Orthopaedic diseases are the most common causes of lost training days or early retirement in racing thoroughbreds, traumatic osteoarthritis being the most common. There are no medical treatments that can reverse cartilage damage. However, the number of treatment options for musculoskeletal pathology in the horse has grown considerably in the last few years, mostly driven by failure to respond to previous treatments, or high recurrence of injury rates.

The term “biologics” used in equine medicine is clearly not specific, but it is generally understood to refer to use of stem cells, blood-derived products such as autologous conditioned serum (IRAP®), autologous conditioned plasma (PRP), or bone marrow aspirate. The equine sector seems to be leading the veterinary industry in the use of cell based therapies in equine practice and orthopedics.

It is important to remember that these products are not drugs, and as such will not have clear and consistent pharmacodynamics as a manufactured drug would. These biologic derived products may produce varying effects when used in different horses, and even within the same horse, the products may produce more effect on one occasion compared to another.

**MESENCHYMAL STEM CELLS (MSC)**

Mesenchymal stem cells have inherent abilities to divide into cells of a variety of different tissues. The theory of stem cell use in therapy is based upon the concept that multipotent (mature) or pluripotent (embryonic) cell populations can be deposited and attach at the site of a tissue injury. It is unclear whether the benefit is due to stem cells implanting to generate new cell lines, or if it is mainly due to causing a local release of biologic factors. A key factor driving the development of stem cells relates to immunity. When cells from another horse are infused into a horse, its body can reject them, just as patients reject organ transplants. Therefore, the most effective therapies must be based on stem cells which are less likely to be rejected.

One option to overcome rejection is to create an individualised bank at the time of birth which can be used if the horse is injured subsequently. Fresh umbilical cord blood and cells from the amniotic membrane can be obtained non-invasively into a standard blood transfusion bag at the time of foaling. Usually 150–200ml can be obtained, and can then be processed and frozen for storage. These MSCs are in much higher concentration, and they have the potential to differentiate into more varied tissue types, and their ability to develop cartilage, bone and tendon has been proven in laboratory tests. However, studies on equine cord blood showed slower and less development in lab cultures. Furthermore, studies with human cord blood show poor MSC numbers in frozen to thawed samples. However, their ability to stay at the site of injection may be better. There are commercial storage centers available for equine cord blood storage for future use.

More commonly, MSCs used in therapy today are derived from bone marrow or adipose tissue (fat) of the patient after it is injured. Stem cells are usually recovered and implanted within one patient (autogenic), but, they might be safe for use in therapy for others (allogenic). In addition, stem cells can allow for the release of growth factors and anti-inflammatory proteins, which in themselves may be the most beneficial factors in the success of stem cell treatments.

**Fig 1.** Obtaining a bone marrow sample from the sternum.
Although stem cells have been applied in a variety of conditions involving bone, tendon, and ligament, the most considerable amount of research into the use of stem cells has gone into tendon and ligament injury, more specifically, core lesions of the superficial digital flexor tendon (SDFT). According to the available research, stem cells seem to improve tendon tissue regeneration, and decrease the incidence of re-injury. MSCs are also now reported in therapy for arthritic joints, and directly into fracture sites, which may be a mechanism to accelerate fracture healing, or re-initiate healing in the case of non-unions.

**AUTOLOGOUS CONDITIONED SERUM (ACS)**

ACS was developed to obtain a concentrated preparation of a protein that is central to the healing process, interleukin-1 receptor antagonist protein (IRAP). We know that pro-inflammatory cytokines play an important role in promoting osteoarthritis, a prominent mediator in inflammation being Interleukin-1 β (IL-1 β), so the goal of IRAP is to inactivate this inflammatory pathway. However this product is generally considered a mixture of biologic factors.

The IRAP II® system works by taking a 50ml venous blood draw into a special syringe containing etched glass beads. The syringe is then stored in an incubator for 24 hours. After this it is removed and undergoes centrifugation for 10 minutes. This process usually yields 8-10 ml of serum (= 8-10 treatments) which give a product rich in growth factors that can be available for immediate injection, or placed in frozen storage.

IRAP II® can be injected locally to aid in reducing inflammation, encouraging regeneration, or can be used in support of a healthy joint with the aim of delaying disease. The product is mainly indicated for use in osteoarthritic joints, or in joints following surgery.

**PLATELET-RICH PLASMA (PRP)**

Platelet-rich plasma (PRP) is a platelet- and growth factor-rich solution made from blood. Platelets are components of blood, and although their primary function is in tissue healing and clotting, they also carry a variety of growth factors which can be
delivered to a site of injury and are released. Venous blood sample typically contains only 6% platelets, while PRP can alter this to having a sample comprised of around 94% platelets.

PRP has been most commonly used in tendon or ligament injuries, either into, or around the tendon/ligament. As these structures generally have poor vasculature, they often have difficulty healing. PRP is also thought to counter this by stimulating blood vessel formation, and collagen production. Horses undergoing this form of treatment could have a series of repeat treatments.

**SUMMARY**

With the limited number of treatment options currently available for equine orthopaedic problems, it is encouraging that we are now keenly exploring new treatments in the field of biologics and regenerative medicine. Many of these treatments hold promise for both the present and future, and although research in this field is still expanding, we still have limited scientific evidence. There are also no studies which produce good direct comparisons amongst these different biologics, so it may be difficult to ascertain which modality may be the most efficacious in a given scenario. However, it is both important and beneficial for today’s equine practitioners and surrounding industry to have a basic understanding, and consider the use of available biologic treatment options.

Photos Courtesy of: Andy Bathe MA, VetMB, DEO, DipECVS, MRCVS