

There are two main strategies for transfer using vectors. In *in vitro* transfer, the vectors are applied directly to the relevant tissue. In *in vivo* transfer involves removal of cells from the body, the gene transfer *in vitro*, and subsequent culture of these cells before they are reintroduced into the target site. Direct transfer is less invasive and technically easier, and can be started during treatment of the acute phase of the injury. A disadvantage is the non-specific infection of cells during the injection process. In addition, owing to the amount of extracellular matrix present, a vector with high transgenic activity is necessary to be able to transfer the gene to enough cells.

Indirect transfer of genes is safer. The relevant cell type is isolated and genetically modified, before reintroduction into the body, cells can be selected and tested for quality. Owing to the work involved in this technique, it would be more suitable for the treatment of degenerative processes rather than acute injuries. The first studies on the feasibility of this procedure have been conducted using marker genes.¹⁴ The main gene used, lacZ, codes for the bacterial β -galactosidase which is not present in eukaryotic cells.

The addition of a suitable substrate changes the staining properties of the cells that express the new gene, enabling the effectiveness of transmission and the duration of expression of the foreign gene to be ascertained. With the vectors currently available, the gene is expressed for six to eight weeks in tendon tissue.¹⁴ Using this strategy, the transfer and expression of the PDGF gene into the patellar tendon of rats lead to an increase in angiogenesis and collagen synthesis in the tendon over four weeks. Gene expression of this duration could influence the whole healing process of tendons and could be the start of an optimised healing process.

Concussion

What advice should we give to athletes postconcussion?

P McCrory

Good early management of concussion in athletes is important for recovery outcomes and return to play

The practical management of concussion can be divided into three broad areas where the issues and treatment priorities differ considerably. These

In summary, tendon healing, even when successful, does not result in normal tendon. Mostly, the result is functionally satisfactory despite morphological differences and biomechanical weakness compared with a normal tendon. The therapeutic use of growth factors by gene transfer seems promising in the quest to produce a new tendon that is biologically, biomechanically, biochemically, and physiologically "normal".

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and the third to the issue of return to play at a later date. It is the second of these areas that this paper will focus on.

IMMEDIATE MANAGEMENT

This is where the clinician is in attendance at a sporting event and is called on to manage the acute brain injury. The major priorities at this stage are the basic principles of first aid. Once these basic aspects of care have been achieved and the patient stabilised, then consideration of removal of the patient from the field to an appropriate facility is necessary. At this time, careful assessment for the presence of a cervical spine or other injury is necessary. The clinical

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management may involve the treatment of a disorientated, unresponsive, unconscious, uncooperative, or combusting patient? The immediate treatment priorities remain the basic first aid principles of "ABC—airway, breathing, and circulation." Once this has been established and the patient stabilised, a full medical and neurological assessment exam should follow.

EARLY MANAGEMENT

This refers to the situation where an athlete has been brought to the medical room for assessment or alternatively to an emergency department or medical facility following a concussive injury. Assessment of injury severity is generally best performed in a quiet of a medical room rather than in the middle of a football field in front of 100 000 screaming fans with television cameras following every move of the doctor.

When assessing the acutely concussed player, various aspects of the history and examination are important. These are summarised in box 1.

Box 1 Early assessment of concussion—history

- History, time and place of injury
- Mechanism of injury (eyewitness account or video)
- Presence or duration of loss of consciousness (LOC)
- Immediate postinjury behaviour
- Acute convulsive symptoms/signs
- Presence of convulsions postinjury
- Post medical history (including history of previous brain trauma)
- Medication use

The common symptoms of concussion have been examined in prospective studies and include headache, dizziness, blurred vision, and nausea.¹ It is worth noting that the presence of headache is not confined to concussion with up to 20% of sporting athletes reporting exercise related headache.² Given that much emphasis is placed upon headache as an important symptom of concussion, medical assessment needs to be accurate in ascertaining the nature and cause of the player's symptoms.

When examining a concussed athlete, a full neurological examination is important. Because the major management priorities at this stage are to establish an accurate diagnosis, and exclude a catastrophic intracranial injury, this part of the examination should be particularly thorough. Although the Glasgow Coma Scale is often used in the setting of head injury to provide a baseline assessment of conscious state, this scale is insufficiently sensitive or specific for the assessment of the majority of sporting concussions.³

In recent times the application of simple neurophysiological tests have created considerable interest as a means to objectively diagnose concussed athletes. The standard approach of asking the orientation items—for example, day, date, year, time, date of birth, etc.—has been shown to be unreliable in following concussive injury. This aspect of memory remains relatively intact in the face of concussive injury and should not be used. More useful, as demonstrated in prospective studies are questions of recent memory. These have been shown to be more sensitive in discriminating between concussed and non-concussed individuals. A typical question battery is that proposed by Maddocks et al (see box 2).⁴ The standardised assessment of concussion (SAC) is less practical but valid alternative.⁵

Box 2 Post concussion memory assessment ("Maddocks questions")

- Which ground are we at?
- Which team are we playing today?
- Who is your opponent at present?
- Which quarter is it?
- How far into the quarter is it?
- Which side scored the last goal?
- Which team did we play last week?
- Did we win last week?

Some clinicians utilise other tests of new learning or immediate and recent memory function, such as three item recall or digit span in order to determine whether post traumatic amnesia (PTA) has resolved.⁶

Having determined the presence of a concussive injury, the patient needs to be serially monitored until full recovery ensues. Consideration of return to play and the role of neuropsychological testing is not relevant at this stage until full clinical and cognitive recovery has occurred. If the concussed player is discharged home after recovery, then he should be in the care of a responsible adult.

The use of computerised tomography or magnetic resonance scanning to ascertain the presence or absence of cerebral pathology is necessary in certain situations. The geographical availability of the various imaging techniques may influence imaging strategies. It is the author's practice not to routinely scan patients with uncomplicated mild concussions—for example, game grade I or Colorado grades 1 and 2.

The treating clinician also must face the decision of who should be referred on to a hospital emergency facility or neurosurgical centre. There are a number of urgent indications that are listed in box 3. Apart from these "redbook" type

Box 3 Indications for urgent referral

- Any player who has or develops the following:
- Fractured skull
 - Penetrating skull trauma
 - Deterioration in conscious state following injury
 - Focal neurological signs
 - Confusion or impairment of consciousness >30 minutes
 - Loss of consciousness >5 minutes
 - Persistent vomiting or increasing headache postinjury
 - Any convulsive movements postinjury
 - More than one episode of concussive injury in a match or training session
 - Where there is assessment difficulty, for example, an intoxicated patient
 - Children with head injuries
 - High risk patients, for example haemophiliacs, anticoagulant use
 - Inadequate post injury supervision
 - High risk injury mechanism, for example, high velocity impact, missile injury

approaches, referral to such a centre depends on the experience, ability, and competency of the physician at hand. If the team physician happens to be a neurologist or neurosurgeon experienced in concussion management, then the clinical referral pathways will be different to a family practitioner called to assist at a football match after an injury has occurred. The overall approach should be "when in doubt, refer".

There is published evidence that the postconcussion recovery rates vary between individuals. Some patients may take days, whereas others may take weeks to recover fully from a concussive injury.^{7,8} The demands and inherent risks of a given sport as well as differences in individual recovery rates, must be taken into account when the medical decision of returning to play is taken. The main areas of cognitive impairment postconcussion relate to the domains of speed of information processing, reaction times, planning, switching mental "set", and disturbances of new learning and memory.⁹ It is the first two of these domains that provides the greatest concern. An athlete in the stages of recovery postinjury will experience several days (or weeks in some cases) of slowed thinking and an inability to process information quickly. This is the principal reason that delays return to sport with the fact that an athlete performing suboptimally will experience further injuries simply because he or she is unable to meet the cognitive demands required for that sport. In the case of motor racing, premature return to sport whilst still

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symptomatic may be fatal. To some degree this is the rationale behind the graded return to sport programmes as recommended for concussion.¹⁰ The often quoted concern regarding the so called second impact syndrome in this setting has been demonstrated to be unfounded.¹¹

When we step outside the world of sport it is clear that athletes in this post-concussive state will be at risk in the real world as well. Driving motor vehicles then becomes a significant concern. No concussed athlete should drive a motor vehicle until they are fully recovered both from a clinical and cognitive standpoint. Dangers exist in the workplace as well and these need to be factored in to the management equation. It seems somewhat bizarre that we devote enormous resources to computerised neurophysiological testing postinjury to accurately predict return to play yet when a footballer leaves our medical room or hospital emergency department, specific management advice is often lacking. The "head injury card" given out by emergency departments is typically designed for more severe brain trauma and to detect possible intracranial complications rather than provide the patient with a useful plan of management. Clearly this is a significant source of potential medicolegal claims against the doctor concerned if such advice is not given.

Does this matter? Recent work from both American and Australian emergency departments has suggested that the provision of detailed information to concussed subjects reduces their period of disability following the injury. As is the case with psychological interventions following all kinds of trauma it seems that if a patient knows what to expect and it is reassured that the symptoms experienced are both real and entirely appropriate during the recovery process then the outcome is better.¹² To some degree this is easier in sport given that most experienced sports physicians

have seen many cases of concussion and can provide a more comprehensive explanation than that by a junior casualty doctor and the athlete usually has peer support from other teammates who have been through similar injuries. The combination of these factors means that psychological disability is often minimised in the sporting setting.

In summary, the steps to good early management of concussion are as follows:

- An accurate diagnosis of concussion and exclusion of intracranial pathology by a thorough history and exam with consideration of neuroimaging if appropriate.
- A detailed (and preferably written) explanation of concussion and the normal symptoms experienced following injury. Such an explanation needs to be written in plain English rather than "medical English". Such an explanation should encompass more than the standard "head injury advice card" as used in emergency departments.
- A clear management plan given to the concussed athletes setting out the period of time off work (or school), driving restrictions where relevant, and any other restrictions to their activity. The period of restriction is should be until full clinical and cognitive recovery occurs and then the recovery should be medically documented for medicolegal reasons. In general terms, a concussed athlete should not play or train until all postconcussive symptoms have fully resolved.

- A medical follow up—for example, an outpatient appointment—where an clinician experienced in concussion and mild brain trauma can assess the recovery of the patient and provide support or guidance where indicated.
- Thorough and contemporaneous documentation of each of the above steps in the patient's medical records.

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