes galloping) confirmed that over a heart rate of 150 bpm, the heart rate was proportional to the effort required as in a normal horse. The contractile function of the left atrium (confirmed with tissue Doppler) during atrial tachycardia was within normal values. Even though it didn't worsen during the exercise, it was treated with TVEC, in order to restore the normal sinus rhythm.

4.2 Exercise testing

Throughout all these ten cases, the standardized lungeing exercise ECG was essential for the formulation of the definitive diagnosis and prognosis of the disease. The value of electrocardiography of horses at rest is limited, because cardiac diseases and disturbances in cardiac rhythm, leading to decreased performance, only rarely manifest themselves during rest (Buhl et al., 2013).

Scheffer & van Oldruitenborgh-Oosterbaan (1996) published a study with the purpose of developing both a satisfactory, standardized computerized method for ECG recording, and a suitable a standardized exercise test on a treadmill based on healthy research horses. A further aim was to evaluate the suitability of the test in horses with a history of poor performance and/or with arrhythmias at rest.
In this study, the horses were put on the treadmill for warming-up of 7 minutes at walk (1.7 m/s), trot (4.0 m/s), and canter (7.0 m/s). After the warming-up period, the exercise ECG was recorded for 15 minutes at walk (1.7 m/s), trot (4.0 m/s), canter (7.0 m/s with 0% and 4% inclination), and at walk again. If the heart rate stayed very high, or if (pathological) arrhythmias developed during exercise, one or more recovery ECGs were recorded after the test. The ECGs were evaluated on quality, and on arrhythmias recorded during exercise. The mean heart rates of each step of the exercise test were calculated, the rhythm was assessed, each complex was examined, and the relationship between the

complexes was evaluated. The blood variables before and after exercise were compared and a possible relationship with the ECG signal was evaluated (Scheffer & van Oldruitenborgh-Oosterbaan, 1996).

They concluded that the possibility for obtaining a reliable ECG during a standardized exercise test had potential for improving the understanding of physical fitness and the significance of resting cardiac abnormalities. An exercise ECG could be helpful in reaching a diagnosis of arrhythmias during exercise. In horses that already had an arrhythmia at rest, it could be possible to evaluate the significance of this arrhythmia during exercise. In horses with a history of poor performance, it could offer an extension of the examination protocol. They concluded that a standardized exercise test in combination with blood sampling made it possible to compare the results with reference values (Scheffer & van Oldruitenborgh-Oosterbaan, 1996). As a matter of fact, this type of protocol has been performed widely ever since.

As described by Durando (2003), and later by Franklin & Allen (2014), on a treadmill the exercise is more controlled, and can be made to replicate the desired work level more easily. With treadmill testing the exercise can be standardized, allowing to repeat examinations to assess the effect of treatment or progression of disease. It also allows more options for testing to be performed at the horse's side, which has been impossible in the field. The test can be individualized to a particular horse's athletic ability, starting from slow speeds for those horses with a history of collapse, to intense speeds for racing animals with subtle performance decreases.

Nevertheless, the horses have to learn to exercise on a treadmill (Scheffer & van Oldruitenborgh-Oosterbaan, 1996; Franklin & Allen, 2014). Franklin & Allen (2014) recommended that the horses should receive two or three acclimatization runs prior to exercise testing, but that final decisions should be based on the animal's ability to adapt to treadmill exercise. In a study be Gehlen et al. (2006), about pulmonary artery wedge pressure during treadmill exercise in warmblood horses with AF, the horses were taught to use the treadmill within three days. On the first day, they were led onto and stopped on the treadmill several times. On the third day, the procedure was repeated with all horses being walked, trotted and cantered.

The use of a treadmill requires the horse to be transported to a facility with appropriate equipment. The necessary equipment is expensive to setup and run, given that a dedicated team of several experienced people is required for each test (Couroucé-Malblanc & van

Erck-Westergren, 2014, Franklin & Allen, 2014; Durando, 2010). Ryan et al. (2005) developed a study about the prevalence of cardiac arrhythmias in horses in training, to identify factors that were associated with the occurrence of exercise-induced premature depolarisations, and to determine whether the current guidelines for interpretation of exercising ECGs in clinical cases require modification in light of findings in normal horses. They considered that the convenient mean to obtain the required data was with digital ambulatory electrocardiograph (ECG) recorders. They considered this equipment could record the ECG during vigorous exercise, avoiding the need for treadmill studies, which could be difficult to explain to the owners of healthy individuals.

According to Couroucé-Malblanc and van Erck-Westergren (2014), exercise tests can be conducted in a treadmill laboratory or in the field. There are advantages and disadvantages for both types of exercise test. An advantage of field studies is the conduct of tests in the environment likely to be used in competition (Couroucé-Malblanc & van Erck-Westergren, 2014; Franklin & Allen, 2014). The surface gaits and speeds used in a field test can be closely aligned to the demands faced during exercise in actual competition. Field tests also consider the effects of the rider, jockey, or driver that in some instances might be the weakest link in the horse's performance (Couroucé-Malblanc & van Erck-Westergren, 2014), allowing a more realistic simulation of the conditions under which the performance is considered jeopardized (McGurrin, 2015). Furthermore, field tests can be easily integrated into training sessions, it is possible to conduct multiple evaluations during a competitive season, and thus enable a regular and rational follow-up of the horse. Of course, there may be difficulties in the standardization of field exercise tests as conditions may vary over time, according to climatic or other external conditions (Couroucé-Malblanc & van Erck-Westergren, 2014; Franklin & Allen, 2014), and electrode motion artefacts are more likely in these situations (McGurrin, 2015). Couroucé-Malblanc & van Erck-Westergren (2014) considered that to reduce the effect of extrinsic variations, field exercise tests should be repeated over time.

Locomotion during treadmill exercise is quite different to that on the track. As a consequence, even if horses are given tasks on treadmills that produce similar HRs, their gaits may be quite different. Stride frequencies at identical trot and gallop speeds are greater on a racetrack. Designing the treadmill exercise tests to replicate field exercise was considered to be a 'fruitless endeavour' (Couroucé-Malblanc & van Erck-Westergren, 2014; Franklin & Allen, 2014).

Environmental conditions are an important consideration during field exercise testing. HR and other variables were compared under high and low ambient temperature and relative humidity during a submaximal incremental field exercise test in horses tested in summer and in autumn. These factors must be considered when using fitness tests in the field. Sudden changes in environmental conditions might have considerable consequences for HR and blood lactate responses during exercise. The type and quality of a track is another feature to consider, as track conditions have been shown to influence physiological variables measured and calculated during a standardized test (Couroucé-Malblanc & van Erck-Westergren, 2014). Therefore, although testing portability continues to improve, limitations still remain (Davidson, 2015).

These disadvantages might be overcome by lungeing exercise, since there's no need to teach the horse to use the treadmill, very low investment is needed in resources and specialized people, and in most cases it already makes part of the horse's training. For some authors, lungeing is considered included in field (or train) testing (Durando, 2003; Munsters et al., 2014; Durando, 2010; Davidson, 2015).

A pilot study by van Denderen (2011), which aim was to determine possibilities and threats using different exercise methods in future hyperflexion research, available in the Utrecht University repository, compared the stress showed by the horses during riding, lungeing or working on a treadmill. It concluded that lungeing and riding are training techniques that gave the horses less stress. Riding was preferred mainly because the hyperflexion posture is mostly used during riding, and during the lungeing horses were less controllable. Although, this condition doesn't apply in the context of the exercise ECG in this study in particular, and this pilot study has led to the conclusion that lungeing the horses while testing certain variables in which additional stress needs to be avoided, was indeed a good option, provided that they are trained considerably on the lunge.

According to Munsters et al (2014), in a study about exercise testing in Warmblood sport horses under field conditions, while measuring HRs, lungeing is considered a field technique of testing which provided reliable results if used consistently. The choice between the techniques (ridden or lunged conditions) was a matter of personal preference and/or pragmatic dealing with logistics or other conditions.

Therefore, to Allen et al. (2016) it was important to note that lungeing can elicit high HR in otherwise normal horses, if they are unfamiliar with being lunged, since it's also

necessary to consider whether other factors, such as anxiety and excitement, are influencing the HR particularly, if an unfamiliar place or unfamiliar exercise is used.

As an additional fact, according to Parkin (2009), lungeing as part of a normal exercise regimen was associated with a reduced likelihood of lameness in the previous two years. Horses that were regularly lunged were 0.8 times less likely to have been lame in the previous two years, than horses that were not normally lunged. This association may be due to adaptation of the musculoskeletal system to different types of exercise and potentially improved proprioceptive conditioning. It is also possible that horses being lunged were fitter or maybe warmed up and cooled down more effectively than those that are not lunged, thus reducing their predisposition to lameness.

However, according to the guidelines: Recommendations for Management of Equine Athletes with Cardiovascular Abnormalities, the work intensity should be at or slightly exceeding the horse's customary activities during exercise ECG (Reef et al., 2014). If we standardize every step of the lungeing test, it's impossible to know whether or not the work intensity was exceeded for a horse in particular with a specific workload. Unless, it can be adapted as possible with the help of the owner or the rider themselves, who can be the ones lungeing the horse in the first place. This can also help them feel more comfortable in an unfamiliar place. Nonetheless, the 'fast gallop' may include the unexpected sympathetic stimulation needed: 'Some method of inducing unexpected sympathetic stimulation should be included in the exercise test to identify an inappropriate HR, aberrant conduction, or ectopy associated with adrenergic stimulation' (Reef et al., 2014), or maybe, additional stress may not be undesirable after all.

In fact, it is a practical technique to perform at the clinic during clinical diagnose, if an arena is available. The environmental conditions at the arena (indoor) can be just the ones where the horses feel comfortable, eliminating the environmental variables. However, the disadvantage that is always present, is the biggest advantage of field testing, which is similarity to the conditions used in competition. Field testing is commonly performed where the horse is stabled for training or competition, which is a convenience for the owners, trainers, and riders (Davidson, 2015). Just not, to all clinicians working at reference veterinarian clinics.

5. Conclusion

The importance of the exercise ECG for diagnose and prognosis during cardiac examination, and the assessment of the severity of an underlying cardiac dysrhythmias, is undeniable.

The electrocardiogram is the test of choice for confirming and diagnosing cardiac arrhythmias. In order to be able to make an appropriate diagnose of a cardiac dysrhythmia, and to predict its impact on the horse's performance, an exercise ECG should always be included in the protocol of cardiac examination, unless the horse's condition doesn't allow it to be performed.

In this study, there were cases in which arrhythmias at rest didn't reveal during exercise, and the opposite as well, which had important repercussions to the treatment and prognosis. As matter of fact, and as referred before, in horses with clinically important structural lesions, and arrhythmias, such as lone AF, that cannot be converted to sinus rhythm, exercise testing can determine if the HR is appropriate for the work performed, or if an arrhythmia deteriorates over the course of the test (Reef et al, 2014). The information given by the ECG at rest alone is very limited.

The reference reliable studies reported mainly consider field exercise test and laboratory exercise test with treadmill. Field exercise tests enable the horse to be examined in the environment in which it normally competes, whilst ridden and with tack modifications that may influence clinical findings. However, the protocols are difficult to standardize and the types of tests that can be performed are limited. Laboratory exercise tests performed in a controlled environment with sophisticated instruments enabling greater precision and accuracy in the measurement of a larger number of physiological response variables (Franklin & Allen, 2014). Although, this might be unaffordable.

Lungeing usually makes part of most horse's training. They can be walked, trotted, and galloped, and create high levels of exertion. It doesn't need sophisticated instruments and very specialized people to perform it, giving the possibility for it to be done in any veterinary clinic, as long as an arena and the wireless ECG recording equipment (Holter or telemetry) are available. This test can be included in a cardiac examination protocol with other procedures, giving good quality ECG recordings, and can also. be standardized and adapted if needed. It provides a simplified method for exercise testing, and a reliable alternative for treadmill and field testing at a clinic. The biggest disadvantage is that the

conditions aren't similar to the ones used in competition. However, it is more similar to the horse's normal exercise than the treadmill.

In the Consensus Statements of the American College of Veterinary Internal Medicine (ACVIM) and the European College of Equine Internal Medicine (ECEIM): Recommendations for Management of Equine Athletes with Cardiovascular Abnormalities, Reef et al. (2014) determined as one of the areas for future research and investigation the refining of the exercise testing for specific sports. This investigation would allow to improve the evaluation of the horse's poor performance variables according to its specific workload, and give better data to analyse slighter changes.

The most important factor, which is independent of the test used, is the diagnostic value of the exercise test according to the patient's condition, the circumstances of the clinical examination, the veterinarian's preferences and experience, and most importantly, the resources available.

Without being the perfect test, and considering its advantages and disadvantages, the diagnostic value of the lungeing exercise test in this study for cardiac evaluation of arrhythmias at the clinic, was considered to be very good, and provided reliable information to formulate both diagnosis, treatment and prognosis.

C. References

Allen K. J., Young L.E., Franklin S.H. (2016). Evaluation of heart rate and rhythm during exercise. Equine veterinary education, 28, 2, (p. 99-112)

Belloli C., Zizzadoro (2006). Atrial fibrillation in horses: difficult diagnosis for a therapeutic orphan. Veterinary Journal, 172, 1 (p. 8-9)

Blissitt K. (1999). Diagnosis and treatment of atrial fibrillation. Equine Veterinary Education, 11, 1, (p.11-19)

Blissitt K. (2010). Auscultation. In: Marr C.M., Bowen M. (Ed.) Cardiology of the horse. (Second Edition) (p. 91), London, UK: Saunders.

Bonagura J.D., Reef V.B. (2004). Disorders of the cardiovascular system. In: Reed S.M., Bayly W.M., Sellon D.C. (Ed.) Equine Internal Medicine (Second Edition) (p. 355-446) London, UK: Saunders.

Bowen M.I. (2014). Ambulatory electrocardiography and heart rate variability. In: Hinchcliff, K.W.; Kaneps, A.J.; Geor R.J. (Ed.); Equine sports medicine and surgery. (Second Edition) (p. 127-149), London, UK: Saunders.

Bright J.M., Marr C.M. (2010). Introduction to cardiac anatomy and physiology. In: Marr C.M., Bowen M. (Ed.) Cardiology of the horse. (Second Edition) (p. 3-19), London, UK: Saunders.

Buhl R. (2015). Cardiac murmurs. In: N. Robinson E.N., Sprayberry K.A. (Ed.) Current therapy in equine medicine (Seventh Edition). (p. 510–515) St. Louis, Missouri, Saunders

Buhl R. (2010). Valvular regurgitations in the horse: the importance of an exercise ECG, The Veterinary Journal, 183, (p. 117-118)

Buhl R., Meldgaard C., Barbesgaard L. (2013). Cardiac arrhythmias in clinically healthy showjumping horses. Equine veterinary journal, 42, (p. 196-201)

Couroucé-Malblanc A., van Erck-Westergren E. (2014). Exercise testing in the field. In: Hinchcliff, K.W.; Kaneps, A.J.; Geor R.J. (Ed.) Equine Sports Medicine and Surgery. (Second Edition) (p. 25-42), London, UK: Saunders.

Davidson E. J. (2015). Evaluation of the horse for poor performance. In: N. Robinson E.N., Sprayberry K.A. (Ed.) Current therapy in equine medicine (Seventh Edition). (p. 77–80) St. Louis, Missouri, Saunders

De Clercq D., van Loon G., Baert K., Tavernier R., Croubels S., De Backer, Deprez P. (2006). Intravenous amiodarone treatment in horses with chronic atrial fibrillation. The veterinary journal, 172, 1, (p. 129-134)

Decloedt A., Verheyen T., Van Der Vekens N., Sys S., De Clercq D., van Loon G. (2013). Long-term follow-up of atrial function after cardioversion of atrial fibrillation in horses. The veterinary journal, 197, 3 (p. 583-588)

Decloedt A., Schwarzwald C.C., De Clercq D., Van Der Vekens N., Pardon B., Reef V.B., van Loon G., (2015). Risk factors for recurrence of atrial fibrillation in horses after cardioversion to sinus rhythm, 29, (p. 946-953)

Durando M.M. (2003). Clinical techniques for diagnosing cardiovascular abnormalities in performance horses. Clinical techniques in equine practice, 2, 3 (p. 266-277)

Durando M.M. (2003). Evaluation of cardiovascular function in the performance Horse. In: N. Robinson E.N. (Ed.) Current therapy in equine medicine (Fifth Edition). (p. 585–591) London, UK: Saunders.

Durando M.M. (2010). Exercise and stress testing. In: Marr C.M., Bowen M. (Ed.) Cardiology of the horse. (Second Edition) (p. 139-148), London, UK: Saunders.

Franklin S., Allen K. (2014) Laboratory exercise testing. In: Hinchcliff, K.W.; Kaneps, A.J.; Geor R.J. (Ed.) Equine Sports Medicine and Surgery. (Second Edition) (p. 11-24), London, UK: Saunders

Gehlen H., Bubeck K., Rohn K., Standler P. (2006). Pulmonary artery wedge pressure during treadmill exercise in warmblood horses with atrial fibrillation. Research in veterinary science, 81, 1, (p. 134-139)

Gilmour R.F. (2015) Electrophysiology of the Heart. In: Reece W.O., Erickson H.H., Goff J.P., Uemura E.E. (Ed.) Dukes' Physiology of Domestic Animals (Thirteenth Edition) (p. 304-314), USA, Wiley Blackwell

Gilmour R.F., Moïse N.S. (2015) The electrocardiogram and cardiac arrhythmias. In: Reece W.O., Erickson H.H., Goff J.P., Uemura E.E. (Ed.) Dukes' Physiology of Domestic Animals (Thirteenth Edition) (p. 315-324), USA, Wiley Blackwell

Hamlin R.L. (1999). Normal Cardiovascular Physiology. In: Fox P.R., Sisson D., Moïse N. S. (Ed.) Textbook of canine and feline cardiology: principles and clinical Practice. (Second Edition) (p. 25-37), Philadelphia, Pennsylvania, WB. Saunders

Hinchcliff, K.W. (2014). The Horse as an athlete, In: Hinchcliff, K.W.; Kaneps, A.J.; Geor R.J. (Ed.) Equine sports medicine and surgery. (Second Edition) (p. 3-10), London, UK: Saunders.

Hodgson D.R. (2014). The cardiovascular system: anatomy, physiology, and adaptations to exercise and training. In: Hodgson D.R., McKeever K.H., McGowan C.M. (Ed.) The athletic horse: principles and practice of equine sports medicine. (Second Edition) (p. 162-173) Elsevier Saunders.

Jensen P.N., Gronroos N. N., Chen L.Y., Folsom A.R., Defilippi C., Heckbert S.R., Alonso A., (2014). Incidence of and risk factors for sick sinus syndrome in the

general population. Journal of the american college of cardiology, 64, 6 (p. 531-538)

Jesty S.A. (2014). Cardiovascular system. In: Orsini J.A., Divers T.J. (Ed.) Equine emergencies: treatment and procedures (Fourth Edition) (p. 124-156) Missouri, Elsevier, Saunders

Jose-Cunilleras E., Young L.E., Newton J.R., Marlin D.J., (2006). Cardiac arrthythmias during and after treadmill exercise in poorly performing thoroughbred racehorses. Equine exercise physiology 7, Equine veterinary journal, S36, (p. 163-170)

Malalana F. (2015). Heart murmurs in horses – what's important and what's not. Livestock, 20, 1, (p. 52-56)

Marr C.M. (2010). Cardiac murmurs: valvular regurgitation and insufficiency. In: Marr C.M., Bowen M. (Ed.) Cardiology of the horse. (Second Edition) (p. 207-216), London, UK: Saunders.

McGurrin M.K.J. (2011). Cardiovascular System. In: Munroe G.; Weese J.S. (Ed.) Equine clinical medicine, surgery and reproduction. (First Edition) (p. 672-690) London, UK, Manson publishing

McGurrin M.K.J. (2015). Investigation of cardiac arrhythmias. In: N. Robinson E.N., Sprayberry K.A. (Ed.) Current therapy in equine medicine (Seventh Edition). (p. 77–80) St. Louis, Missouri, Saunders

McGurrin M.K.J., Physick-Sheard P. W. (2005). How to perform transvenous electrical cardioversion in horses with atrial fibrillation. Journal of veterinary cardiology, 7, (p. 109-119)

McSloy A. (2011). Cardiac auscultation and diagnostics in the poorly performing horse. Companion animal, 16, 7, (p.4-7)

Miller M.S., Tilley L.P., Smith F.W.K.J, Fox P.R (1999). Electrocardiography. In: Fox P.R., Sisson D., Moïse N. S. (Ed.) Textbook of canine and feline cardiology: principles and clinical Practice. (Second Edition) (p. 67-103), Philadelphia, Pennsylvania, WB. Saunders

Munsters C.B.M.C., van Iwaarden A., van Weeren R., Sloet van Oldruitenborgh-Oosterbaan M.M. (2014). Exercise testing in Warmblood sport horses under field conditions. Veterinary journal, 202, 1 (p. 11-19)

Parkin. T. (2009). How not to train sport horses: detrimental regimens and exercises. In: Lindner A. (Ed.) Applied equine nutrition and training: Equine nutrition and training conference (ENUTRACO) 2009 (p. 131-137), The Netherlands, Wageningen Academic Publishers

Patterson M. (2002). Equine Cardiology. Consulted at: 1st of March 2016; available at: http://www.provet.co.uk/equinecardiology/

Physick-Sheard P.W. (2013). Seek and ye shall find: Cardiac arrhythmias in the horse. Equine Veterinary Journal, 45, 3 (p 270-272)

Physick-Sheard P.W. (2016). Equine electrocardiography revisited. Equine veterinary education, 28, 2, (p. 65-67)

Physick-Sheard P.W., M.K.J. McGurrin (2010). Ventricular arrhythmias duringa race recovery in standardbred racehorses and associations with autonomic activity. Journal of veterinary internal medicine, 24, (p. 1158-1166)

Pool, D.C.; Erickson H.H. (2014). Heart and vessels: function during exercise and training adaptations. In: Hinchcliff, K.W.; Kaneps, A.J.; Geor R.J. (Ed.) Equine sports medicine and surgery. (Second Edition) (p. 667-689), London, UK: Saunders.

Rastagi S.C. (2007). Essentials of animal physiology. (Fourth Edition) (p. 248-257), New Delhi, New Age International

Reef V.B., Bonagura J., Buhl R., McGurrin M.K.J., Schwarzwald C.C., van Loon G., Young L.E. (2014). Recommendations for Management of Equine Athletes with Cardiovascular Abnormalities. J Vet Intern Med 2014; 28, (p. 749–761)

Reef V.B., Marr C.M., (2010). Dysrhythmias: assessment and medical management. In: Marr C.M., Bowen M. (Ed.) Cardiology of the horse. (Second Edition) (p. 159-178), London, UK: Saunders.

Reef V.B., Reimer J.M., Spencer P.A. (1995). Treatment of atrial fibrillation in horses: new perspectives. Journal of Veterinary Internal Medicine, 9, 2, (p. 57-67)

Riedesel D.H. (2015). Mechanical activity of the heart. Gilmour R.F. (2015) Electrophysiology of the Heart. In: Reece W.O., Erickson H.H., Goff J.P., Uemura E.E. (Ed.) Dukes' Physiology of Domestic Animals (Thirteenth Edition) (p. 327-339), USA, Wiley Blackwell

Ryan N., Marr C.M., McGladdery J. (2005). Survey of cardiac arrhythmias during submaximal and maximal exercise in Thoroughbred racehorses. Equine veterinary journal, 37, 3, (p. 265-268)

Scheffer C.J.W., Sloet van Oldruitenborgh-Oosterbaan M.M. (1996). Computerized ECG recording in horses during a standardized exercise test. The veterinary quarterly; 18 (p. 2-7)

Schwarzwald C.C., Hardy J., Buccellato M. (2003). High Cardiac Troponin I Serum Concentration in a Horse with Multiform Ventricular Tachycardia and Myocardial Necrosis. J Vet Intern Med; 17, (p 364–368)

Sisson D.D., Ettinger S.J. (1999). The Physical Examination. In: Fox P.R., Sisson D., Moïse N. S. (Ed.) Textbook of canine and feline cardiology: principles and clinical Practice. (Second Edition) (p. 46-64), Philadelphia, Pennsylvania, WB. Saunders

Slack J., Boston R., Soma L.R., Reef V.B. (2014). Occurrence of cardiac arrhythmias in standardbred racehorse. Equine veterinary journal, 47, (p. 398-404)

Solis C. N., Schaer B. L. D., Boston R., Slack J. (2015). Myocardial insult and arrhythmias after acute haemorrhage in horses. Journal of Veterinary Emergency and Critical Care, 25, (p. 248–255)

Stephenson R.B. (2013). Electrical activity of the heart. In: Klein B.G. (Ed.) Cunningham's textbook of veterinary physiology (Fifth Edition) (p. 171-186), Missouri, Saunders

Stephenson R.B. (2013). The electrocardiogram. In: Klein B.G. (Ed.) Cunningham's textbook of veterinary physiology (Fifth Edition) (p. 188-198), Missouri, Saunders

Stephenson R.B. (2013). The heart as a pump. In: Klein B.G. (Ed.) Cunningham's textbook of veterinary physiology (Fifth Edition) (p. 200-211), Missouri, Saunders

Van Denderen J.G. (2011). Do horses show more stress during riding, lunging or working on a treadmill?. Consulted at: 28th of March, available at: http://dspace.library.uu.nl/bitstream/handle/1874/192734/Do_horses_show_more_stress_during_riding,_lunging_or_working_on_a_treadmill,_Judith_van_Denderen

Van Loon G. (2011). Atrial Premature Complexes and Atrial Tachycardia. In: Wilson D. A. (Ed.) Clinical Veterinary Advisor – The Horse (First Edition) (p. 54–55), Missouri, Saunders

Van Loon G. (2014). Clinical significance of cardiac murmurs: get the sound and rhythm!, 10th Veterinary sport horse conference, Amsterdam, The Netherlands

Van Loon G., Patterson M. (2010). Electrophysiology and arrhythmogenesis. In: Marr C.M., Bowen M. (Ed.) Cardiology of the horse. (Second Edition) (p. 59-73), London, UK: Saunders.

Verheyen T., Decloedt A., De Clercq D. Deprez P., Sys U.S., van Loon G., (2010). Electrocardiography in horses – part 1: how to make a good recording. Vlaams Diergen. Tijds. 79, 331-336.

Verheyen T., Decloedt A., De Clercq D. Deprez P., Sys U.S., van Loon G., (2010). Electrocardiography in horses – part 2: how to read the equine ECG. Vlaams Diergen. Tijds. 79, 337-344.

Verheyen T., Decloedt A., Vekens N.V., Sys S., De Clercq D., van Loon G. (2013). Ventricular response during lungeing exercise in horses with lone atrial fibrillation. Equine Veterinary Journal 45**,** 309–314.

Young, L.E.; Van Loon, G. (2014). Diseases of the heart and vessels. In: Hinchcliff, K.W.; Kaneps, A.J.; Geor R.J. (Ed.) Equine sports medicine and surgery. (Second Edition) (p. 695-743), London, UK: Saunders.