

IGSRV

International Group of Specialist Racing Veterinarians

Newsletter October 2013

ICRAV 2014 MAURITIUS

Peter Symons

Have you presented at either of the last two ICRAVs?

If not, perhaps it's your turn.

The ICRAV is, and always has been, primarily supported by its delegates.

If you expect independent experts to be flown in to present ... then be prepared for:

- Very high registration fees (to pay their airfares/accommodation); OR
- No ICRAV (because of the high cost of organisation/attracting experts)

The sensible and viable alternative is for each delegate to develop an interest in a topic ... and then present it to their peers.

Currently, a small number of speakers ... Parkin, Knight, Stover ... hold the Vet program. This can't go on.

Everyone has the education, opportunity and support to do this (statistics - Tim Parkin; access to journals – Peter Knight; help with English/presenting/writing papers – various). Just find a topic ... and then ask.

We respectfully suggest that IGSRV members should look at presenting at least:

- once every two conferences (if English-speaking); OR
- once every three ICRAVs (if non-English-speaking).

This ICRAV we're looking for IGSRV members to present papers on Standardbreds; on things like:

- Pre-race scratching criteria;
- Tongue-ties;
- Particular injuries and issues associated with Standardbred horses.

Novice regulatory veterinarians

Roland Devolz is keen to encourage the next generation of regulatory veterinarians.

Do you know any of these people? ... good veterinarians that we can encourage and support? Vets that haven't been, and aren't planning to attend this ICRAV?

If so, let us know (Peter Symons; kptg@globaldial.com). The Organising Committee are considering a reduced registration fee; and lower-cost shared accommodation for those that qualify.



AUSTRALIA, NEW ZEALAND AND SOUTH AFRICA BAN ANABOLIC STEROID USE

There has been a considerable shift in the attitudes to the use of anabolic steroids over the past few months. In April this year the British Horseracing Authority announced that 11 horses, all trained by Mahmood Al Zarooni under Sheikh Mohammed's Godolphin banner in Newmarket, had tested positive for steroids in out-of-competition testing. Seven of the horses were positive for Ethylestrenol while four tested positive for Stanozolol. Al Zarooni was subsequently found to have been solely responsible for the administration of the drugs, and was disqualified for 8 years. In response to the findings Sheikh Mohammed announced a ban on the use of all performance-enhancing steroids in equine sports in the UAE.

In September the Australian Racing Board (ARB) announced a total ban on the use of anabolic steroids in racehorses both in and out of training, a step that was followed by New Zealand Thoroughbred Racing in October. The ban will be introduced on 1 November in Australia and by 1 December in New Zealand, with the ruling taking effect from 1 May 2014 in order for any treated horses to be free of anabolic steroids. Anabolic androgenic steroids are banned from birth. There are no time or therapeutic exemptions of any kind. The ban applies to all unregistered juveniles and registered racehorses until their retirement as a racehorse. The ban was introduced after lengthy consideration of veterinary and scientific advice and consultation with trainers' and owners' associations. The British Horseracing Authority has undertaken to review the use of anabolic steroids and report their position to the IFHA by early 2014.

The following statement on the use of anabolic steroids was released by the Executive Council of the IFHA following its recent meeting in Paris.

1. IFHA considers that anabolic steroids have no place in horse racing.
2. The use of anabolic steroids should not be permitted in or out of competition.
3. IFHA will work with jurisdictions that may permit exceptional use for therapeutic purposes only, subject to stringent controls and a minimum stand down period to eliminate performance enhancing effects.

Modifications to the Australian Rules of Racing required to implement the ban were released on 30 October 2013.

AR 178H. (applicable to registered racehorses)

- (1) A horse must not, in any manner, at any time, be administered an anabolic androgenic steroid.
- (2) Any person who:
 - (a) administers an anabolic androgenic steroid;
 - (b) attempts to administer an anabolic androgenic steroid;
 - (c) causes an anabolic androgenic steroid to be administered; and/or
 - (d) is a party to the administration of, or an attempt to administer, an anabolic androgenic steroid, to a horse commits an offence and must be penalised in accordance with AR 196(5).
- (3) Where the Stewards are satisfied that a horse has, or is likely to have been, administered any anabolic androgenic steroid contrary to AR 178H(1), the Stewards may prevent the horse from starting in any relevant race, official trial or jump-out.
- (4) When a sample taken at any time from a horse has detected in it an anabolic androgenic steroid the horse is not permitted to start in any race or official trial:
 - (a) for a minimum period of 12 months from the date of the collection of the sample in which an anabolic androgenic steroid was detected; and
 - (b) only after an Anabolic Androgenic Steroid Clearing Certificate is provided in respect of a sample taken from the horse, such sample having been taken at a date determined by the Stewards.
- (5) Any owner, lessee, nominator, trainer and/or person in charge of a horse registered under these Rules must, when directed by the Stewards or other official appointed by the Principal Racing Authority, produce, or otherwise give full access to, the horse so that the Stewards or other official appointed by the Principal Racing Authority may take or cause a sample to be taken and analysed to determine whether any anabolic androgenic steroid is present in the system of the horse.
- (6) For the avoidance of doubt and without limitation, sub-rule (5) requires an owner, lessee, nominator and/or trainer to produce the horse, or otherwise give full access to the horse, even if the horse is:
 - (a) under the care or control of another person; and/or
 - (b) located at the property of another person.
- (7) Any person who fails to produce, or give full access to, a horse to provide a sample as required by sub-rule (5) may be penalised.

- (8) In respect of a horse registered under these Rules, where an owner, lessee, nominator, trainer and/or person in charge of a horse is in breach of sub-rule (5), the relevant horse will not be permitted to start in any race or official trial:
- (a) for a period of not less than 12 months following the day on which the horse is in fact produced to the Stewards, or full access to the horse is otherwise given to the Stewards, so that a sample may be taken and analysed for anabolic androgenic steroids; and
 - (b) only after an Anabolic Androgenic Steroid Clearing Certificate is provided in respect of a sample taken from the horse, such sample having been taken at a date determined by the Stewards.

AR 15D. (applicable to unregistered horses)

- (1) This rule applies to all horses:
- (a) born on or after 1st May 2014; and
 - (b) which are eligible to be registered under these Rules but have not yet been registered under these Rules.
- (2) The Stewards or other official appointed by the Principal Racing Authority may, at any time, direct that a horse be produced to provide a sample to be analysed to determine whether any anabolic androgenic steroid is present in the system of the horse.
- (3) Where a horse is not produced to provide a sample as directed pursuant to AR 15D(2), that horse is ineligible to start in any race or official trial:
- (a) until at least 12 months after the latter of:
 - (i) the date on which the horse, having been registered under these Rules, is allowed to start in a race under AR 45A (subject to any further conditions imposed by the Stewards in their discretion); and
 - (ii) the date on which the horse is in fact produced to provide a sample to be analysed to determine whether any anabolic androgenic steroid is present in the system of the horse; and
 - (b) only after an Anabolic Androgenic Steroid Clearing Certificate is provided in respect of a sample taken from the horse, such sample having been taken at a date determined by the Stewards.
- (4) Where a sample taken at any time from a horse has detected in it an anabolic androgenic steroid (other than an anabolic androgenic steroid which is present at or below the relevant concentrations set out in AR 178C(1)), that horse is ineligible to start in any race or official trial:
- (a) until at least 12 months after the latter of:

- (i) the date on which the horse, having been registered under these Rules, is allowed to start in a race under AR 45A (subject to any further conditions imposed by the Stewards in their discretion); and
 - (ii) the date the relevant sample was taken; and
 - (b) only after an Anabolic Androgenic Steroid Clearing Certificate is provided in respect of a sample taken from the horse, such sample having been taken at a date determined by the Stewards.
- (5) Any person must, when directed by the Stewards or other official appointed by the Principal Racing Authority, produce, or otherwise give full access to, the horse so that the Stewards or other official appointed by the Principal Racing Authority may take or cause a sample to be taken and analysed to determine whether any anabolic androgenic steroid is present in the system of the horse.
- (6) For the avoidance of doubt and without limitation, sub-rule (5) requires an owner, lessee, nominator and/or trainer to produce the horse, or otherwise give full access to the horse, even if the horse is:
- (a) under the care or control of another person; and/or
 - (b) located at the property of another person.
- (7) Any person who fails to produce, or give full access to, a horse to provide a sample as required by sub-rule (5) may be penalised.

South African Press release

The board of the National Horseracing Authority in South Africa has taken the decision to ban the use of anabolic steroids. This decision falls in line with the recent position taken by the International Federation of Horseracing Authorities.

Rule 73.4 will be introduced on 1 December 2013, with the ban taking effect from 1 June 2014, thereby giving six months for a treated horse to be free of anabolic steroids. Out of competition testing for anabolic steroids will take place randomly from 1 June 2014 onwards.

73.4 ANABOLIC STEROIDS

73.4.1 Notwithstanding anything to the contrary contained in the RULES, the TRAINER and/or the OWNER of a HORSE shall be guilty of an offence if an anabolic steroid is administered to that HORSE or if a SPECIMEN taken from that HORSE at any time contains an anabolic steroid, except in the circumstances provided for in RULE 73.4.2.

73.4.2 In exceptional circumstances, the TRAINER and/or the OWNER of a HORSE may apply in writing to a veterinary surgeon employed by the NATIONAL HORSERACING AUTHORITY ("NHA Vet") for permission to allow the administration of a single-dose of an anabolic steroid to the HORSE if there is a justifiable and recognisable therapeutic reason for such administration. Should the NHA Vet in his/her sole discretion decide to grant such permission, then:

73.4.2.1 the administration shall be supervised by the NHA Vet who shall record the details of such administration in a register specifically kept by the NATIONAL HORSERACING AUTHORITY for this purpose; and

73.4.2.2 the HORSE in question shall be ineligible to race for a minimum period of 90 DAYS after such administration.

Brief exposure to performance-enhancing drugs may be permanently 'remembered' by muscles

From: <http://jp.physoc.org/site/misc/mediacentre.xhtml>

Brief exposure to anabolic steroids may have long lasting, possibly permanent, performance-enhancing effects, shows a study published today [28 October, 2013] in The Journal of Physiology.

Previously, re-acquisition of muscle mass – with or without steroid use – after periods of inactivity has been attributed to motor learning. However, this new data from the University of Oslo suggests that there is a cellular 'memory mechanism' within muscle of brief steroid users.

The team investigated the effects of steroids on muscle re-acquisition in mice and discovered greater muscle mass and more myonuclei – which are essential components for muscle fibre function – were apparent after returning to exercise.

Professor Kristian Gundersen explains how they carried out the study and the results found:

"Mice were briefly exposed to steroids which resulted in increased muscle mass and number of cell nuclei in the muscle fibres. Three months after withdrawal of the drug

(approximately 15% of a mouse's life span) their muscles grew by 30% over six days following load exercise. The untreated mice grew insignificantly."

The findings might have consequences for the exclusion time of doping offenders as brief exposure to anabolic steroids might have long lasting performance-enhancing effects.

Prof Gundersen says:

"The results in our mice may correspond to the effects of steroids lasting for decades in humans given the same cellular 'muscle memory' mechanism. The new results might spur a debate on the current World Anti-Doping Agency (WADA) code in which the maximum exclusion time is currently two years." Additionally, the data suggests that strength training when young might be beneficial later in life since the ability to generate new myonuclei is impaired in the elderly.

Future studies should include human muscles and further investigation into the cellular and molecular mechanism for muscle memory.

THE CONTROL OF INTRA-ARTICULAR CORTICOSTEROIDS

Presented by Brian Stewart to 47th International Conference of Horseracing Authorities, Paris, October 2013.

The presentation was based on on the initiative and work of the IGSRV membership and the subsequent deliberations of the IFHA Welfare committee.

The therapeutic use of Intra-Articular Corticosteroids

The veterinary procedure of intra-articular administration of corticosteroids is a legitimate and useful treatment for joint inflammation when used appropriately and judiciously. The use of these medications is appropriate because they 'normalize' the joint environment and minimize ongoing joint damage, when combined with rest and appropriate modification of

the exercise regime. An adequate rest period from training and racing must be provided for sick or injured horses to recover.

Corticosteroids should not be used to enable the racing, training and abuse of sick or injured racehorses, nor should they be used to try to enable healthy horses to be trained harder than nature would allow.

The Problems associated with inappropriate use of Corticosteroids

There are a number of issues around the use of corticosteroids in racetrack practice.

- They may be used in the absence of a definite diagnosis.
- They may suppress the signs of joint inflammation and permit a horse to continue to cause damage to the injured joint during exercise. Continued over-use of an injured joint may lead to injury and / or the early onset of osteoarthritis and possibly catastrophic racing injury.

Arguments used to support the frequent use of IA Corticosteroids

1. "Helping the Horse"

It is sometimes argued that because of the stresses of training and racing, joint injury and the onset of degenerative disease is inevitable. Therefore the argument goes, it is humane and proper to 'help the horse' by medicating it to provide pain relief and enable it to continue training and racing as comfortably as possible. However, this approach discounts the value of working harder to minimise the risk of injury and, if it does occur, providing both treatment and modification of the training regimen to allow the horse to recover and heal.

2. Improving the profitability / viability of racehorse ownership and training

It is sometimes argued that joint disease is an occupational disease of the racehorse, therefore it is necessary to use medication to 'get horses to the track on the day' to enhance the financial viability of horse ownership (and horse training). While this argument clearly places the owner's and trainer's financial interests above that of the safety and welfare of the horse, if racehorses are 'production animals', this position may be reasonable. However,

it raises questions about how the industry wants to be perceived and whether the 'production animal' approach is sustainable in a rapidly changing social environment. The challenge is to achieve a reasonable balance.

The use of medication is often a support for less skilled training and inadequate veterinary diagnostics

The over-training / inappropriate training of racehorses is a common cause of injury. Instead of monitoring horses carefully and being sympathetic to the training needs and responses of the individual, there is a tendency for horses to be trained to a formula. There may be an over-reliance on medication to mask training problems, thus removing the motivation to adapt the training programme to the individual needs of the horse. Thus inappropriate training and treatment of the resulting injury without appropriate adaptation of the training regimen is one of the major welfare issues in horseracing. An important skill of the art and science of training racehorses is to be able to achieve peak fitness while maintaining the horse in a sound and healthy condition. The use of medication as a substitute for skilful training and preventative medicine narrows the differential between very good trainers and others, which is not consistent with the 'spirit' of sporting competition.

Is current laboratory testing for the control of IA corticosteroids adequate?

Administration of corticosteroids directly into a joint compartment means that high levels of the drug are present and confined within the inflamed joint but that blood and urine levels may be so low as to be undetectable. Therefore, blood and urine levels of corticosteroids are not an accurate reflection of persistence of the drug and its effect within the joint. As a result, laboratory testing of biological samples collected on race day at current levels of sensitivity alone does not provide an adequate level of control of abuse.

Control of IA corticosteroid use

There is scientific evidence that corticosteroids (and their pharmacological actions) persist within the joint well beyond the time the substances may be detected in plasma and urine. If regulatory authorities cannot control the abuse of a treatment by analytical testing on race day, an alternative is to impose a compulsory stand down period after treatment that protects the health and welfare of the horse (an approach that is already applied to

treatments such as shockwave treatment). The IFHA Welfare Committee has assessed that a minimum 14 day stand down period after any type of IA corticosteroid treatment achieves the objective of protecting the horse while permitting the appropriate treatment of horses in training. The formulation of the proposed minimum stand-down period for IA corticosteroids was based on the results of research and clinical observation by international experts.

The implementation of a stand down period raises the issue of how it can be enforced. Although this is a difficult problem to solve, it may be managed by:

- Out of Competition Testing
- Auditing of veterinary records
- Substantial penalties

It also raises questions about how practitioners will respond. It is possible that a 'stand-down' period after IA corticosteroid treatment may cause them to substitute other joint therapies such as IRAP, PRP (which are effectively undetectable) and NSAIDs. It can be argued that IRAP and PRP are restorative and therefore more desirable than inappropriate 'masking' treatment with corticosteroids. Although it inevitable that alternative therapies will be tried, this is not a reason to do nothing to control the abuse of corticosteroids.

Making a statement

IA corticosteroid medication is often used as a substitute for diagnosis and for the provision of an appropriate recovery period. It is important that horse racing authorities clearly state what they consider to be unacceptable safety and welfare practices....otherwise we are providing tacit approval of the practice. If we don't do something about a practice we know to be deleterious to the safety and welfare of the racehorse, who else will be the advocate for the horse (and rider)? Difficulties in enforcement should not be an excuse to abdicate leadership responsibilities

Relevant to Brian's presentation is recently published retrospective cohort study that compared the rates of musculoskeletal injury (MSI) in horses receiving local corticosteroid injection (LCI) with those that were untreated and those prior to treatment. An MSI was

defined as any limb injury identified by a veterinarian following which the horse did not race for at least 6 months, or was retired. A LCI was defined as any injection of corticosteroid into or adjacent to a synovial structure, muscle, or tendon/ligament. Of the 1911 study horses, 392 had been treated. Most LCIs were bilaterally (70.9%) and intra-articularly into the carpal (49.7%) or fore fetlock (29.3%) joints. There were 219 MSIs of which carpal injuries (47%), fore fetlock (22%) and forelimb tendon injuries (16%) were the most common. The incidence rate of MSI in untreated horses and those prior to injection was 1.22 injuries/100 horse-months, and to 4.83 following the LCI. The hazard ratio returned to levels indistinguishable from before treatment after 49 days. The hazard of MSI in horses following second and subsequent LCIs in the data collection period was greater than in horses following their first LCI.

R.C. Whitton M.A. Jackson, A.J.D. Campbell, G.A. Anderson, T.D. Parkin, J.M. Morton, L.A. Boden Musculoskeletal injury rates in Thoroughbred racehorses following local corticosteroid injection. *The Veterinary Journal*. Accepted Manuscript

HORSES RACING LEAD THE WORLD IN THE INTRODUCTION OF DRUG TESTING

Brian's presentation also raises the issue of the ethical issues surrounding medication use. It has recently been argued that horse racing lead the world in the introduction of drug control measures. The following is based on

Gleaves, J., & Llewellyn, M. (2013). Sport, Drugs and Amateurism: Tracing the Real Cultural Origins of Anti-Doping Rules in International Sport. *The International Journal of the History of Sport*, (ahead-of-print), 1-15.

Gleaves, J. (2012). Enhancing the Odds: Horse Racing, Gambling and the First Anti-Doping Movement in Sport, 1889–1911. *Sport in History*, 32(1), 26-52.

The horse racing industry has always lead the way in the regulation of drug use, and the earliest concerns expressed about doping in sport occurred in American and British horse racing near the start of the twentieth century. The issues and events that stirred interest

related primarily to the need to provide a fair gambling environment rather than the typical twentieth century concerns about safety or preserving the spirit of sport. According to Gleaves and Llewellyn, gambling influenced the development of sport rules in two ways: by necessitating both equality of opportunity to win and regulations to eliminate cheating.

In the late nineteenth century, human athletes sought to enhance their performance by using stimulants such as alcohol, strychnine, narcotics or digitalis. However, few objections were raised to the use of these performance enhancers. In fact, nothing was done to hide their use and it was not until 1928 that the first organisation controlling human sport - the International Amateur Athletic Federation banned doping among its athletes. The IOC subsequently introduced a ban on doping in 1938.

In contrast, criminal charges had been laid against alleged horse dopers in Canada as early as 1890. The eastern branch of the Jockey Club in the United States introduced a rule designed to 'put an end to the reprehensible practice of "doping" horses' in 1897. The use of drugs in horses, in contrast to humans, was at this time principally designed to impair performance – hence the origin of the term doping, which was defined by the Oxford English Dictionary in 1889 as "to administer dope to (a person, a horse); to stupefy with a drug; to drug". By 1900, a new definition had been added – "the administration to a horse of certain medical preparations, with the object of either stimulating or retarding the animal's progress in a race". The additional emphasis on enhancing performance was largely the result of the success of trainers from the United States who brought horses to the UK to race, success which prompted widespread claims of doping amongst the British aristocracy who controlled racing at the time. In 1903, the Jockey Club in the UK formally banned doping, following the lead of the US Jockey Club which had, in 1902, introduced a rule stating that 'any person who shall be proved to have affected the speed of a horse by the use of drugs or stimulants administered internally and who shall have used appliances, electrical or mechanical, other than the ordinary whip and spur shall be ruled off'. By 1912, saliva testing of horses had been introduced with the intention of detecting substances such as cocaine or opium.

Although subsequent studies have suggested that the 'doping' agents of the day had little effect on performance, Gleaves and Llewellyn believe that

“the new concern over doping in horse racing was part of a larger cultural turn towards science that had begun with the Scientific Revolution. The belief that humans increasingly could control their environment, including their horse's performance, meant that people were ready to believe that such practices worked. Although no empirical evidence supported such claims, the mindset of the horse racing community reflected the wider social belief that people could control performance through substances and injections.”

They further suggest that society's increasing concerns about the use of drugs and alcohol in the latter half of the nineteenth century may have also been significant. In contrast, they believe that bans on the use of performance altering agents by humans first emerged “to defend amateurism against the perceived nefarious forces of gambling, commercialism, professionalism and totalitarianism that were supposedly overrunning amateur sport”.

Gleaves and Llewellyn conclude that “numerous historians have noted the impact that horse racing had on modernizing sport. Indeed, much before other sports, horse racing embodied Allen Guttmann's seven characteristics of modern sport: standardization, rationalization, bureaucratization, quantification, equality, secularization and the quest for records.”

UPCOMING AMENDMENTS OF JAPAN RACING ASSOCIATION MEDICATION RULES

Fumiaki Mizobe, Kanichi Kusano (Japan Racing Association: JRA)

1. 2014 Updates on List of 'Prohibited Substances'

Effective April 1, 2014, 37 drugs are to be added to the list of 'Prohibited Substances'. Subsequent to the last year's revision of the list of 'Restricted Drugs', it is aimed to reorganize these two different categories of controlled drugs in accordance with pharmacological property.

Stimulants (21 drugs): Adrafinil, Aminorex, Amphetaminil, Ethylamphetamine, Clobenzorex, Cyclazodone, Dimethylamphetamine, Selegiline, Dextroamphetamine, Deprenyl, Fanprofazone, Fenethylamine, Furfenorex, Prenylamine, Benzphetamine, Mesocarb, Mefenorex, Modafinil, Lisdexamfetamine

Narcotics (3 drugs): Ethylmorphine, Codeine, Heroin

Tranquillizers (6 drugs): Benzodiazepine derivatives (Ketazolam, Demoxepam, Nordazepam, Halazepam, Pinazepam, Fosazepam)

Anabolic Steroids (3 drugs): Quinbolone, Testosterone, Boldione

Skeletal Muscle Relaxants (2 drugs): Guaifenesin, Methocarbamol

Beta-Agonists / Beta-Antagonists (4 drugs): Alprenoxime, Ibuterol, Bambuterol, Betaxolol

Bronchodilators (2 drugs): Aminophylline, Choline Theophylline

Psychotropic Drugs (1 drug): Carbamazepine

Opioids (1 drug): Tramadol

2. 2014 Commencement of 'Out-of-Competition Testing' by JRA

This is another newly adopted regulation that is going into effect from April 1, 2014. Out-of-Competition Testing (OCT), which is regarded as a useful method to control long acting drugs such as anabolic steroids (AS), and drug abuse during training period, has been conducted in many racing authorities worldwide. Since the AS positive scandal in the UK Godolphin stable spotlighted the issue this spring, it's now becoming a common sense internationally to consider anabolic steroids to be completely banned from birth to retirement of racehorses. OCT is expected to work as a deterrent for these drug abuses.

LATEST RESEARCH

Movement of water into the lungs of exercising horses

In horses during high intensity exercise approximately 4% of the cardiac output leaves the pulmonary circulation due to increases in hydrostatic forces and subsequent increase in perfused alveolar capillary surface area and/or reversible alterations in capillary permeability (termed stress failure) under conditions of high flow and pressure. The purpose of this study was to test the hypothesis that the movement of Cl^- from the red cell in association with CO_2 elimination into alveolar gas partially determines transvascular fluid fluxes during exercise (the Jacobs-Stewart cycle). Five horses underwent maximal exercise to exhaustion on a treadmill to exhaustion with and without acetazolamide. The study showed that acetazolamide attenuated pulmonary transvascular fluid and Cl^- fluxes during exercise, indicating that transvascular fluid fluxes in the lung are dependent on the Jacobs-Stewart cycle and that transmural hydrostatic (Starling) forces make a minor contribution.

Vengust, M., Staempfli, H., Viel, L., Swenson, E. R., & Heigenhauser, G. (2013).

Acetazolamide attenuates transvascular fluid flux in equine lungs during intense exercise. *The Journal of physiology*, 591(18), 4499-4513.

Bone Remodelling in Racehorses

The ability of bone to adapt to increased loading depends on modelling and remodelling. In bones exposed to high repetitive loads, modelling increases cortical and trabecular thickness conferring strength, stiffness and resistance to fatigue damage. Remodelling removes fatigue-damaged bone and replaces it with new bone. Stress fractures are the result of loading of a skeleton that is not adapted to its loading environment. Repetitive loading inhibits remodelling, allowing the accumulation of fatigue damage. The bones of the horse undergo intracortical remodelling. They have low cortical porosity at sites subjected to high loads, but focal cortical porosity consistent with remodelling is observed at fatigue fracture sites suggesting that the suppressive effect of repetitive loading can be overcome. Cortical bone fatigue fracture sites are also characterised by surrounding callus formation. Subchondral bone is subjected to repeated high magnitude compressive loads generated by wrapping forces from muscles and tendons. Post-mortem specimens of the

distal third metacarpal bone in 11 racehorses with condylar fractures (cases) and eight racehorses in training without fractures (controls) were compared. Under conditions of repetitive loading, the authors observed approximately double the level of erosion surface at the fatigue fracture site in cases compared with controls. Fractured bones had greater total bone volume, and remodelling at the fracture site was associated with a higher surrounding trabecular and subchondral bone area. Despite subchondral remodelling being inhibited by high magnitude repetitive loading, focal remodelling occurs at sites of fatigue failure, perhaps due to remodelling in surrounding trabecular and subchondral bone focally unloading the damaged region.

Whitton, R. C., Mirams, M., Mackie, E. J., Anderson, G. A., & Seeman, E. (2013). Exercise-induced inhibition of remodelling is focally offset with fatigue fracture in racehorses. *Osteoporosis International*, 1-6.

Risk factors for injury in young horses

The aim of this study was to identify exercise-related risk factors for carpal and metacarpal and metatarso-phalangeal (MCP/MTP) joint injury occurrence in young Thoroughbreds in flat race training. This was a 2-year prospective cohort study that collected daily exercise and joint injury data from horses in 13 training yards in England. A total of 647 horses spent 7785 months at risk of joint injury and 184 injuries were recorded. Increasing daily canter distance reduced the risk of injuries affecting the carpal or MCP/MTP joints that did not require diagnostic imaging and abnormalities of subchondral bone and/or articular margin(s) that were identified using diagnostic imaging. However, increasing canter distance increased the risk of fracture or fragmentation identified by diagnostic imaging. MCP/MTP injury risk reduced with increasing daily canter distance but increased with accumulation of canter or high-speed exercise since entering training, whereas accumulation of canter exercise was marginally associated with reduced carpal injury risk. Risk of all injury types varied significantly between trainers. The results of this study suggest that regular canter exercise is generally beneficial for joint health, while accumulation of high-speed exercise detrimentally affects MCP/MTP joints.

Reed SR, Jackson BF, Wood JLN, Price JS, Verheyen KLP. (2013) Exercise affects joint injury risk in young Thoroughbreds in training. *The Veterinary Journal* 196 (2013) 339–344

Detection of ITPP administration

Myo-Inositol tris pyrophosphate (ITPP) increases oxygen-releasing capacity of red blood cells. It is capable of crossing the red blood cell membrane. Systemic administration of ITPP has been found to increase the exercise capacity in mice. This paper reports the findings of a study in which a Standardbred mare was administered 200 mg of ITPP intravenously. Urine and plasma samples were collected up to 120 hours post administration and analyzed for ITPP by liquid chromatography-tandem mass spectrometry. ITPP was detected in post administration plasma samples up to 6 hours. The peak concentration was detected at 5 min post administration. In urine, ITPP was detected up to 24 h post administration. The peak concentration was detected at 1.5 h post administration.

Lam G, Zhao S, Sandhu J, Yi R, Loganathan D, Morrissey B (2013) Detection of myo-inositol tris pyrophosphate (ITPP) in equine following an administration of ITPP. *Drug Testing and Analysis*. DOI 10.1002/dta.1473

Prolotherapy for osteoarthritis

Prolotherapy is an injection therapy for chronic musculoskeletal pain such as osteoarthritis. The study reported was a randomized controlled trial designed to assess the efficacy of prolotherapy for knee osteoarthritis. Ninety adults with at least 3 months of painful knee osteoarthritis were randomized to blinded injection (dextrose prolotherapy or saline) or at-home exercise. Various scales were used to assess the therapeutic response – the Western Ontario McMaster University Osteoarthritis Index (WOMAC); knee pain scale (KPS; individual knee), medication use, and participant satisfaction. No baseline differences existed between groups and all groups reported improved WOMAC scores over the one year study. Adjusted for sex, age, and body mass index, WOMAC scores for patients receiving dextrose prolotherapy improved more than patients in other groups and exceeded the WOMAC-based minimal clinically important difference. Individual knee pain scores also

improved more in the prolotherapy group. Satisfaction with prolotherapy was high and there were no adverse events.

Rabago, D., Patterson, J.J., Mundt, M., Kijowski, R., Grettie, J., Segal, N.A., Zgierska, A. (2013) Dextrose prolotherapy for knee osteoarthritis: A randomized controlled trial. *Annals of Family Medicine* 11 (3) ,. 229-237.

Exercise and meloxicam metabolism

This study investigated the influence of running exercise training on pharmacokinetics of meloxicam (MXM) in rats. Animals were divided into three groups (1) sedentary group, (2) 4 weeks exercise group and (3) 8 weeks exercise group. Progressive training was adopted on a rodent treadmill machine. After single dose administration of MXM, blood samples were taken at different time points. Plasma was subjected to liquid-liquid extraction and further analyzed by a high-performance liquid chromatography (HPLC) method. Because CYP2C9 is one of most important enzymes affecting the metabolism of NSAIDs in the liver CYP2C9 activity was also measured. The results revealed that long term running exercise can increase T_{max} and decrease C_{max} and the area under curve (AUC), which could be associated with the liver microsomal CYP2C9 activity.

Wang, F. A. C. (2013). The influence of running exercise training on pharmacokinetics of meloxicam in rats. *Life Science Journal*, 10(3).

NSAIDs and Exercise

This study examined the combined effect of indomethacin (IND) and exercise on muscle and brain inflammation in mice that were exercised on a treadmill (run at 25 m min, 8% grade for 90 min) or rested for 5 consecutive days. Muscle and brain were examined for gene expression of inflammatory mediators after 5 days of treatment. While IND and exercise alone had little effect on inflammation, the combination treatment produced substantial increases in the muscle (IL-1, MCP-1 & TNF-) and brain (IL-1 & MCP-1) (P 0.05). Hematocrit and hemoglobin were decreased along with body weight (days 3-5), and run time to fatigue (days 3-5) (P 0.05) and in general, these were correlated with the increased expression of muscle and brain inflammatory mediators. The combination of IND and exercise can lead to

inflammation in both the muscle and brain that is associated with serious side effects and impaired performance in mice.

Enos, R. T., Davis, J. M., McClellan, J. L., & Murphy, E. A. (2013). Indomethacin in Combination with Exercise Leads to Muscle and Brain Inflammation in Mice. *Journal of Interferon & Cytokine Research*.

Parathyroid hormone and bone strength

Intermittent low-dose treatment with parathyroid hormone (PTH) analogues has become widely used in the treatment of severe osteoporosis. During normal physiological conditions, PTH stimulates both bone formation and resorption. However, when given intermittently, PTH has strong anabolic effects in bone. The stimulatory effects of PTH on bone formation have been explained by the so-called 'anabolic window', which means that during PTH treatment, bone formation exceeds bone resorption during the first 6 – 18 months. PTH changes gene expression in bone cells, drives bone lining cells to differentiate into osteoblasts, and enhances stem cell adhesion to bone surfaces. PTH has a direct antiapoptotic effect on osteoblasts and when PTH interferes with remodelling, the osteoblasts over-compensate. IGF is essential for PTH's anabolic effect.

Aslan, D., Andersen, M. D., Gede, L. B., de Franca, T. K., Jørgensen, S. R., Schwarz, P., & Jørgensen, N. R. (2012). Mechanisms for the bone anabolic effect of parathyroid hormone treatment in humans. *Scandinavian Journal of Clinical & Laboratory Investigation*, 72(1), 14-22.

Lactate stimulates some training adaptations

This study focused on lactate's ability to mediate changes in bioenergetic-associated parameters in liver and brain. In one group of experiments, mice underwent 7 weeks of treadmill exercise sessions at intensities intended to exceed the lactate threshold. Over time, the mice dramatically increased their lactate threshold. In the liver, mRNA levels of gluconeogenesis-promoting genes increased PGC-1 α expression increased Brain tumour necrosis factor alpha expression fell, whereas vascular endothelial growth factor A expression rose. In another group of experiments, exogenously administered lactate was found to reproduce some but not all of these observed liver and brain changes. The data

suggest that lactate, an exercise by-product, could mediate some of the effects exercise has on the liver and the brain, and that lactate itself can act as a partial exercise mimetic.

Lu, J., Selfridge, J. E., Burns, J. M., & Swerdlow, R. H. (2013). Lactate administration reproduces specific brain and liver exercise-related changes. *Journal of neurochemistry*, 127(1), 91-100.

Do something for yourself

Moderate consumption of beer is associated with lower cardiovascular (CV) risk. In a randomized, single-blind, crossover study, 17 healthy, non-smoking, men (ages 28.5 ± 5.2 years with body mass index $24.4 \pm 2.5 \text{ kg/m}^2$) consumed on three separate occasions, at least 1 wk apart: 400 mL of beer and 400 mL water; 800 mL of dealcoholized beer), and 67 mL of vodka and 733 mL water (same amount of alcohol as in the 400 mL of beer). Aortic stiffness was significantly and similarly reduced by all three interventions. The authors concluded that beer acutely improves parameters of arterial function and structure in healthy nonsmokers. This benefit seems to be mediated by the additive or synergistic effects of alcohol and antioxidants and merits further investigation.

Karatzi, K., Rontoyanni, V. G., Protogerou, A. D., Georgoulia, A., Xenos, K., Chrysou, J., ... & Sidossis, L. S. (2013). Acute effects of beer on endothelial function and hemodynamics: A single-blind, crossover study in healthy volunteers. *Nutrition*.