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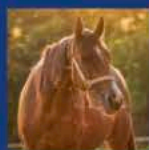
THE QUARTERLY MAGAZINE

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REDUCING THE RISK OF EXERCISE-ASSOCIATED SUDDEN DEATH (ESAD) WILL TECHNOLOGY HELP?

In racehorses, exercise-associated sudden death – or EASD – is a very rare event but, the miserable events at Cheltenham last November where three horses died on the same day, drew considerable negative attention to the condition and highlight a need for better understanding of why it happens as well as motivating vets, researchers and horsemen to do more to prevent it.



Cheltenham drew a spotlight to the problem but EASD was already the focus of international effort: in June 2024, Woodbine Racecourse, Toronto hosted the International Horseracing Federation's (IFHA) Global Summit on Equine Safety and Technology where EASD was one of two major workshop topics. This international event was sponsored by Cornell University's Harry M. Zweig Memorial Fund for Equine Research, The Hong Kong Jockey Club Equine Welfare Research Foundation, and Woodbine Entertainment Group. Specialist veterinary clinicians, pathologists and researchers spent two days sharing knowledge and ideas and debating how tangible improvements to equine safety and welfare in racing could be made towards reducing the prevalence of both EASD incidents and severe musculoskeletal conditions.

► What is EASD?

The term EASD is used to describe a fatal collapse in a previously healthy horse either during or shortly after exercise. Currently, across the world, different time-windows are used by regulators which makes quantification of the problem challenging. A benchmark definition is needed so that the occurrence rates can be audited and the EASD workshop team advised that an international definition is adopted to define EASD as within approximately one hour after exercise. Figures from the BHA show that in the UK, the 2024 EASD incident rate was 0.04% or 4 horses per 10,000 starts – which with just under 90,000 runners translates to 36 EASD losses for the year which is why the triple Cheltenham deaths were so extraordinary. The UK's rate is comparable with other nations such as Australia and a little lower than the USA although the different definitions used in different racing jurisdictions make direct comparisons challenging.

► Four broad EASD categories

The most authoritative international study looking at causes of EASD was performed with the Horserace Betting Levy Board supported by a group in the University of Edinburgh's Royal Dick School of Veterinary Studies. This report showed that



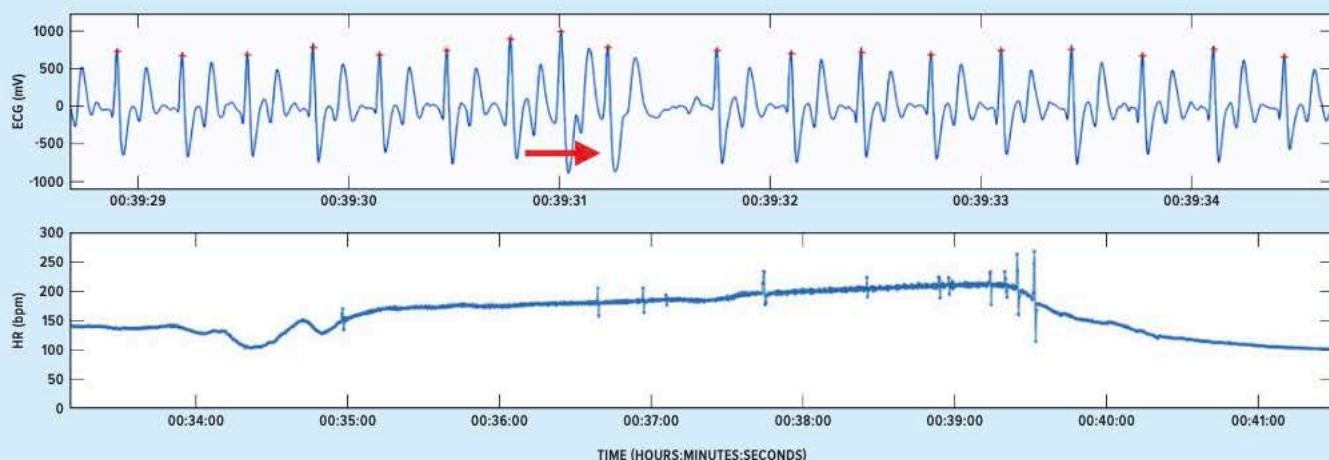
determination of cause of death is significantly impacted by individual pathologist's interpretation of findings, however, in broad terms about a quarter of cases of EASD have a clear and definitive diagnosis of cardiopulmonary failure and a further 10-15% have necropsy findings which are strongly suspicious of cardiac or pulmonary failure; around 10% of EASD cases are due haemorrhagic shock brought on by rupture of a major blood vessel which is most commonly within the abdomen, while unfortunately around 20% of cases are unexplained despite detailed examination. A range of other rare conditions including brain and spinal problems, often relating to trauma, account for the remainder.

Within the cardiopulmonary failure category, it is generally accepted that the majority relate to cardiac arrest. This means that the cardiac rhythm is disrupted but, in fact it is actually very difficult to prove that a cardiac rhythm disturbance has been the trigger mechanism of death during a post-mortem examination. In the June 2024 IFHA summit, a significant amount of the workshop was dedicated to discussing current knowledge of cardiac rhythm disturbances, why they occur and how they might be detected in future.

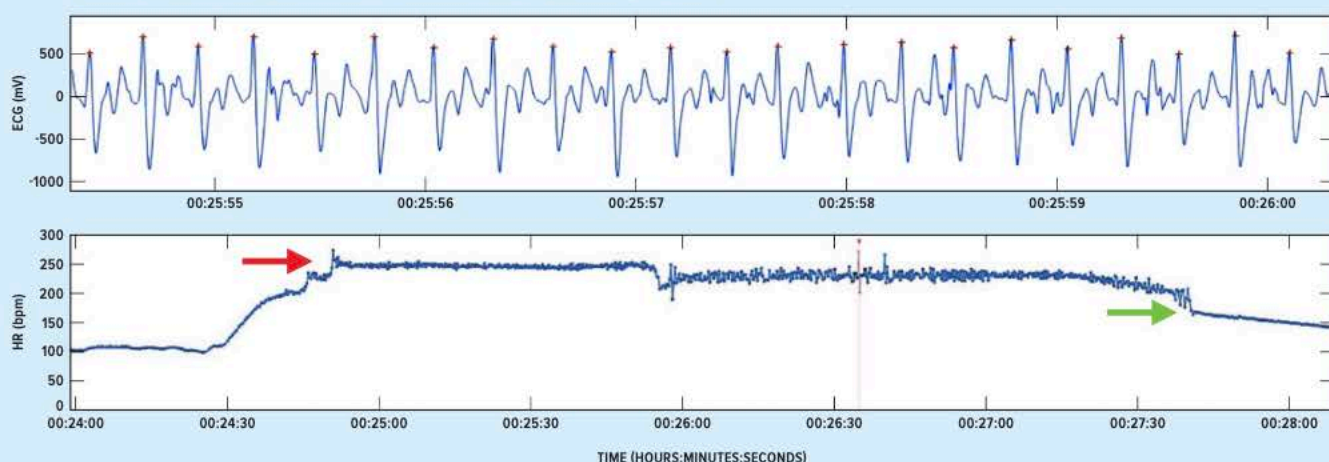
► Cardiac arrest: a "perfect storm"

Cardiac arrest can be likened to a perfect storm where multiple adverse factors combine with devastating impact. Unlike catastrophic bone fractures or tendon injuries, cardiac arrest does not necessarily relate to an accumulating pathway of built-up microdamage and because of this, it is very difficult to predict cardiac arrest might occur.





ABOVE: This horse had an episode of distress on the racetrack when vets detected that the cardiac rhythm was irregular. Looking back over its training record, episodes were noted when the heart rate was higher than usual and examination of the ECG traces showed that there were cardiac rhythm disturbances. In this example, the lower panel shows a plot of heart rate over time: the spikes in the heart rate indicate individual premature depolarisations which is confirmed by examining the ECG above which shows a premature complex followed by a pause.



ABOVE: This horse has had episodes of atrial fibrillation previously: on the day this ECG was recorded, his rider and trainer noted that he was not working well. The heart rate during the training session was excessively high, approaching 250 beats per minute. The lower panel shows a plot of heart rate over time and this shows first the heart rate takes a sudden jump upwards (red arrow) and becomes fuzzy, indicating there the intervals between beats are varying. As the heart rate slows down this variation from beat to beat becomes more obvious and the ECG above confirms the rhythm is very irregular. The rhythm disturbance self-corrects at a heart rate just over 150 beats per minute (green arrow) and thereafter the plot is smooth indicating a regular heart rate. The case shows that without the training wearable, the diagnosis could not have been made because well before the horse returns to his stable, the cardiac rhythm is entirely normal again.

< For a cardiac rhythm disturbance (aka an arrhythmia) to develop three elements are required: a substrate, triggers and, in some cases, one or more modulators. A substrate refers to the structure of the heart, this can be an area of scar tissue but the heart structure does not necessarily need to be pathological and the changes in muscle content which arise as a result of athletic training may also be a substrate.

A trigger reflects a change in the cellular and tissue environment such as alteration in concentrations of different electrolytes or development of low oxygen concentrations in the tissues yet changes in electrolytes and lowering oxygen concentrations occur every time a horse gallops. Modulators are an electrophysiological characteristic of the heart which might be a permanent feature of an individual's cell make-up or more often might be a transient state such as a variation in the nervous system brought on by excitement, stress or perhaps pain.

The key point is all these independent factors have to combine to precipitate a cardiac arrest – indeed a horse might go through its life uneventfully despite the presence of a particular substrate

or it may experience these triggers on a daily basis and come to no harm. It is the coalescing of multiple factors at a given moment that precipitates the rhythm disturbance that leads to cardiac arrest.

► EASD at the molecular level

Arguably the biggest challenge we currently face in this arena is lack of knowledge of what is normal in the exercising horse. There is very little understanding of structural and electrical remodelling of the equine heart in response to exercise. We do know that the heart, just like any other muscle, will increase in size in response to training and we also know that in horses competing over longer distances such as steeplechasers, a big heart confers an athletic advantage. Exercise training can also lead to scar-tissue formation but in both human and equine athletes the importance of this pathology is uncertain. There is some evidence that fit horses also have altered cardiac electrical characteristics but again, knowledge in this field is very sparse.

Electrical activity in the heart muscle cells is controlled by ion channels – these are proteins that are sited within the cell



ABOVE: Vets currently rely on resting and exercising electrocardiograms (ECG's) to identify horses with arrhythmias.



ABOVE: Increasingly more trainers have been using wearable devices during routine training to refine their training programmes.

membranes which effectively act as gates opening and closing to allow electrolytes such as sodium, potassium and calcium to move in and out of the cell and in doing so the electrolytes carry the electrical current.

Channelopathies – or abnormalities in these ion channels - have an important role in the development of rhythm disturbances but right now, research on equine ion channels has been limited... but that is changing rapidly. Researchers in Surrey, Copenhagen and various US universities are working to understand equine channels and the genetic and acquired factors that determine how they function. As knowledge accumulates it may be possible to include tests for the molecular make-up of an affected individual in post-mortem exams – the so-called “molecular autopsy” which is improving diagnosis rates in human cardiac arrest sufferers.

So far equine studies have not found conclusive evidence of genetic mutations associated with EASD. But there is evidence for heritability in the thoroughbred: observations from Australia which have shown some stallions' and at least one mare's progeny have higher rates of EASD associations suggesting that it is likely that there are genetic elements at play in EASD. One of the key recommendations of the IFHA's EASD workshop was that tissues from both horses impacted by EASD and those dying of other causes should be banked and shared amongst researchers to underpin and promote research studies in this area.

► ECG is the cornerstone of arrhythmia diagnosis

Currently vets rely on resting and exercising electrocardiograms (ECG's) to identify horses with arrhythmias. However, there are a number of limitations to using ECG as a screening and diagnostic tool:

- ECGs can be technically difficult to perform during exercise as they are affected by motion artefact; leading to reduced quality of the trace.
- ECGs currently must be manually interpreted, which is time consuming and leads to significant intra- and inter-observer variability.
- There are no universal guidelines on how to perform the ECG; i.e. exactly where to place the electrodes, which affects the trace produced.

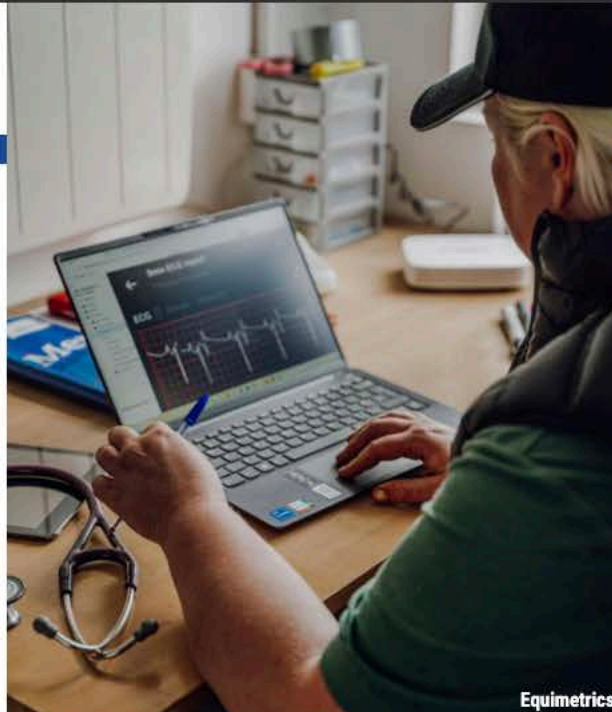
There is no consensus on interpretation of the results of an ECG examination in terms of the clinical significance of any abnormalities detected and whether the clinical presentation impacts criteria for interpretation. Indeed, we need to understand more about what is 'normal', before we can identify horses with an 'abnormal' trace.

► Will wearables change the diagnostic landscape?

Over recent years, increasingly racehorse trainers have been using wearable devices during routine training. Generally, the trainer's motivation is to collect data on speed and fitness variables in their horses to refine their training programmes but several of these devices also have the capacity to include an ECG trace. The ECG can then be accessed if the horse has a problem during a training session and, usefully, the horse's past record can also often be interrogated. The large numbers of recordings that are currently being made represents an untapped resource for collecting ECG information from large numbers of horses to better understand cardiac responses during exercise in both healthy and unhealthy individuals.



BELOW: There is an urgent need to develop AI systems which can screen training ECGs to identify those that warrant further attention.



It has been known for some time that healthy horses frequently have mild rhythm irregularities – generally described as premature complexes or premature depolarisations – these minor fluctuations in rhythm occur at all phases of exercise and particularly as their heart rate is slowing rapidly at the end of a gallop. But the dividing line between what is normal variation and what is clinically concerning is not clear-cut. We do not know exactly how much beat-to-beat variation can be classed as normal versus a sign of significant arrhythmia and we have little understanding of the relationship between premature depolarisations and other factors such as stress, exercise intensity, medical interventions and adverse clinical events.

As a result, veterinary clinicians are looking forward to the ongoing expansion of wearables as an exciting new window into equine cardiac function. Yet, the scale of the unexplored data collection currently going on in training brings with it a challenge – with so many ECG traces being rapidly collected, how can we address the mammoth task of actually looking at them? Artificial intelligence (AI) is revolutionising many aspects of modern life, including medical diagnosis. There is an urgent need to develop AI systems which can screen training ECGs to identify those that warrant further attention. And, although a large number of wearable devices are available on the commercial market, these products often lack validation which is needed before we can use the data they collect to make clinical decisions on individual animals and use the data as a research resource.

► Could we deal with EASD cases better?

Racetrack arrhythmia/collapse are, in reality, low probability but high impact events which can be difficult to manage due to their traumatic nature and the fact that they are often played out in the public eye. This is compounded by the availability of medical equipment and limited treatment options that may be futile.

However, when these events do unfortunately occur, they represent a golden opportunity to collect diagnostic information and biological samples which could be used to prevent future EASD events in other horses in the future. The combination of an ECG history, a video of the horse as it suffers the event, information from necropsy if the horse dies, and tissue banking offers valuable research insights.

The nearest parallel event from human sport is the cardiac arrests which are occasionally seen in footballers. Through the effort of football's regulators, today pitch-side emergency medical facilities are excellent and large numbers of trained staff are in attendance, all leading to the best possible outcomes for sportsmen when medical problems arise. When looking to perform cardiopulmonary resuscitation and treatment attempts in the collapsed horse, the animals' size is a major challenge; human defibrillators simply do not work in large animals.

We need more information on emergency medications that can be used in the presence of arrhythmias of unknown origin. These drugs need to be quick to administer, available and suitable to be carried by a racecourse vet, safe, effective and affordable. The IFHA's EASD group identified that in pressurised situations, pre-determined protocol approaches to both emergency treatment and necropsy procedures are invaluable and the group is working to develop these protocols for dissemination across racing jurisdictions.

► Will EASD risk always be present?

As EASD is such a rare event, it is impossible to believe that the risk of EASD can ever be removed entirely, but given the recent technological development in both veterinary science and wearables for training, there is reason to be optimistic that in the coming years, we will at last be able to improve diagnosis rates, identify some of the contributing risk factors and even potentially provide more effective emergency treatment options for these unusual but tragic episodes in our horses. **■**



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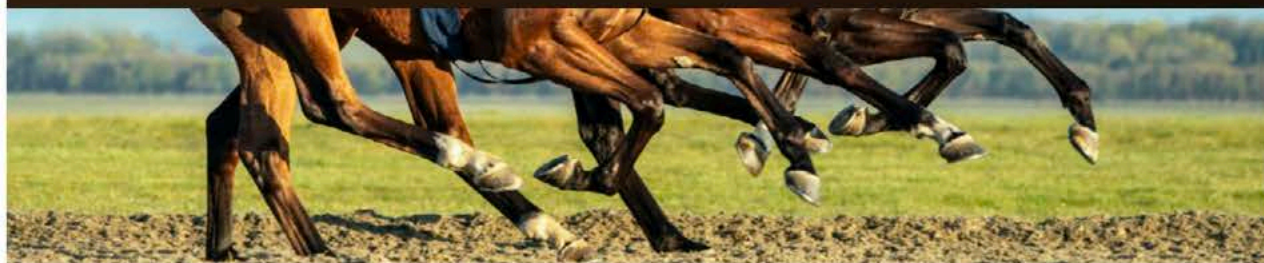
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