Head, Low-Back and Muscle Injuries in Athletes: PRP and Stem Cells in Sports-Related Diseases


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S. Zaffagnini et al. (eds.), ESSKA Instructional Course Lecture Book,
DOI 10.1007/978-3-642-53983-1_19, © ESSKA 2014
19.1 Introduction

In this chapter, we will discuss some particular topics about sports medicine. In particular, we will focus on:

Head injury:
- Skull fracture
- Facial injury
- Twitch on the pitch
- Concussion

Low-back pain and sacroiliac joint disorders:
- Strains and sprains
- Degenerative disc disease
- Disc herniation
- Spondylosis and spondylolisthesis
- Posterior element overuse syndrome
- Sacroiliac joint dysfunction

Muscle injuries:
- Sites of injury
- Epidemiology
- Treatment
- Complication
- Injury prevention

PRP and stem cells:
- PRP
- Stem cells

19.2 Head Injury

Head injury is an inherent component of combat/fighting sports such as boxing, karate and tae kwon do and may occur as a result of unintentional contact during sports such as rugby football and soccer. In other sports such as American football (NFL), the head may be used as a weapon to strike the opponent.

Concussion is thought to occur most commonly in girls soccer, American football and ice hockey [1]. Concussion comprised 33% of the injuries sustained in amateur and professional boxers observed over a 12-month period [2]. In tae kwon do championships, the head and neck was identified as the second most common area injured with rates of 18.3/1,000 athlete exposures [3]. Concussion injury rates during professional rugby union matches were 4.1/1,000 player-hours, and most of these were sustained tackling head on (28%), collisions (20%) or being tackled head on (19%) [4]. In international football, the incidence of all head and neck injuries was 12.5/1,000 player-hours with aerial challenges being the most common cause of injury (55%) [5]. Head injury rates in collegiate American football are not directly comparable although head injuries occurred at a rate of 0.21 per 100,000 participants [6].

During the sport of horse racing, riders may both sustain falls from above head height onto the head and in addition suffer the risk of being kicked or trodden on by the horse. Professional horse racing suffered six deaths due to head injuries between 1975 and 2000. Concussion occurred in 1.8–2.7 per 100 falls from 1992 to 2000. In jump racing, 126 concussive injuries occurred per 100,000 rides [7].

The majority of this chapter involves standard pitch or event side and prehospital management, which are reproduced in texts and course manuals.

The initial assessment of head-injured athletes follows the same standard safe to approach with airway and consideration and control of the cervical spine, breathing with supplementary oxygen therapy, circulation assessment with control of exsanguination, disability assessment and exposure and environmental control.

The response of the player following the head injury may change rapidly, and so a careful repeated assessment is needed particularly with airway opening and the administration of supplementary oxygen therapy.

When assessing disability, the level of consciousness may be determined by using the AVPU scale [8]. These are graduated scales of consciousness based upon the patient’s response to verbal and painful tactile stimuli. Limb movement can be noted at the point of injury together with looking at the player’s eyes. The presence of movement and alteration of papillary size with time may represent intracranial haemorrhage and increased
pressure over time. Noting these at the point of injury provides a baseline for future reference.

During the secondary survey, a more formal Glasgow Coma Scale can be determined [9]. As can be seen below, the GCS is complicated and difficult to remember; however, there are several key important thresholds. These are whether the player is confused or drowsy (GCS 13 and 14) or the patient is so deeply unconscious that they are unable to maintain their own airway (GCS ≤8) approximately equal to unresponsive on AVPU. Patients who are not verbalising may be considered to be unconscious.

The deterioration of patients on this scale may be more reliably noted than the finite score.

<table>
<thead>
<tr>
<th>Glasgow Coma Scale</th>
<th>AVPU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td></td>
</tr>
<tr>
<td>Open spontaneously</td>
<td>4 Alert</td>
</tr>
<tr>
<td>Open to speech</td>
<td>3 Responds to voice</td>
</tr>
<tr>
<td>Open to painful stimulus</td>
<td>2 Responds to pain</td>
</tr>
<tr>
<td>Remain closed</td>
<td>1 Unresponsive</td>
</tr>
<tr>
<td>Voice</td>
<td></td>
</tr>
<tr>
<td>Appropriate conversation</td>
<td>5</td>
</tr>
<tr>
<td>Confused conversation</td>
<td>4</td>
</tr>
<tr>
<td>Inappropriate words</td>
<td>3</td>
</tr>
<tr>
<td>Incomprehensible sounds</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td>Responds appropriately</td>
<td>6</td>
</tr>
<tr>
<td>Localises to pain</td>
<td>5</td>
</tr>
<tr>
<td>Flexes to pain</td>
<td>4</td>
</tr>
<tr>
<td>Decorticate posturing</td>
<td>3</td>
</tr>
<tr>
<td>Decerebrate posturing</td>
<td>2</td>
</tr>
<tr>
<td>No response</td>
<td>1</td>
</tr>
</tbody>
</table>

The management of confused players is difficult as they may not comply with simple advice and instructions. This can be a difficult area regarding cervical spine immobilisation as they have potential for a cervical spine injury at the time of their head injury and yet may not tolerate oxygen therapy or cervical spine immobilisation. Players who are combative should clearly not have their head immobilised for fear of causing iatrogenic damage. In practice, combative players should be treated with care to calm them, make them compliant and encourage them from the field of play with the consideration that a cervical spine injury may have occurred and immobilised once they have calmed to the extent that they can now be managed. A combative player is unlikely to have sustained an unstable cervical spine fracture. The greatest deformation and risk to the cord is likely to have occurred during injury. Protection against subsequent injury must be undertaken.

Event side providers are able to respond within seconds of a player sustaining a head injury. The majority of episodes of loss of consciousness are short lived, and by manually opening the airway, providing supplementary oxygen therapy with cervical spine immobilisation for a short period of time, the player rapidly recovers to an alert state in which their airway is no longer compromised. Remember not all head injuries result in a loss of consciousness and the player may present with an altered state of consciousness. These players then need to be transferred from the field of play with cervical spine precautions to allow a more thorough assessment to exclude concussion and cervical spine injury.

During a prolonged episode of unconsciousness, the patient’s airway may be considered to be in jeopardy. Manual airway opening techniques or simple adjuncts can successfully maintain the airway for short periods of time; however, for prolonged unconsciousness, a definitive airway may be required. In these situations, the player will be transferred to the hospital for further care, treatment and investigation.

Careful observation and repeated assessment must be performed in any player who sustains a head injury. Intracranial bleeding has been noted to occur after minimal force [10] and may take some time for its effects to be realised. The bleeding may be either venous or arterial with rupture of the extradural middle meningeal artery following a skull fracture. The increase in pressure from the bleeding may present as delayed-onset drowsiness following a head injury after the player has recovered from the loss of consciousness associated with the initial impact. These patients have been described as ‘talking and dying’ on account of the lucid interval. Other signs of increased intracranial pressure include reduced pupil reflexes in response to light and a fixed dilated pupil due to third cranial nerve compression. The sluggish response upon shining a penlight into the pupil in the presence of an
intracranial collection is caused by compression of the outer parasympathetic neural fibres of the oculomotor nerve with sparing of the central sympathetic nerves. Subdural accumulation is usually caused by the gradual collection of venous blood commonly presenting as drowsiness. Intracerebral haemorrhage may present with a focal neurological deficit. The distinction between these at the event side is academic, and it is vital to note deterioration early and seek expert help.

19.2.1 Skull Fracture

Typical signs of a skull fracture include the presence of a scalp haematoma, palpable step or deformity to the cranial vault; however, other less obvious signs may become apparent as time progresses. These include:

Visual changes including field defects and double vision/diplopia due to either bleeding within the occipital cortex or optic nerve compression. Diplopia due to orbital muscle dysfunction may also occur.

Bruising around the eyes in the absence of facial injury. This is commonly known as raccoon/panda eyes and together with a retro-auricular haematoma is a sign of skull fracture. However, this is a late sign and not usually seen pitchside.

A persistent clear discharge from the nose or ear. This is a leak of cerebrospinal fluid producing CSF rhinorrhoea or otorrhoea.

Hearing change due to blood accumulating behind the tympanic membrane: haemotympanum.

A facial muscle weakness could occur due to cranial nerve VII compression together with loss of facial nerve sensation. This could also occur with an inferior orbital blowout fracture.

19.2.2 Facial Injury

Clearly, any player sustaining a facial injury has received an injury above the clavicle and as such has the potential to both be concussed and have a cervical spine injury. Haemorrhage and fracture from facial injuries have the potential to place the patient’s airway in jeopardy. Alert players with such injuries typically wish to sit forward so that any blood can be spat out or can drain from the mouth. In the primary assessment of these patients, airway management is the first concern with consideration of the cervical spine. If the patient wishes to sit forward, he may be considered to have head control. In this situation, the injured player will be unwilling to tolerate triple cervical spine immobilisation, and the application of this may be detrimental to their overall care. Once again, consideration that cervical spine injury may have occurred is required.

19.2.3 Twitch on the Pitch

It is common for players to suffer a short seizure or convulsive episode following a head injury. When this occurs in sport, it is commonly termed a ‘twitch on the pitch’. These are benign, do not represent a form of epilepsy and usually settle after a few seconds. If this is still in progress by the arrival of the medical team, supplementary oxygen therapy can be provided. During this seizure activity, the cervical spine should be considered while the airway is maintained; however, the rigid immobilisation of the cervical spine during a convulsion may actually be detrimental.

Most seizure activity is short lived and will terminate within a few seconds particularly after an airway manoeuvre and the provision of supplementary oxygen. The Rugby Football League mandatory equipment list includes ampoules of diazepam for IV/rectal administration to stop seizures; however, this is primarily for prolonged epileptic seizures. Seizure activity relating to a head injury is likely to spontaneously terminate particularly with oxygen therapy. Again the straight pointing of an upper or lower limb, called a ‘fencing response’, may be indicative of a head injury and may allow recognition from afar. A brief loss of consciousness and impact seizures do not reliably predict outcomes following concussion although a cautious approach should be adopted following their occurrence [11].
19.2.4 Concussion

Over the past decade, there have been advances in the understanding and terminology of concussion; however, concussion is considered by many to be the most complex injury in sports medicine to diagnose, assess, and manage. Experts in concussion research have met at three international conferences to produce consensus statements and guidelines for the management of concussion. The first of these was in Vienna in 2001 [12], the second in Prague in 2004 [13] and the most recent in Zurich in 2008 [14]. At each meeting, the groups have appraised and modified their initial statements in light of advances in research. A fourth symposium convened in Zurich in November 2012 [15]. The American Medical Society for Sports Medicine and the American Academy of Neurology have recently produced guidelines for the diagnosis and treatment of concussion in sport [16, 17]. The American Medical Society for Sports Medicine reviewed the literature and made recommendations based upon the Strength of Recommendation Taxonomy (SORT). The American Academy of Neurology performed a systematic review based upon a Grading of Recommendations, Assessment, Development and Evaluation (GRADE) based upon evidence-based methodology and a subsequent Delphi process. The distinction of the Zurich Consensus working group is that the group provided recommendations for all aspects of concussion management even if there is little or no evidence.

West and Marion have recently compared these three published guidelines. Despite the different methodologies used [1], key similar guidelines have been produced in each case, and these will be discussed below.

Concussion is defined as a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces. Several common features that incorporate clinical, pathologic and biomechanical injury constructs that may be utilized in defining the nature of a concussive head injury include:

Concussion may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an “impulsive” force transmitted to the head.

Concussion typically results in the rapid onset of short-lived impairment of neurologic function that resolves spontaneously.

Concussion may result in neurophysiological changes but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury.

Concussion results in a graded set of clinical symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course; however it is important to note that in a small percentage of cases however post concussive symptoms may be prolonged.

No abnormality on standard structural neuro-imaging studies is seen on concussion.

The consensus groups have also given guidelines on the on-field or sideline evaluation of acute concussion. The key principles are based upon the recognition of injury, assessment of symptoms, cognitive and cranial nerve function and balance tests. It is recommended that when a player shows any features of a concussion:

The player should be medically evaluated on-site using standard emergency management principles, and particular attention should be given to excluding a cervical spine injury.

The appropriate disposition of the player must be determined by the treating health-care provider in a timely manner. If no health-care provider is available, the player should be safely removed from practice or play and urgent referral to a physician or emergency department arranged.

Once the first aid issues are addressed, then an assessment of the concussive injury should be made using the Sport Concussion Assessment Tool 3 (SCAT3) or other similar tool. Comparison with a preseason baseline is advantageous.

The player should not be left alone following the injury, and serial monitoring for deterioration is essential over the initial few hours following injury.

A player with diagnosed concussion should not be allowed to return to play on the day of the injury.

Players are well aware that if they are concussed they will be removed from the field of play and so may not complain of symptoms. Any player therefore sustaining a head injury should be carefully observed for the signs of concussion.
Observable signs include behavioural changes and cognitive impairment, as demonstrated by them lacking their usual clarity of thinking while performing their sport.

The pitchside assessment of concussion may be formed by brief neuropsychological test batteries assessing attention and memory function. These tests include the commonly used Maddocks questions [18] and the Standardized Assessment of Concussion. Standard orientation questions have been shown to be unreliable in the sporting situation when compared to memory assessment. The Maddocks questions are more relevant to athletes during a game and more specific than standard orientation questions. The use of the SCAT3 card and Pocket SCAT3 will help determine whether a player has been concussed and give good advice following a concussion.

Even in the presence of negative neuropsychological test results, the clinical impression of the attending sports physician is paramount. Knowledge of individual players and athletes, in particular to their mood, mannerisms and character, is much more important.

The Maddocks Questions:
Which ground are we at?
Which half is it?
Which side scored the last goal?
Which team did we play last week?
Did we win last week?

The player can then be removed from the field of play for assessment or substituted. In some sports, officials have the ability to remove players from the field of play following injury, irrespective of the player’s or the coach’s opinion.

In this respect, although a loss of consciousness has been acknowledged as a predictor of outcome in moderate to severe traumatic brain injury, it is not noted as a marker of severity for concussion. The most recent consensus meeting determined that prolonged (>1 min duration) LOC would be considered as a factor that may modify management. LOC is however a useful objective marker that a head injury has occurred and that the player is likely to be concussed. Thus, the consensus group recommends that those sustaining a loss of consciousness do not return to play. However, a player may still demonstrate concussive symptoms and need to be removed from the field of play, even if they have not sustained an LOC.

Asking patients about symptoms is facilitated by the use of a checklist as patients may be unable to recall if they have had the symptom or not.

It involves three balance tests, which should be performed on the SCAT3 form: the double-leg stance, the single-leg stance and the tandem stance.

The mainstay of concussion management involves physical and cognitive rest until all symptoms resolve and a graded programme of exertion prior to medical clearance and return to play.

The player should be observed during this period of rest and ensure they are well hydrated, eat regularly and take simple analgesics, e.g. paracetamol. In more severe cases, minimising cognitive input and maintaining a regular routine should be advised. It must be remembered that the effects of concussion can have delayed onset.

Patients should be referred to an emergency facility if they:
Have worsening headache
Become very drowsy or cannot be easily awakened
Cannot recognise people or places
Develop significant nausea or vomiting
Behave unusually more confused or irritable
Develop seizures
Develop weakness or numbness in the arms or legs
Develop slurred speech or unsteadiness of gait

The graded programme should typically take about a week following a concussion with 24 h required to complete each stage. The player/athlete should only progress a stage onwards if symptoms do not reoccur. The additional use of neuropsychological testing and the interpretation of the results are beyond the scope of this manual.

Since the guidelines in 2013, the consensus is that any player who has sustained or is suspected to have sustained a concussion may not return to play on the same day as injury. ‘When in doubt, sit them out!’ is a useful mantra to follow. From the work within the NFL, it must be noted that
the majority of players sit out rather than the 15.2% of players who return immediately and 39% of those playing in high school and collegiate football admit to playing with residual symptoms from a prior head injury.

Nonelite athletes may not have the same resources available as elite athletes (such as the presence of trained medical staff during practice and competition, a concussion programme as part of sideline preparedness, the benefit of neuropsychological or postural testing as well as consultants with expertise readily available) and as a result tend to be managed more conservatively. Younger athletes often have a greater incidence of concussion with longer recovery time frames; however, they are often managed with less expertise and with limited resources. It is safer to not return these athletes to play on the same day and be more conservative with their management.

Legislation now mandates that any child or adolescent removed from the field of play or game with suspected concussion may not return. Unfortunately, data on this group of patients is limited.

Ten to fifteen percent of patients will have ongoing post-concussive symptoms for more than 10 days. This could be even higher in some sports typically ice hockey and some populations of children. It must be remembered that many of the symptoms of concussion are not specific to concussion and it is important to consider and manage coexistent pathologies. Further investigation is required consisting of formal neuropsychological and conventional neuroimaging to exclude structural pathology. There is insufficient evidence for the use of advanced neuroimaging or genetic markers. There is potential benefit of sub-symptom threshold activity as part of a comprehensive rehabilitation programme.

Patients should be managed in a multidisciplinary manner by health-care providers with experience in sports-related concussion. Important components of management after an initial period of physical and cognitive rest include associated therapies such as cognitive vestibular physical and psychological therapy assessment for other forms of prolonged symptoms and consideration of a graded exercise programme at a level that does not exacerbate symptoms [11].

The assessment of any player after a head injury should progress along the management principles of airway with consideration of the cervical spine, breathing, circulation with haemorrhage control, disability assessment and finally exposure and environmental control.

Assessment of concussion is complex and is facilitated with the use of the Standardised Assessment Concussion Tool (SCAT3).

Any player who is concussed or has symptoms of concussion should be removed from the field of play. They may only return once they are symptom-free at rest and on exertion and preferably after being reviewed by a physician or experienced clinician.

19.3 Low-Back Pain and Sacroiliac Joint Disorders

Not only sedentary individuals are afflicted by back pain; it has significant effects on athletes as well, but they differ from nonathletic population in their will to return to activity that may vary from will to win through significant financial considerations. Low-back pain represents one of the most common reasons for missed playing time by professional athletes.

Athletes are typically well conditioned in spite of low-back pain, because of greater flexibility of the lumbar spine and higher pain thresholds, but they have higher demand on their lumbar spine and cannot tolerate any kind of limitations on their activities.

Low-back pain is a common musculoskeletal disorder that is almost ubiquitous and that may be either acute or chronic. It is important to remember that it’s a symptom, not a diagnosis. Pain could be related to problems with the lumbar spine, intervertebral disc, ligaments around spine and discs, spinal cord and nerves, paravertebral muscles, pelvic and abdominal organs or skin (Table 19.1); in most cases of low-back pain, an anatomical abnormality is not identifiable.

Accurate history and physical examination are essential for evaluating low-back pain in an
Table 19.1 Low-back pain in athletes: differential causes

<table>
<thead>
<tr>
<th>Spinal pathologies</th>
<th>Nonspinal pathologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle strain/ligament</td>
<td>Sacroiliac joint dysfunction</td>
</tr>
<tr>
<td>strain sprain</td>
<td></td>
</tr>
<tr>
<td>Degenerative disc disease</td>
<td>Intrapelvic, gynaecologic</td>
</tr>
<tr>
<td>(no slip)</td>
<td>conditions (e.g. ovarian cysts)</td>
</tr>
<tr>
<td>Isthmic spondylolisthesis</td>
<td>Renal disease</td>
</tr>
<tr>
<td>Facet syndrome</td>
<td></td>
</tr>
<tr>
<td>Ring apophyseal injury</td>
<td></td>
</tr>
<tr>
<td>(adolescents)</td>
<td></td>
</tr>
<tr>
<td>Sacral stress fracture</td>
<td></td>
</tr>
<tr>
<td>Central disc herniation</td>
<td></td>
</tr>
<tr>
<td>(without radiculopathy)</td>
<td></td>
</tr>
<tr>
<td>Sacralisation of L5/</td>
<td></td>
</tr>
<tr>
<td>transverse process</td>
<td></td>
</tr>
<tr>
<td>impingement</td>
<td></td>
</tr>
<tr>
<td>Facet stress fracture</td>
<td></td>
</tr>
<tr>
<td>Acute traumatic lumbar</td>
<td></td>
</tr>
<tr>
<td>fracture</td>
<td></td>
</tr>
<tr>
<td>Discitis/osteomyelitis</td>
<td></td>
</tr>
<tr>
<td>Neoplasm</td>
<td></td>
</tr>
</tbody>
</table>

In case of acute symptoms, it is important to understand the mechanism of injury; otherwise, duration of symptoms, location and irradiation and rate of onset of symptoms must be investigated in case of chronic low-back pain. If pain is localised in the lower back, it’s more probably a mechanical back pain, while if symptoms predominantly affect the legs, it may be due to nerve compression/irritation.

Lifetime prevalence of low-back pain in the general adult population is estimated to be between 85 and 90%.

47%, while disc-related disorders are quite uncommon; instead an adult athlete often suffers low-back pain due to degenerative conditions (48%) or to unspecified causes [20]. In order to establish a proper diagnostic process and treatment, it’s important to underline that common causes of low-back pain in athletes are different between ages [21], as shown in Table 19.2.

Prevalence of low-back pain was shown to be different depending on the practised sport: Granhed and Morelli [22] found a significantly higher prevalence of low-back pain in retired wrestlers and heavyweight lifters than in a control population. Other studies [19, 20] showed a different occurrence of low-back pain in football players (27%), artistic gymnasts (50%) and rhythmic gymnasts (86%). Similarly, also other causes of low-back pain such as sacroiliac disorders show a higher prevalence in rowers [23].

Low-back pain can occur either from an acute traumatic injury, more commonly in athletes, or from a repetitive microtrauma that produces an overuse injury. It’s immediately understandable that contact sports tend to produce acute injuries from high-energy impacts, whereas sports involving repetitive flexion, extension and torsion of the spine result in overuse injuries [20].

Large forces are produced in the lumbar spine region during various athletic manoeuvres; these forces act on the muscles and ligaments, on the intervertebral disc and on the posterior elements.

Mechanical strain on spinal ligaments leads to tears and produces pain. This pain leads to decreased motor unit recruitment and reduced activity due to fear of producing pain that produce muscle wasting and weakness. This condition creates a muscle imbalance that leads to further mechanical disruption and muscle wasting [24].

During sports, the intervertebral disc is always under load as a result of body weight and muscle activity; under certain conditions, these loads exceed the tolerance of the disc and may cause degenerative or traumatic changes (degenerative disc disease or disc herniation) that are represented by progressive disc dehydration and loss of proteoglycans in the nucleus; these changes reduce the ability of the nucleus to absorb loads and could decrease the space available for the
### Table 19.2 Causes of low-back pain by age

<table>
<thead>
<tr>
<th>Prepubescent</th>
<th>Adolescent</th>
<th>Adult</th>
<th>Elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>Trauma</td>
<td>Discogenic</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Tumour or other malignancy</td>
<td>Spondylosis</td>
<td>Mechanical back pain</td>
<td>Spinal stenosis</td>
</tr>
<tr>
<td>Trauma</td>
<td>Hyperlordosis back pain</td>
<td>Unspecified</td>
<td>Discogenic</td>
</tr>
<tr>
<td>Developmental</td>
<td>Discogenic</td>
<td>Osteoarthritis</td>
<td>Medical cause</td>
</tr>
</tbody>
</table>

neural elements producing irritation or compression [19]. In this case, a long history of low-back pain is usually reported by the athletes, with or without radicular pain; over time, the radicular pain becomes more severe because initially the disc material pushes on the annulus, activating pain receptors, and then the disc material herniates and irritates or compresses nerve roots [24]. Other authors found that these changes are sports and training related; in particular, they found that lumbar flexion was the most influential factor in developing disc degeneration.

Many authors [25, 26] consider that pars interarticularis lesions arise from mechanical stress due to repetitive hyperextension and axial loading applied to posterior elements of the spine, and they believe that the increased rate of spondylolysis in athletes is related to increased forces acting on the lumbar spine during sport activities.

In a young athlete, growth cartilage and secondary ossification centres are particularly vulnerable to injury; these areas are susceptible to compression, distraction and torsion injury. An incomplete ossification of the posterior column could be present in the lower lumbar vertebrae, particularly L5, predisposing to spondylolytic stress fractures; the presence of an unknown spina bifida represents an additional risk factor for spondylolysis [26]. So a growing athlete may potentially be at higher injury risk, in particular in contact sports [20]. Vulnerability of the growing spine was shown by Goldstein et al. [27] in an MRI study of female gymnasts and swimmers: they found that back pain complaints were more common in gymnasts, with increased age and level of competition, than in swimmers that did not have such a repetitive loading on their spine.

As mentioned previously, the type of sport or activity and position played must be elicited because it correlates with the prevalence of low-back pain [19, 20]. Also athletic background should be explored: volume of training and level of competition should be investigated, as well as any increase of volume or intensity of training because it could reveal a poor conditioning, an excessive or repetitive loading, an improper techniques or an inadequate equipment [20].

History of back pain should be investigated: onset and duration of symptoms should differentiate between acute trauma and overuse injuries. Pain quality, location and severity should be determined, as well as eliciting any associated neurological symptoms and aggravating factors. Previous episodes of low-back pain should be investigated: as reported by Greene et al. [28], athletes with previous history of low-back pain had three times the risk for subsequent episodes if compared to those with no history of pain.

It is also very important to consider other more sinister causes of back pain, such as infection (Figs. 19.1 and 19.2), tumours or inflammatory conditions, in particular if ‘red flag’ symptoms...
such as fever, malaise, weight loss, neurological abnormalities, night pain and morning stiffness are present. Moreover, numerous conditions can affect bone metabolism contributing to stress fractures or metabolic bone pain: steroids (asthma, allergies), endocrinological dysfunctions (amenorrhoea, thyroid irregularities, disordered eating, illicit use of hormones) and chronic disease (inflammatory bowel, HIV) [20].

Physical examination should include inspection of the spine and also athlete’s gait and posture; any ataxia, antalgic gait, limp or Trendelenburg gait should be noted.

Looking the patients from behind shoulders and pelvis should be aligned; bony and soft tissue should be symmetrical on both sides of the spine. Any abnormalities such as cysts, hairy patches, dimples, growth, haemangiomas or café au lait spots could be associated with congenital malformation (e.g. tethered cord).

Scoliosis, kyphosis or excess lordosis should also be noted: a gentle lumbar lordosis should be appreciable from the side. A forward-bending test should be performed to assess for any asymmetry suggestive of scoliosis.

Range of motion in all planes should be evaluated in flexion, extension, rotation and lateral bending. It’s supposed that an athlete should be able to flex forward and come close to touch his toes without bending knees; tight hamstring can cause a reduction of forward flexion. If pain is evoked with flexion, an injury of the anterior elements of the spine is suggested or a muscle strain/spasm or a disc-related condition. Pain with extension indicates an involvement of the posterior elements or the sacroiliac joint; also a single-legged hyperextension test can be performed [20].

The spine and sacroiliac joint should be palpated looking for any tenderness point. Also paraspinal muscles and buttocks should be palpated for any tenderness or muscle spasm.

Examination of the lumbar spine should include special tests like figure-4 or FABER (flexion, abduction, external rotation) (Fig. 19.3) and Gaenslen sign (Fig. 19.4). If these tests provoke ipsilateral pain, this is suggestive of a sacroiliac joint pathology.

Neurological examination is necessary to complete investigation and should include deep tendon reflexes and lower extremity strength (heel and toe walking); during physical examination for low-back pain and radiculopathy, most useful tests are the straight leg raise (Fig. 19.5) and the cross-table straight leg raise; moreover, if used together [29], any abnormalities indicated a compression or irritation of nerves that could be originated from a degenerative disc disease or a disc herniation.

Any kind of imaging studies cannot substitute an accurate and complete physical examination. In selected patients with acute low-back pain and without signs or symptoms of an underlying serious condition, imaging studies are not indicated, as shown by several authors [24, 30], because they did not find any improvement in clinical outcome in these patients. Henschke et al. [30, 31] evaluate that in nonathletic patients even if some weaker ‘red flags’ are present, a 4–6-week period of treatment is suggested before any imaging study; but if an athlete suffers low-back pain,
in particular if he is an elite athlete, a proper and rapid treatment is requested. So an imaging study, to avoid any delay in diagnosis and treatment and soon return to sport activity, is maybe suggested when this kind of patient is involved.

Plain radiographs in two projections could be useful for screen for serious conditions; because of low sensitivity and specificity, they had little diagnostic value but could provide information to rule out any structural abnormalities: oblique view allows evaluation of pars interarticularis, while flexion/extension radiographs assist in assessing dynamic instability.

MRI represents the gold standard for the lumbar spine and sacroiliac joint, in particular if neurological symptoms are present or a serious condition is suspected. An alternative could be represented by CT scan, if MRI is contraindicated or unavailable [30], but it’s necessary to remember that they are different exams: MRI is more useful in evaluating discs, neural structures or other soft tissues and can also provide information regarding possible occult fractures or the presence of neoplastic disease, while CT helps define bony structures [32], and it should be reserved for confirming diagnosis or in case of significant trauma or to evaluate spinal canal impingement [24, 33].

Bone scan is very sensitive to rule out metabolic activity, such as with a neoplastic lesion, fractures of indeterminate age or spondylolytic defects. Scintigraphic tracer is abnormally accumulated where repetitive stress causes local bone remodelling [34].

A good clinician should never forget that any findings in MRI or computer tomography, or in any other imaging study, should be correlated with clinical findings, especially in older patients because the likelihood of false positives is increased [30]. Moreover, as shown by Graw and Wiesel [19], a ‘nonspecific low-back pain’ should be included in differential diagnosis: patients who suffer low-back pain could have no specific signs of any pathology on imaging studies, or they could present abnormalities that don’t correlate with symptoms; instead, patients without low-back pain could present abnormalities on MRI nevertheless. These possibilities underline the importance of correlating imaging and clinical findings together; otherwise, the risks of incorrect diagnosis and under- or overtreatment increase.

The majority of low-back pain cases are self-limiting in the general population and resolve within 6 weeks regardless of treatment, but 5–10 % of patients will develop chronic back pain [30]. An athlete hardly accepts any kind of limitation on his sport activity, which can lead to a shortened career and financial loss, so an adequate treatment should be rapidly undertaken in order to return to play as soon as possible and reduce the possibility of developing chronic pain.

Although low-back pain is a common cause of inability in general population, there are few data in literature that analyse proper treatment and criteria for return to play when an athlete is involved.
19.3.1 Strains and Sprains

Strains and sprains are stretch injuries that involve respectively ligaments and muscles. These are quite common injuries in athletes that cause low-back pain, but diagnosis is usually made by exclusion.

Strains and sprains occur when loads exceed the resistance of involved structure. Typically, pain is acute and worst in the first 24–48 h and improves with time; chronic strains and sprains present a gradual onset of symptoms persisting for longer periods [32]. Muscle spasm is often present, and point of tenderness is generally localised; in particular, they are worsened by particular movements. Neurological examination doesn’t show any abnormalities.

Acute strains and sprains could be simply diagnosed by acquiring accurate history of injury and performing physical examination. Any imaging study is not necessary, and the result is generally negative. When chronic strains and sprains occur, onset of symptoms is gradual and insidious, and pain persists for a longer period; in these cases, imaging studies are still generally negative, but they are used to rule out other pathologies [32].

These kinds of injuries represent the principal cause of low-back pain in athletes.

These are typically acute injuries, and patients report pain immediately consequent to the injury that increases in few hours (increased stiffness and pain the morning following the incident). Conservative treatment is the choice. Cryotherapy and heat offer benefits in decreasing spasm and pain; transcutaneous electric nerve stimulation and electric stimulation (high-voltage pulse galvanic stimulation) may be useful in the acute stages, but their efficacy has not been conclusively demonstrated [32].

A brief period of rest is needed: it should be limited to 1–2 days to prevent muscle atrophy that could lead to muscle imbalance and consequent lengthening of the period before restart of sport activity [24, 32].

Medications could be administrated; nonsteroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors are a good choice: in a large Cochrane review [35], they showed statistically better effects compared with placebo; NSAIDs have more side effects than COX-2 inhibitors.

Glucocorticosteroids are not more effective than placebo in acute injuries with straight leg raise test negative at 1 month [24]; moreover, they are banned by the World Antidoping Association.

Other drugs could be used. There is little evidence on the efficacy of muscle relaxants on low-back pain, and they have a high incidence of side effects (oversedation) that can hinder their use [36]. Also antidepressants could be administrated, but results are not consistent with all of them; the most effective antidepressant in reducing pain in chronic condition is selective serotonin reuptake inhibitor, in particular duloxetine [35].

These drugs have significantly higher adverse events: drowsiness, dry mouth, dizziness and constipation are the most common [35].

One trial comparing opioid to naproxen found that they were significantly better for relieving pain but not improving function. They commonly cause headaches and nausea; moreover, they are banned by the World Antidoping Association.

These initial interventions are followed by a physical therapy programme: as reported by Burns et al. [36], it would be started with direction-specific exercises; patients are invited to perform exercises or movements that decrease pain, and the primary goal is centralisation of symptoms (from distal to proximal). In another study Long et al. [37], 84 % of patients had significant reduction in pain and disability within the first 2 weeks of treatment.

When pain disappears or is at least reduced and centralised, the rehabilitation programme is continued with trunk, back and lower extremity strengthening, stretching exercises to restore function and then progressive return to sport [38]. In order to have better outcome results, physical therapy should be individualised and supervised [35].

To prevent recurrence of low-back pain, it is important that the athlete understands the importance of adherence to the rehabilitation programme and maintains a proper training; avoidance of overtraining is essential [36].
19.3.2 Degenerative Disc Disease

As in general population, degenerative disc disease is a segmental dysfunction: initially, pain originates from synovitis of facets or intervertebral disc (circumferential or radial annular tears); afterwards disc annular functionality, due to dehydration, is reduced and facet capsules become lax, influencing vertebral stability, and finally the degenerative process may be accompanied with listhesis and segment instability [19, 32].

History and physical examination are relatively nonspecific of degenerative disc disease. This pathology could be suggested by worsening of symptoms during flexion activities and improving with extension. So to diagnose degenerative disc disease, imaging studies are necessary.

Neural elements, including the spinal dura centrally and the nerve roots in the lateral recess, could be compressed by annulus fibrosus and by ligamentum flavum and facet joint capsule hypertrophy, with consequent symptoms irradiated to lower limb [19].

Plain radiographs may demonstrate an indirect sign of disc degenerative changes represented by loss of disc space height. MRI (Fig. 19.6) is the gold standard in demonstrating degeneration of the disc: loss of disc hydration on T2-weighted images on sagittal plane is the typical sign of degenerated disc [32]. According to Pfirrmann’s classification [39] based on the evaluation of disc homogeneity, height, signal intensity and distinction between the nucleus and annulus, there are 5 MRI degrees of lumbar intervertebral disc degeneration; de Schepper et al. [40] showed how low-back pain is strongly associated with disc space narrowing more than other radiographic features, in particular if more spaces are involved.

Considering athletic population, several studies [32] found a significantly higher prevalence of disc signal changes in athletes than in nonathletes, confirming the highest demand on the spine of athletes.

Discogenic low-back pain should be initially treated nonsurgically. Resolution of acute symptoms generally occurs within weeks [32].

First of all, abstinence from practice and competition is recommended; the period of inactivity should be balanced against the risk of losses in trunk muscle and general fitness [24].

Pain relief is achieved with the administration of NSAIDs with or without muscle relaxants, in relation with muscle spasm presence. In consideration of symptoms and possible side effects, other drugs could be used, as previously described [24, 35].

The use of lumbosacral corset or orthoses is still controversial: although it may offer benefits in controlling extremes of motion, muscle wasting can occur [30].

After the initial period of rest, patients should be encouraged to regain mobility through passive and active stretching exercises, followed by isometric exercises, in particular emphasising abdominal muscles and lumbar extensors. Once neutral position could be attained and maintained, muscle strengthening is encouraged to gain greater strength. Then, sport-specific exercise is emphasised to hasten return to sport and prevent recurrence [32].
If conservative treatment doesn’t obtain pain relief or recurrences are frequent, surgery should be considered. The choice of spinal fusion is not optimal for an athlete, because the loss of function of one segment should be compensated by other segments leading to an overloading and increasing the risk of degenerative changes to those levels; moreover, the lengthy postoperative period is poorly tolerated by most athletes [41]. Possibility of return to play following a spinal fusion is related to the level and the type of sport: most authors suggest to return to play in limited contact sports at least 1 year after fusion; full contact sports or highly competitive is much less likely, especially if 2 or more levels are involved, due to increased risk of subsequent injury to the adjacent levels [24].

A new surgical option is represented by total disc replacement (TDR). Some authors conducted a randomised trial comparing lumbar fusion and TDR: both groups showed significant improvements after surgery, but they were greater in the TDR group; at 2-year follow-up, there were no more differences between groups. Siepe et al. [42] reviewed 39 athletes who underwent TDR: return to play rate was 94.9%, and 9 of 12 professional or elite athletes returned to play at competitive level and reported they achieved full recovery and peak fitness at an average of 5.2 months postoperatively. Tumialan et al. [43] compared 12 military patients who underwent TDR to an age- and level-matched cohort who underwent lumbar fusion: 83% of TDR group were able to return to unrestricted full duty at an average of 22.6 weeks, while in the fusion group only the 67% return to full duty at an average of 32.4 weeks.

These studies showed a better outcome at short follow-up of TDR if compared to spinal fusion. Longer follow-up is still not available, but these promising results lead to the possibility of employing total disc replacement in athletes.

19.3.3 Disc Herniation

Disc herniation is due to the escape of nuclear material from the annulus fibrosus. It is often related to peripheral annulus injury associated with traumatic disruption; initially, only low-back pain could be present that could progress to radicular symptoms if irritation or compression of surrounding neurological structures is present.

Patients with disc herniation present radicular symptoms: most common levels involved are L4–L5 and L5–S1. Pain is worsened by flexion and Valsalva manoeuvre and improved by lying supine.

Motor and sensitive tests are mandatory: if L5 root is involved, weakness of ankle and toe dorsiflexion could be noted, and sensory changes may be experienced on the lateral aspect of the lower leg and middorsum of the foot; if S1 root is involved, weakness in ankle eversion and planter flexion, sensory changes on the lateral aspect of the foot and a decrease in Achilles tendon reflex should be present. Tests to investigate radiculopathy, such as straight leg raise test, are typically positive.

Cauda equina syndrome, caused by the compression of the nerves in the lower portion of the spinal canal, is uncommon. Usually, it presents with the characteristic findings of saddle paresthesia, loss of bowel and bladder function [20].

X-rays could be useful to rule out other pathologies. MRI (Figs. 19.7 and 19.8) represents the study of choice because it can demonstrate the herniation and its extension and moreover can show any nerve root compression [20]. MRI could be oversensitive for disc herniation, so it’s important to correlate with clinical symptoms [30].

As shown by Hsu et al. [44], 82% of athletes that suffered lumbar disc herniation successfully returned to play regardless of treatment: performance scores within each group were equal before and after treatment, either conservative or surgical. Anakwenze et al. [45] compared NBA players who underwent lumbar discectomy to a control group matched for experience, position, age and BMI who did not require surgery and found that both groups achieved the same level of performance.

As shown by these results, it’s initially suggested to treat patients conservatively, including limited rest, activity modification, NSAIDs and
exercises (extension and isometric exercises are performed first, and when sufficient strength and pain relief are achieved, flexion exercises are begun). Surgery is needed only if severe or progressive neurological deficit is present and if pain is refractory to conservative care. As long as patient shows improvements, surgery is deferred [24].

Microdiscectomy is widely recommended in athletes with lumbar disc herniation, because of less invasiveness and less disruption to muscles, bone and neural structure.

Wang et al. [46] showed that patients who underwent single-level microdiscectomy returned to play in 90% of cases, whereas multiple-level microdiscectomy showed the worst rate of returning to play.

In literature, all authors emphasise the importance of postoperative physical therapy and rehabilitation; Watkins et al. [47] permitted professional and Olympic athletes who underwent lumbar microdiscectomy once they complete truck stabilisation programme, achieve an excellent aerobic condition and perform sport-specific stretching and strengthening exercises; Eck and Riley [24] allow return to sport once sufficient pain relief and range of motion are achieved.

Typically, 6–8 weeks are needed to return to noncontact sports and 4–6 months to contact sports postoperatively [41].

Spinal fusion is recommended for cases of multiple recurrences or if spinal instability coexists; this procedure increases the risk of degenerative changes and injury to adjacent levels; moreover, the ability to return to sport is related to level of play and type of sport involved, as previously said for disc degenerative disease.
19.3.4 Spondylolysis and Spondylolisthesis

Spondylolysis is defined as a defect of the pars interarticularis; sometimes a forward slipping of one vertebra on another (spondylolisthesis) is associated. Spondylotic spondylolisthesis is the most common in athletes, interesting in most cases L5 and sometimes L4.

Spondylolysis is classified in four groups: dysplastic, developmental, traumatic (acute or chronic) and pathological. Typically, athletes suffer from spondylolysis due to a stress fracture (chronic traumatic) [38].

Risk of injury of the posterior elements is higher in sports involving repetitive extension and rotation of the lumbar spine: dancers, figure skaters, gymnasts and football linemen [32].

Insidious onset of low-back pain, in particular if extension related, is typical in athletes with spondylolysis and often associated with hamstring flexibility reduction that produces gait described as ‘stiff-legged’. Pain is enhanced by spine extension: single-legged hyperextension test (Fig. 19.9) can localise spondylolysis when standing on the ipsilateral leg [32].

Pain irradiation to lower limb, with numbness or weakness, is occasionally present; in this case, differential diagnosis with disc herniation should be considered [20].

Classical sign of spondylolysis on radiographs is a radiolucent defect in the pars interarticularis: in an acute injury, edges are irregular and gap is narrow, whereas in a chronic injury, lesions are smooth and rounded [48]. When the defect is large, on radiographs, in particular on oblique view, diagnosis is easy (the ‘Scotty Dog’ visual is a useful aid, with the defect appearing at the dog’s neck that represents the pars interarticularis); however, if the defect is narrow, spondylolysis could be missed, because a 45° oblique view demonstrates a pars defect well only if it is perpendicular to the pars [38].

When forward displacement of the vertebra on the other occurs, spondylolisthesis is diagnosed on lateral view radiograph (Fig. 19.10) and classified according to the percentage of anterior slippage (Meyerding system). If spondylolisthesis is suspected with normal static radiographs, flexion and extension views should be obtained: a dynamic translation greater than 3.0 mm is considered abnormal, suggesting spinal instability [24].
predictive indicator of bony healing after conservative treatment. MRI has the advantage of being noninvasive and the lack of radiation exposure, but Masci et al. [49] reported a significant major number of false negatives if compared with single photon emission computed tomography (SPECT). Also bone scintigraphy is very sensitive for detection of bone stress, but it’s not useful for diagnosis; moreover, once forward slippage develops, bone stress couldn’t be any more present (however, bone remodelling and tracer uptake may occur at the pars interarticularis immediately above or below the level of fracture).

Nowadays, when spondylolysis or spondylolisthesis is suspected, SPECT in addition to bone scintigraphy increases sensitivity and improves disease localisation without exposing the patient to additional radiation. Moreover, SPECT can identify early pars stress before any bone abnormality is detected with CT [34].

Spondylolysis and low-grade spondylolisthesis (<grade 3), associated with a recent injury and acute back pain, could be successfully treated conservatively: first of all, restriction to sport activity is necessary for at least 2 months or until patients can achieve painless lumbar extension [48]; the use of bracing is suggested in acute or delayed symptomatic spondylolysis, low-grade spondylolisthesis and unilateral pars fractures: Steiner and Micheli [50] treated adolescent athletes with spondylolysis or low-grade spondylolisthesis for a mean of 2.5 years with a modified Boston brace and noted good or excellent results in 78% of cases despite a union rate on radiographs of only 25% at follow-up. Anderson et al. [51] noted that patients with spondylolysis showing greater signal intensity on SPECT had a better outcome with bracing treatment than patients with lower intensity signal indicating that early bracing may offer advantages compared to delayed treatment.

In addition to bracing, a physical therapy programme is suggested: it is started with flexion and stretching exercises that improve abdominal strength and flexibility, reducing hamstring contracture; extension exercises are initially avoided. NSAIDs are administered if radicular pain complaints are present [48].

Fig. 19.11 Spondylolisthesis RMN

On axial CT scans, an unclosed neural arch is diagnostic of spondylolysis (incomplete ring sign). At this level, it is important to differentiate spondylolysis from facet joint analysing cortical contours, cortical margins and landmarks of joint capsule; on sagittal views, differences between pars defect and facet joint are more evident, and also incomplete fractures are better diagnosed [48].

The use of MRI (Fig. 19.11) is still unclear, because it has limitation in evidencing the cortical integrity of an incomplete stress fracture, but, as reported by Sairyo et al. [33], high signal on T2-weighted images is useful in early diagnosis of spondylolysis and could be used as a good
As reported in literature, majority of athletes can be effectively treated conservatively, but a long period of sport inactivity and physiotherapy is needed that could not be accepted by professional athletes. Generally, surgery should be suggested if back pain persists despite conservative treatment, or if spondylolisthesis is >grade 3 or progressive, or if neurological symptoms are present [32].

There are two main options of surgical treatment: spinal fusion and direct pars repair. Spinal posterolateral fusion, with or without instrumentation, is widely studied in literature in general population, but few information are available on athletes. Recently, interbody fusion has been reported more frequently, but no clinical advantages are not yet demonstrated if compared with posterolateral fusion. Proceeding with a spinal fusion leads to loss of motion of that segment overlapping adjacent segments, and return to sport could be conditioned.

Direct pars repair offers a major advantage on spinal fusion: less restriction on motion of the segment involved with reduced subsequent overlapping of adjacent ones.

Several techniques have been described for direct pars repair including Scott wiring technique, hook–wire constructs, translaminar interfragmentary screw (i.e. Buck screw) technique and pedicle screw–rod–hook constructs with autogenous bone grafting [48].

Nozawa et al. [52] describe better outcomes of Scott wiring technique in 20 competitive athletes with spondylolysis or grade 1 spondylolisthesis; all athletes returned to sport, but not all to their preoperative level of activity, while Debnath et al. [53] showed a better outcome in athletes treated with Buck screw technique.

Other series [41] of competitive athletes treated with both techniques showed good or excellent results with over 90 % of patients who returned to the same level of sport activity. In the achievement of good success with multiple techniques, it is likely that the critical aspect of surgery is resection of fibrous tissue within the defect, decortication to a bleeding surface and autogenous bone grafting of the defect. Once healing is achieved, a rehabilitation programme, as previously described, should be considered [48].

Return to sport criteria after surgery for spondylolysis or spondylolisthesis is still debated: Radcliff et al. [54] proposed a rehabilitation protocol with core strengthening and nonimpact aerobic activity at 2 weeks postoperatively with exercises performed with a neutral spine during the first 3 months; after those higher-impact exercises are started, sport-specific training could be introduced at 4–6 months. Return to play is allowed when athletes have normal strength and range of motion and they are pain-free during sport activity; this usually occurs from 6 to 12 months after surgery.

Recommendations for return to noncontact or low-impact sports after spinal fusion are controversial. Many authors allowed their patients to return to low-impact sports after 6 months; Eck and Riley [24] disagree and suggested delaying return to noncontact sport after 1 year. Criteria to return to high-impact sports are even more controversial: some authors did not recommend return to this kind of sports after spinal fusion; otherwise, there are authors who permitted return to high-impact sport after 1 year [41].

After spondylolisthesis fusion, many authors agree to forbid sports that require extreme mobility or involve heavy loads such as gymnastic, football, rugby, wrestling, weightlifting, skydiving and bungee jumping. Other authors [48, 54] did not forbid return to these sports, but they advise that athletes could be limited after surgery.

19.3.5 Posterior Element Overuse Syndrome

It is known also as hyperlordotic low-back pain, mechanical low-back pain or muscular low-back pain [26, 38]. After spondylolysis, it is the most common cause of low-back pain in adolescents.

This syndrome is not a well-defined condition: a lot of structures such as muscle–tendon units, ligaments, facet joints and joint capsules could be involved in causing low-back pain. Clinical presentation of athletes with posterior element overuse syndrome is completely similar to spondylolysis [49].
This syndrome is clinically similar to spondyloysis, and the same imaging studies are suggested, but differently to spondyloysis, they are negative. Imaging studies are necessary to exclude other causes of low-back pain originating from posterior elements [20].

Treatment does not require surgery. In order to control pain, a brief period of rest is suggested, but muscle wasting should be prevented. The use of ice and NSAIDs may be helpful in reducing inflammation. A lumbar support brace, which often is required for up to 6 weeks, may help to reduce pain and reduce hyperlordosis, which often is the cause of this syndrome. Physical therapy consists of abdominal strength exercises, antilordotic exercises and hamstring and lumbo-dorsal fascia stretching; extension exercises are initially avoided. Return to sport is allowed; pain-free extension is obtained, but training should be modified to avoid recurrences [20].

### 19.3.6 Sacroiliac Joint Dysfunction

The sacroiliac joint functions as a shock absorber and disperses forces between the trunk and the lower extremities. Sacroiliac joint dysfunction can be a cause of low-back pain due to disease, inflammation, movement dysfunction (hypermobility or hypomobility) or leg length discrepancy. The influence of proximal or distal structures is poorly appreciated but must be considered. A sacral stress fracture could be a very rare cause of pain in sacroiliac joint region, in particular in elite athletes [55]. Provocative tests for the sacroiliac joint are numerous, such as distraction test, FABER test, thigh thrust test and Gaenslen test, but they are not specific, so it’s necessary to perform them together to make a proper diagnosis. Signs and symptoms of seronegative spondyloarthropathies, such as Crohn’s disease, psoriatic arthritis and juvenile ankylosing spondylitis, should be addressed when the sacroiliac joint is involved [23].

A specific gold standard imaging study to evaluate sacroiliac joint dysfunction is still not identified, because of joint location and presence of overlying structures.

If pain has been present for more than 3 weeks, standard radiographs taken at a 25–30° from AP axis and lateral view should be obtained: they may show degenerative changes, ankylosis, demineralisation or a fracture. On radiographs, degenerative changes are usually first on the iliac side; if sclerosis involves the lower two-thirds of the joint on both sides, sacroiliitis is common [23]. Irregularity and widening of the sacroiliac joint could be present in an adolescent patient.

Computerised tomography is useful in identifying fractures, degenerative changes and osteoid osteomas. The high sensibility of bone scans in detecting osteoblastic activity could be exploited in the suspect of infection, fracture or a metabolic process [20].

Magnetic resonance imaging helps to diagnose soft tissue pathology, lumbar disc disease, fractures and tumours. MRI is helpful and the most sensitive for diagnosing inflammatory sacroiliitis.

Few information are available on management of sacroiliac joint dysfunction.

Ice and drugs, in particular NSAIDs, help alleviate pain and inflammation. If a sacral stress fracture is present, protected weight bearing is necessary until pain resolves. The use of bracing could be useful to stabilise the joint [20].

The influence of proximal and distal structures should be considered during physical therapy. To achieve a successful return of the athlete to sport, its mechanical demands must be evaluated carefully. Rehabilitation must focus on postural retraining of the entire abdomino-lumbo-sacro-pelvic-hip complex. The transversus abdominis has been shown to be the key muscle to functional retraining; some studies [23] demonstrate lower recurrence rates and lower pain. Recently, Richardson et al. [56] analyse that clinical benefits focusing on the transversus abdominis occur due to significantly reduced laxity in the sacroiliac joint.

Before starting any postural retraining, considering the entire abdomino-lumbo-sacro-pelvic-hip complex, a leg length discrepancy should be corrected.

Intra- or periarticular sacroiliac joint injections of corticosteroids and/or anaesthetic,
with or without fluoroscopy, have not been consistently shown to be effective [23], although they theoretically should help to treat sacroiliac joint dysfunction.

Return to sport is allowed when pain is controlled and good balance of the abdomino-lumbo-sacro-pelvic-hip complex is achieved through postural retraining.

19.4 Muscle Injuries

Muscle injuries within sport are both a common and problematic occurrence. This will be acknowledged by everybody that works within sport, regardless of which sport they are involved whether that be soccer, swimming, cricket, rugby, canoeing, athletics, fencing, Australian rules football, gymnastics and Gaelic football, to list those whose epidemiology has been described within the literature since the start of 2012 [57–65]. Nevertheless, muscle injury potentially affects all sport participants, and an understanding of the injury, subsequent treatment and ultimately any injury prevention mechanisms is essential for the physician working within sport.

The category of muscle injuries often incorporates the entire musculotendinous complex and thus concerns injuries anywhere along the length of a muscle from the bone and tendon interface at the origin, along the tendon, the proximal musculotendinous junction, the muscle belly itself, the distal musculotendinous junction and the insertion of the distal tendon into bone. The general acceptance is that tendon avulsions and tears in the sportsperson are best treated by surgical intervention whether it is the Achilles [66], quadriceps [67], hamstrings [68] or biceps [69]. Therefore, the focus of this piece will be regarding injuries to the muscle belly.

It has been previously suggested that little descriptive information exists regarding the description and therefore classification of muscle injuries. Indeed, the term ‘muscle strain’ has been interesting commonplace yet also vague and nondescriptive. To grade muscle injuries into one of three groups has gained popularity and has been described by more than one author: O’Donoghue in 1962, Takebayashi in 1995, Peertrons in 2002 and Stoller in 2007 [70–73]. However, each of these whether being clinically based or imaging based (either ultrasound or MRI) has a very broad middle grade, which is essentially nondescriptive. This was the stimulus for the introduction of a much more descriptive classification system that was formed from a consensus of a group of experts within the field of sports medicine. The Munich classification [74] has been introduced and displays a more detailed and consistent description of muscle injuries that have already been shown to be useful and ultimately validated by the UEFA Study Group when describing return to play following muscle injury in elite soccer players [59]. It is suggested that the research community adopt the Munich classification for the foreseeable future in order to permit progression in our understanding of muscle injuries.

19.4.1 Sites of Injury

19.4.1.1 Adductor Muscles ('Groin Strain')

Collectively, the adductor muscle groups may be divided into further three muscle groups by depth of layer of muscle. The superficial group may comprise of the pectineus, gracilis and adductor longus muscles; the middle layer, of the adductor brevis; and the deep layer, of the adductor magnus. However, pain in the groin region may be attributed to more than one of these muscles or potentially none of them at all. As a result, the presentation of a patient with groin pain requires very specific attention and exclusion of other pathologies such as abdominal wall pathology (e.g. hernia), intra-abdominal disorders (e.g. appendicitis or inflammatory bowel disease), genito-urinary pathology (e.g. urinary tract infection, sexually transmitted infection, testicular abnormalities), lumbosacral pathology (e.g. nerve root irritation or compression from bony or disc disease) or hip pathology (e.g. labral tear, femoroacetabular impingement, osteoarthritis, osteochondritis dissecans, iliopsoas tendinopathy) [75].
As a result, a thorough history, examination and imaging studies are important in deciding what the source of the pain is. Regarding an abductor strain, which is one of the more common muscle injuries among soccer players [60], a patient may present with decreased abductor range of movement and decreased abductor strength. It has also been speculated that biomechanical irregularities of the lower limb, such as overpronation and fatigue of accessory muscles around the hip, contribute to the risk of adductor injuries [76]. The physical examination findings are essentially tenderness to palpation of the muscle and pain on resisted contraction, in this case resisted abstraction. Imaging is thought to be useful in determining the difference in the potential diagnoses; however, it has been suggested that more consistent and systematic terminology be used when describing imaging findings [77] in order to achieve a better framework for treatment planning.

19.4.1.2 Quadriceps Muscle
The quadriceps muscles are formed by the rectus femoris, vastus lateralis, vastus intermedius and vastus medialis. Collectively, an injury to the quadriceps muscles accounts for the most common muscle injury in soccer [60]. In particular, as the quadriceps (rectus femoris) spans two joints in the hip and the knee, it is susceptible to a higher rate of injury as it will be caused by excessively forceful hip flexion and/or knee flexion [75]. An increased rate of injury is observed within the player’s kicking leg, with a history of previous injury and an increase in player age.

Rupture of the tendinous origin or insertion at the tendon bone interface is identifiable as this is the area of pain and tenderness. An injury to the muscle itself is well described by the patient as during a manoeuvre of forceful quadriceps contraction as a sharp pain in the area of muscle tear with or without the sensation of a popping or tearing sensation. There is tenderness in the area of muscular tear with associated swelling and ecchymosis that may be visible after 24 h [78].

19.4.1.3 Hamstrings
The hamstring complex comprises of the semitendinosus, semimembranosus and biceps femoris, both short and long heads. All but the short head of the biceps femoris are bi-articular. This is likely to be a contributing factor into why injuries of the hamstrings are common in soccer and demonstrated no bias between kicking and non-kicking legs [60]. Commonly the injury is during running, and it is hypothesised that this injury occurs as a result of high eccentric forces and moderate muscle strain [79]. In addition, many other factors have been suggested as being contributory to hamstring injury. These include anatomical factors, muscle fibre type distribution, muscle architecture and degree of anterior pelvic tilt [79] in addition to the phase of the activity involved [80]. Of specific interest is the high rate of hamstring injuries in Australian rules football that may be accounted for by the nature of the sport where a sprinting player may have to reach down for the ball [80]. There is again an increase in the rate of injury in those that have suffered a previous hamstring injury [81].

Presentation of these injuries is often following a classical history of injury that is seen with a sudden acceleration followed by pain in the posterior thigh. It is often accompanied by a tearing sensation. Tenderness over the area of the tear is seen with associated swelling and ecchymosis as seen with other types of muscle tear. A review of the imaging of hamstring injuries suggested that the majority (86%) occur in the muscle belly and within the biceps femoris (80%) [82].

19.4.1.4 Gastrocnemius (Calf Strain)
The ‘calf’ muscle refers to the gastrocnemius and soleus complex. While again being observed at a fairly common rate in soccer [83], this injury type may again be observed in many different sports. In particular, the term ‘tennis leg’ [84] has been mentioned to describe this injury in the tennis player. This refers to the serving motion that fully extends the knee with sudden ankle dorsiflexion, which results in the maximum stretch of the gastrocnemius. Tennis leg typically refers to the distal myotendinous junction although the term may be used when describing any injury to the calf region. Again the fact that the muscle is bi-articular is likely to be a reason as to why it is a fairly commonly injured muscle [82].
The clinical presentation is consistent with other types of muscle injury; a particular event is often noted with pain and potential tearing sensation felt. Then follow the examination findings of swelling and ecchymosis with tenderness to palpation over the area of torn muscle fibres.

The injury tends to occur in younger patients following a period of heavy exercise, whereas in older patients, it may occur following a much more insidious episode such as stepping out of a car which may not have registered with the patient as being a specific injury [82]. As a result, an important differential diagnosis includes deep venous thrombosis (DVT), particularly in the absence of a specific injury, as this is also more likely in older patients. Interestingly in a study of patients with ultrasound evaluation of tennis leg, 10% of patients were found to have a DVT without any other finding and a further 5% in addition to another finding [85]. Another important differential diagnosis is an Achilles tendon rupture, which should be differentiated upon clinical examination with a palpable gap at the site of tendon failure. In the event of any doubt regarding the diagnosis, an ultrasound scan is suggested, as the management of the two possibilities is extremely different, with the mainstay of muscle belly injury being nonoperative compared to a low threshold for surgical intervention in the athlete with Achilles tendon rupture.

19.4.2 Epidemiology

In essence, any of these injuries may occur in any sport. Indeed, if one considers the functional chain to be of significance, then any muscle injury will have an impact on any sport, e.g. a quadriceps injury in the overhead athlete. The next section will summarise some of the epidemiology findings specific to some of the most common sports in the world.

19.4.2.1 Soccer

The world game has been investigated extensively with regard to the epidemiology of muscle injury, mainly in the form of the UEFA Study Group. A review of 2,123 muscle injuries concluded that intrinsic factors found to increase muscle injury rates in professional soccer were previous injury, older age and kicking leg and that injury rates varied during different parts of the season and also depending on match location [60]. However, importantly, further UEFA studies have shown that while ligament injury rate has decreased over the last decade, muscle injury remains high [60]. This may be associated with another finding from the group that has shown fixture congestion to be associated with high muscle injury rates [86].

19.4.2.2 Swimming

A recent study has shown the rates of injury in elite Paralympic swimmers with visual impairment. As one may expect, the muscular injuries are more prevalent in the trunk and spine muscles and the upper than the lower limb although of interest 19.9% of injuries were seen in the lower limbs [87].

19.4.2.3 Rugby Union

In rugby, and in particular sevens rugby union (an Olympic sport in 2016), the rate of injury has been described as being 55.4 injuries per 1,000 playing hours with 14.6% of all injuries being in the lower extremity in terms of site and 10.4% being muscular injuries in terms of type [62]. The sport of rugby itself is interesting, as it has moved from an amateur era into a modern professional sport. This change has accounted for an increase in injury risk [88]. A meta-analysis has confirmed that an increase rate of injury is observed with an increase in the level of rugby that is played; in addition, most injuries were muscular and equivalent in rate to other collision sports [89].

19.4.2.4 Tennis

An extensive review article concerning tennis has shown a general trend that acute injuries in tennis were more likely to occur in the lower extremity rather than the upper extremity. There was no association with age, sex, skill level and injury rate although the volume of play was associated with the risk of injury. Tennis leg itself accounted for between 4 and 9% of all tennis injuries discussed [90].
19.4.2.5 Ice Hockey
A study of 1292 National Hockey League (NHL) players demonstrated that low levels of sport-specific training in the off-season (as compared to high levels) and previous injury were factors associated with increased risk of groin injury [91]. This was the basis for potential injury prevention strategies to be introduced in the sport.

19.4.2.6 Australian Rules Football
While not being potentially a worldwide sport, ‘Aussie rules’ has led the way in terms of injury surveillance with over 20 years of data from the elite league governing 13,606 injuries [64]. During this time, hamstring injuries have featured most commonly, and interestingly recurrence rates of injury have decreased each season. The authors concluded that such annual surveillance of injury rates was well received and crucially was instrumental in aiding rule changes that improved player safety.

19.4.3 Treatment

19.4.3.1 Traditional Methods
The mainstay immediate treatment of muscle injury for many years has been the ‘RICE’ method incorporating rest, ice, compression and elevation [92]. The aim of which is principally to decrease the risk of injury-induced bleeding into the muscle beyond the initial zone of injury with the result to minimise the extent of the injury [93]. This also decreases the inflammatory process in its earliest phase and helps with the pain that a patient will experience following injury. Subsequently to RICE, the term PRICE has evolved in order to add the use of ‘protection’ in the form of soft padding to the injured area of muscle to decrease the risk of impact injury with other objects [93].

It is recommended that the rest phase of activity restriction be present for 48–72 h post injury and that through this time ice be applied in 15- to 20-min spells every 60–90 min. It is also suggested that the compression bandage be applied during the periods where icing is not used (ACSM). The duration of rest and immobilisation is limited to this time as it is a period sufficient enough to produce a form of scar with sufficient strength to bear the forces that will be experienced by the next phase of treatment, namely, commencing mobilisation [93].

Beyond 72 h and dependent upon the severity of the injury, the next phase of rehabilitation will begin with a gradual increase in activity, which may begin with gentle movement of the muscle, mild resisted exercise, proprioception exercise and continued icing. Following this phase, a gradual increase in activity is permitted with pain being the indicator of speed of progression (ACSM). The recommendation is to progress from isometric to isotonic to isokinetic muscle contraction training through this time with again pain being the guiding factor [93].

An early return to activity is required in order to optimise the regeneration of healing muscle and promote the recovery of flexibility and strength of the injured skeletal muscle to pre-injury levels. The rehabilitation protocol should also incorporate core stability exercises, as these exercises appear to result in a better outcome for injured skeletal muscle than programmes based exclusively on stretching and strengthening of the injured muscle alone [93].

Following this early phase of treatment, the specifics of the muscle rehabilitation are dependent upon the muscle group involved, e.g. the use of Nordic hamstring exercises [94, 95]. Such exercises can be initiated in order to help rehabilitation and prevent recurrence.

In spite of these treatments being considered traditional and the basis of most management plans for the treatment of muscle injury, little in the way of objective evidence exists within the literature to suggest this is the optimum treatment. As a result, other techniques have been suggested and attempted in an effort to decrease the healing time from injury.

19.4.3.2 Medication
Few controlled studies exist to demonstrate the effects of nonsteroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids in the patient with muscle injury. Some have suggested a transient improvement in recovery from exercise-induced muscle injury [96]. In addition, short-term use of
NSAIDs in the early phase of muscle healing has been shown to lead to a decrease in inflammatory cell reaction without any adverse effect on muscle healing, tensile strength or contraction [93]. However, the long-term use of NSAIDs is potentially detrimental to the regenerating skeletal muscle, with the suggestion that it is harmful in the eccentric contraction-induced strain injury model [97].

19.4.3.3 Ultrasound
Once again, while being well recognised as a treatment for muscle injury, the role of ultrasound has very little supportive objective evidence existing within the literature. Some animal-based studies suggest a benefit from continuous therapeutic ultrasound in accelerating the healing response [98], whereas others suggest that while ultrasound will promote the satellite cell proliferation phase of myoregeneration, it did not display any benefit in the overall morphology of muscle regeneration [99].

In the absence of any randomised controlled trial that offers definitive evidence as to the effects of ultrasound in muscle healing, studies continue to emerge with the most recent in the literature again supporting the use of low-intensity pulsed ultrasound (LIPUS). The suggestion is that it induced an organised tissue structure at the site of injury and stimulates expression of cyclooxygenase-2 (COX-2) and the formation of new muscle fibres [100].

19.4.3.4 Hyperbaric Oxygen Therapy
Scientifically, it makes perfect sense that by increasing the concentration of oxygen within the body, there would then be more oxygen availability for the cellular processes of muscle healing and regeneration [93]. However, in spite of some experimental studies showing that its use may significantly improve the rate of repair of injured skeletal muscle [101], a subsequent Cochrane review has stated that there is insufficient evidence from randomised controlled trials that will identify the effects of hyperbaric oxygen therapy on delayed-onset muscle soreness [102], which was the closest review found in the literature to muscle injury in the athlete.

19.4.3.5 Kinesio Tape
The use of colourful taping has gained popularity among athletes in recent times. This has particularly been seen in the elite athlete population. That being said, very little exists in terms of scientific evidence as to the benefits of the taping. A systematic review performed in October 2011 and published in November 2012 concluded that there was insufficient evidence to support the use of kinesio tape following musculoskeletal injury due to there being few high-quality studies that have investigated its use [103]. Interestingly, however, the review was unable to discount a perceived benefit that the athlete may have. No ill effects were perceived; therefore, it may be that the use of such taping may provide a placebo effect for the athlete.

19.4.3.6 Platelet-Rich Plasma (PRP)
PRP has become very popular as a method of treatment for a number of different diagnoses. One is to treat muscle injuries. The possibility has received much coverage in the medical literature without any convincing conclusion to whether or not it carries a benefit. Scientifically, it stands to reason that PRP injections into muscle would carry a benefit; however, comment is made of a single poster presentation that showed benefit in a case series of 20 professional athletes with hamstring injury without subsequent publication [104]. Little else exists within the literature that would convincingly suggest a beneficial effect from PRP injection into muscle in the clinical setting. A review article has suggested that no PRP formula has yet been proven to result in good-quality evidence of muscle healing and recovery following injury in sports [105]. This feeling appears to be shared by the International Olympic Committee Sports Medicine consensus group as well, with a warning to proceed with caution in the use of PRP and the statement that further clinical trials are required [106]. Interestingly, one study is progressing and appears to be of suitable design quality in order to provide and answer to the question as to how much benefit PRP will provide as treatment to an injured muscle.
19.4.4 Complication

19.4.4.1 Myositis Ossificans
Although being rare, this is an important complication of muscle injury or repetitive muscle injury where bone or cartilage is laid down at the site of trauma. Clinically, it should be suspected if pain and swelling have not subsided by 10–14 days after a muscle injury and the normal pattern of injury recovery is not being observed. The ossification itself is unlikely to be visible on radiographs for around 6 weeks, as per any standard bone formation. The treatment is debated, and NSAIDs may be used in an attempt to decrease the rate of ossification as demonstrated within the literature for the process of heterotopic ossification [93]. Other treatments that have been successful, albeit on a case report basis, include extracorporeal shock wave therapy [107] and acetic acid ionophoresis, which has been described previously [108] and again in recent times [109].

19.4.5 Injury Prevention

It was said by Benjamin Franklin that an ounce of prevention is worth a pound of cure. This certainly appears to be the trend with muscle injury as well. It has been shown that the use of eccentric hamstring exercises (Nordic hamstring exercise) as a part of a 10-week prophylactic training programme resulted in a reduction in the rate of overall, new and recurrent hamstring injuries in professional and amateur male soccer players in a randomised controlled trial [95]. Similarly, a preventative exercise programme has been shown to be of benefit in reducing adductor muscle injuries in soccer as well [110].

The FIFA 11+ is a series of warm-up exercises designed by the FIFA Medical Assessment and Research Centre (F-MARC) that has since been popularised and integrated into the framework of soccer coaching and subsequently adopted by many soccer associations across the world due to its success at decreasing the rate of a number of injuries [111]. It has been demonstrated to be of benefit in terms of reducing a large spectrum of lower limb injuries in the sport of soccer, including muscle injuries [112, 113]. Further, widespread incorporation of the FIFA 11+ is likely to be of benefit in further decreasing the rate of injury in other sports as has already been demonstrated in basketball [114].

Finally, core stability appears to have an associated effect of risk of injury to the lower limbs. A study in American football suggested that suboptimal core stability might be a contributory factor towards an increased risk of injury in a preliminary study [115] and the previously mentioned study that decreased the frequency of adductor muscle injuries also utilised a programme that improved core stability [76].

Ultimately, muscle injury has a traditional approach to its treatment, which is accepted. It also has a number of potential improvements to this standard treatment that may yet be shown to be of benefit. However, it would appear that the greatest benefit is seen with a structured preventative exercise programme and as such should be considered by those involved with the medical care of sports teams.

19.5 PRP and Stem Cells

In recent years, many developments on the treatment of musculoskeletal injuries/diseases have been done within the scope of regenerative medicine. Several reports have been published regarding the use of platelet-rich plasma (PRP) and stem cells, alone or in combination with delivery carriers and/or biomaterial matrices also known as scaffolds. These have shown great promise for treatment of damaged meniscus, ligaments, tendons, skin, bone, cartilage and osteochondral tissues. The main aim of this review is to highlight the most recent and relevant reports on the use of PRPs and current role of stem cells in clinical orthopaedics (autologous treatments). Herein, the tremendous advances in the clinical applications of PRP, namely, the aspects related with the processing techniques, formulations and administration, are briefly overviewed. Moreover, the regenerative potential of stem cells (and its sources) and the control of their cellular fate by
means of using different biomolecules and clinical use (mostly in knee joint) are also analysed. Finally, new promising regenerative treatment solutions based on tissue engineering (TE) strategies are also briefly discussed. The global concept of tissue engineering requires the combined roles of a triad: cells, scaffolds and bioactive molecules (including several growth factors). When trying to figure out ‘how any tissue functions’ and what is necessary to put its ‘repair mechanisms’ at work, one cannot focus only on an isolated factor. It is necessary to understand the different roles of these different protagonists at different times to envision influencing the role of events necessary for tissue repair. There is no such thing as a ‘panacea’ of modern times capable to solve every problem using the same method. It is still necessary to further investigate the tissue’s biology in order to achieve more effective and reproducible methods of their repair.

For the present time, it is not possible to provide neither evidence-based indications nor guidelines concerning the clinical use of PRP and/or MSCs. Despite promising early results, these are still in the early phase of its clinical experience, and there is a long way in the field of research concerning these issues.

19.5.1 PRP

Autologous platelet-rich plasma (PRP) is a generic term referring to any sample of autologous plasma with platelet concentrations above baseline blood values [116]. Being a source of concentrated autologous platelets, after degranulation of their alpha granules, PRP provides a source of several different growth factors and other cytokines [117, 118].

PRP has been under development as a theory since the 1990s and has been increasingly used in clinical applications [118, 119]. However, one must understand that this technology is still in the early phase of its development and further research is required in either basic science or clinical perspectives. PRP technology basically relies in providing fibrin and high concentrations of a ‘cocktail’ of growth factors with ‘a certain’ potential to aid in selected tissue healing, including bone and soft tissues [119]. The role of multiple growth factors (GFs) in different biologic repair mechanisms as well as the variety and raised concentrations of these GFs found within PRP is the theoretical basis supporting the use of PRP in tissue repair [120]. The growth factors and other cytokines present in PRP include platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), fibroblast growth factor (FGF), insulin-like growth factors 1 and 2 (ILGF-1, ILGF-2), epidermal growth factor (EGF), interleukin 8 (IL-8), vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), keratinocyte growth factor (KGF) and connective tissue growth factor (CTGF), among many others [121]. However, there is no current effective method to control the availability or concentration of any of them prior to application. There are inter- and intra-individual differences as well as inherent to the method of preparation [122].

Moreover, according to Langer and Vacanti, the principles of tissue engineering and biologic repair mechanisms not only depend on the presence of bioactive proteins (e.g. growth factors) but also include cells and scaffolds [123]. It is necessary to make this ‘magic triad’ work properly in order to achieve successful tissue regeneration [124].

Considering the aforementioned, one should have no doubts about the critical role of ‘growth factors’ in biologic repair mechanisms. What must be appreciated and better understood is the effectiveness of all clinical methods aiming to use these proteins in clinical setting. The rationale supporting this method is that by delivering an amount of GFs, we might influence the cascade of events leading to the recovery of a tissue after an injury. One effective way to jeopardise a promising technology is to promote its incorrect use since the beginning of its application.

One should be aware that, up to now, it has not been possible to confirm in large-scale and long-time controlled clinical trials all the observations and suggestions arising from basic science research and preclinical studies [125].
There is no consensus on the ideal dosage of platelets to be delivered through PRP preparations. However, the principle of ‘the more, the better’ does not apply in this sense [126]. A wide range of platelet concentrations from 200×103 platelets/mL up to 1,000×103 platelets/mL are considered therapeutic for tissue healing, whereas much higher counts appear to have biologic deleterious effects [127–129]. The platelets collected in PRP can be activated by the addition of factors such as thrombin and/or calcium chloride, which induces the release of these factors from alpha granules.

Plasma, the fluid portion of blood, contains ions, inorganic and organic molecules as well as same proteins which assist in healing process of connective tissues [130]. Plasma is different from serum once plasma still contains fibrinogen as well as certain clotting factors. When plasma is exposed to thrombin, either by the adding exogenous thrombin or by contact with tissue thromboplastin, the clotting cascade is initiated and platelets are activated [130].

Creating such a platelet-rich fibrin matrix, one might achieve benefits in selected situations. A fibrin scaffold might play the role of conductive matrix for cells’ migration as well as provide a GF reservoir that indirectly binds growth factors, thus prolonging their delivery [126].

Differences between preparations further include the presence or absence of white blood cells (WBCs). WBCs are known to play a role on the initial phases of inflammation, namely, removal of bacteria and/or biologic debris [126]. There is no consensus on this issue, with some methods developed for intentional removal of leukocytes while others promote leucocyte-rich PRP preparations [122]. Some in vitro studies have reported some antibacterial effects related to inclusion of WBCs in PRP [131, 132]. However, it is also recognised that WBCs can release matrix metalloproteinases and produce reactive oxygen species that might lead to increased tissue damage [133]. This represents another key issue, determining a significant difference among the standard methods for the PRP preparation.

It is possible to describe PRP preparation according to the method of production. Single- and two-step centrifugation processes have been described to fraction whole blood and concentrate the platelets [122]. PRP preparation systems have recently gathered for clinical use (http://www.fda.gov/).

Some proponents of PRP therapy argue that negative clinical results are associated with poor-quality PRP produced by inadequate devices; however, there are poor evidences or guidelines favouring any method over another [122]. There are inter- and intra-individual differences in human donors affecting the quality and quantity of PRP preparations [122]. Moreover, variability in platelet-concentrating techniques may alter platelet degranulation characteristics that could affect clinical outcomes [134].

Dose–effect is also a relevant variable to consider. In a recent in vitro study [135], certain doses of PRP could inhibit adipogenic differentiation while inducing the proliferation and osteogenic differentiation of bone marrow mesenchymal stem cells derived from osteoporotic bone marrow, thus promoting fracture healing. However, high concentration of PRP inhibited osteogenic differentiation and callus remodelling [135].

Combining all the previous, the possibility of ‘a la carte’ PRP seems somewhat feasible, in a near future [136]. That is, if several methods exist, if different products are obtained accordingly, maybe, after development of our ability to fine-tune and control these differences, one might choose the ‘type’ of PRP product that best adapts to a specific clinical model. It must be recognised and understood that this plethora of methods to harvest GFs from PRP products creates difficulties in evaluating clinical outcome and in interpretation of published literature.

The use and clinical validation of PRP in orthopaedics and sports medicine are still in their early stages [137]. There are few controlled clinical trials that have adequately evaluated the safety and efficacy of PRP treatments. Most published literature remains on the level of expert’s opinion or small case series without control [125].

PRP has a promising profile for injection therapy permitting minimally invasive, nonoperative approaches for several conditions [138, 139]. Its proposed applications include shoulder cuff
pathology, epicondylitis, Achilles tendinopathy, plantar fasciitis, jumpers knee, muscle injuries or even joint arthritis [138]. There has been some controversy around clinical results. However, one must consider that these results have been obtained from different injuries or pathological models, involving different tissues, many times different preparations of PRP which limits the possibility for further widespread conclusions or guidelines [119]. Once PRP is not supposed to be the ‘panacea’ of modern times, it is difficult to expect that it will always have to ‘work’ no matter the strategy of therapeutic model.

A recent meta-analysis considering rotator cuff tears suggests that PRP has no benefits on the overall clinical outcomes and retear rate after arthroscopic repair of large- and massive-sized defects. However, it was observed a decrease in the rate of retears among patients treated with PRP for small- and medium-sized rotator cuff tears (level II study) [140]. Focused on lateral epicondylitis, a small controlled trial described promising results for ‘tennis elbow’ after failure of previous conservative treatment [141]. Some limitations inherent to study protocol must be considered including the small number of patients considered for results.

However, concerning Achilles tendon disease, modest improvement in functional outcome measures was observed in a small case series following PRP injection [142]. On another clinical trial enrolling patients with chronic Achilles tendinopathy (after failure of physiotherapy), PRP injection did not result in better outcome in pain nor activity when compared to a saline injection [143].

In a randomised trial with a small number of patients, PRP presented favourable results in improving patellar tendon healing after harvesting for ACL repair [144]. A small case series without control reported clinical improvement after PRP in treatment of jumper’s knee [145]. Once more, design of the studies must be carefully considered.

Contradictory results have been reported regarding the influence of PRP in graft integration after ACL repair. Tendon-to-bone healing (osteoligamentous interface) after ACL repair has presented nonsignificant differences [146, 147]. Nevertheless, some improvement in MRI signal concerning graft maturation has been described [147].

A recent single-blinded, randomised, controlled study comparing PRP injections to dextrose prolotherapy for the treatment of chronic recalcitrant plantar fasciitis achieved similar results with only slight better initial improvement in function for PRP group [148].

Once more, in favour of clinical application for PRP, intra-articular knee injections produced favourable functional results on degenerative cartilage lesions as well as pain decrease and quality of live improvement [149].

PRP has also been tempted to improve outcome after traumatic injuries (Fig. 19.12) including fracture healing. PRP combined with allograft achieved similar outcome when compared to autograft and significantly better than allograft alone in the treatment of displaced intra-articular calcaneal fractures [150].

In brief, PRP technology has been recently tested in a wide range of musculoskeletal
pathologies in orthopaedics but also in sports medicine particularly aiming to improve outcome and fasten recovery in high-level athletes.

The issue concerning PRP implications in antidoping rules by either the World Antidoping Agency or the International Olympic Committee (IOC) has been continuously appreciated [151, 152]. It has been discussed if local injections of PRP could have a systemic impact affecting doping tests as well as possible anabolic effects affecting performance [152]. In 2011, the World Antidoping Agency removed intramuscular injections of PRP from its prohibitions after determining that there is a ‘… lack of any current evidence concerning the use of these methods for purposes of performance enhancement’ [153]. Similarly, the IOC tolerates the use of PRP given the lack of evidence concerning systemic effects affecting performance and however recommends caution with the use of these methods [152, 154]. Conversely, the use of PRP is still illegal according to medical care law in countries such as Korea [155].

PRP technology is a promising technology for sports medicine and musculoskeletal application. It is clear that GFs can influence tissue’s repair mechanism. PRP is a method for harvesting autologous GFs whose source each one of us always carries around. What remains unclear is the best method for each tissue, what must be included and what should be excluded in each specific clinical case. Moreover, the timing, the dose and the conjunction with other therapeutic agents are also issues that should be considered. It is necessary to develop appropriate guidelines and increase evidence level prior to its widespread application as treatment option for joint, tendon, ligament and muscle injuries [125]. Results of clinical studies on PRP are difficult to interpret given the methodological quality and limitations of most published clinical trials [154]. More attention should be paid to methodological issues when designing, performing and reporting clinical trials assessing outcome of PRP technology.

To improve clinical application, several authors have been trying to tune and control some aspects. It has already been shown that an innocuous agent like anti-VEGF antibody can play a role to modulate and control some effects of PRP [116]. Moreover, a combination of PRP injections and oral administration of losartan (an antifibrotic agent) could enhance muscle healing by stimulating muscle regeneration and angiogenesis and by preventing fibrosis in skeletal muscle from mice model [156]. Research in this field still has a long way to go.

Future directions of PRP application may concentrate on seeking an appropriate method to control their effects (either by favouring one effect over another or by controlling different effects at different times). Moreover, given the multiplicity of different methods providing different PRP products, in future we might be able to provide guidelines in selection of different products best suited for specific effects: the ‘a la carte’ PRP technology. It is now consensual that more controlled trials are required describing properly the method of PRP tested in order to permit higher level of evidence and indications for use.

### 19.5.2 Stem Cells

The different types of cells found in our body can be generally categorised as germ cells, somatic cells and stem cells. Germ cells give rise to gametes, while somatic cells are the differentiated cells that constitute the adult body. By its turn, stem cells are characterised by cell types possessing the ability of dividing indefinitely, in vitro. Actually, stem cells may become a specialised cell upon differentiation, under the action of specific growth factors/bioactive agents. Therefore, stem cells can proliferate and differentiate beyond the tissues in which they normally reside or may be implanted. An interesting work has been reported by López-Ruiz et al. [157], which showed that chondrocytes extract from patients with OA can induce chondrogenesis in infrapatellar fat pad–derived stem cells.

In respect to its body location, stem cells have been identified and isolated from germ cells, embryo, fetus and many adult tissues (e.g., adipose tissue, skeletal muscle, Wharton’s jelly) [158], including those of diarthrodial joints.
Nevertheless, stem cells that express embryonic and adult stem cell markers have also been found in amniotic fluid, for example [159].

Thus, stem cells may be classified according to the tissue source or, alternatively, their capacity of differentiation (plasticity), as follows:

- Totipotent stem cells are present in the early embryo, and it can differentiate in all types of specialised cells of the body, including the entire fetus and placenta (e.g. zygote and immediate daughter cells).
- Pluripotent stem cells are isolated from the fetus, and it can differentiate in several cell types of all three germ layers (ectoderm, mesoderm and endoderm), but not the whole organism (e.g. embryonic stem cells derived from the isolated inner cell masses of mammalian blastocysts, embryonic germ cells (until 8th week) and embryonic carcinoma cells are some examples of pluripotent cells).
- Multipotent stem cells are cells that can differentiate in a limited type of specialised cells (e.g. mesenchymal stem cells (MSCs), neural stem cells and haematopoietic stem cells).
- Unipotent stem cells are also obtained from adult organs giving rise to one differential cell lineage (e.g. immature oligodendrocytes and keratinocytes).

Recently, Yamanaka’s group [160, 161] has found that mature specialised cells also known as induced pluripotent stem (iPS) cells can be reprogrammed into immature cells capable of differentiating into all tissues of the body. iPS cells are particularly interesting for use in vitro models of disease since it does not present the ethical problems of the use of human embryos. Another advantage of iPS cells is that creation of cell lines that are genetically tailored to a patient became also possible. With this significant progress, musculoskeletal regenerative medicine can be fully addressed. Still, several hurdles have to be overcome before its use in therapeutic applications, namely, the need for a fast and efficient reprogramming [162]. Besides, this technology makes use of traditional viral vectors (some are oncogenes), which should be avoided.

Despite the great developments in stem cell research for orthopaedics [163], fundamental studies are still needed to better understand its tissue location, differentiation pathways, paracrine signalling, mechanism of action and more importantly the regenerative potency of different stem cell types [164]. Another important issue is related to the poor knowledge of stem cell fate once implanted at a defect site. Therefore, all these issues must be clarified before it’s fully acceptance by clinicians and regulators as potential therapy.

Joint disease and repair (trauma) are some of the major challenges that orthopaedic surgeons have to face in their daily activities. Most treatments include pain control with administration of drugs and injection of biomaterials such as hyaluronan or chondroitin sulphate (viscosupplementation strategy) and other natural-based polymers [165–168]. Despite symptomatic improvements in most cases, these treatment solutions have failed in regenerative results, thus leading to progressive loss of joint functioning and ultimately requiring patients’ joint replacement [169].

It is well known that mammal’s tissue repair mechanisms result from the activation of pre-existing stem cells or progenitors cells. In addition, endogenous MSCs contribute to the maintenance of healthy tissues by playing as repairing reservoirs or immunomodulators to reduce inflammation processes [170, 171]. Thus, stem cells use promise to revolutionise traditional clinical practice with a striking impact on patients’ quality of life [172], i.e. from simple symptom control and repair approaches towards the whole tissue or organ regeneration. Despite the use of stem cell-based therapies in clinics is still limited due to the legislative/regulatory constraints and socio-economic factors [162, 173], adult stem cell application has been increasing in the area of joint disease/repair, in the last few years. Actually, adult stem cells have been found in bone marrow, synovium, synovial fluid, meniscus, articular cartilage, ligament and fat pad [174, 175]. Figure 19.13 shows the typical stem cells after being isolated from human knee fat pad.

Clinical trials using MSCs have been stimulated [176–178] by animal studies that showed a beneficial effect of MSC’s transplantation to the osteoarthritic or damaged joint. The clinical trials
were aimed to investigate the therapeutic effects of autologous MSCs as intra-articular injection (mostly in the knee) [175] or after transplantation upon cells seeding into matrices for the treatment of diseased/damaged cartilage tissue. In the following sections, a comprehensive overview of the clinical reports indicating the potential for stem cell therapies and combination of stem cells with scaffolds (TE strategy) in the treatment of joint defects/disorders will be provided.

As aforementioned, MSCs can be found in almost all tissues of the diarthrodial joints and have been exploited for their self-renewal capacity and ability to differentiate towards osteogenic, chondrogenic and adipogenic lineages and apparent myogenesis [174].

A great deal of attention has been given to stem cell-based therapies by means of delivering MSCs in vitro cultured into the defect/diseased areas. Recently, Mirabella et al. [170] has shown that amniotic fluid stem cells (AFSCs) are not osteogenic in vivo, although AFSCs can recruit more host CD31- and VEGF-R2-positive cells as compared to BMSCs. In that work, the authors concluded that AFSCs do not contribute to the deposition of de novo bone, but it can modulate a host response beneficial for enhancing the vascularisation of the bone environment.

Another beneficial application of autologous MSCs has also been reported for meniscus repair. Centeno et al. [179] showed regeneration of meniscus in a knee treated after percutaneous implantation of MSCs.

McIlwraith et al. [180] has investigated the effect of intra-articular injection of MSCs for treatment of microfractured chondral defects, in a horse model. In this preclinical study, a histological improvement was evident, which indicates that intra-articular injection of BMSCs enhances cartilage repair quality. In respect to clinical cartilage regeneration, Saw et al. [181] reported on a pilot study involving 180 patients (grade III and IV lesions of the knee joint, ICRS) that underwent arthroscopic subchondral drilling. Intra-articular injections of autologous peripheral blood progenitor cells (PBPCs) in combination with hyaluronic acid (HA) (8: 2 ml) were administered 1 week after surgery. A total of 5 weekly intra-articular injections were given. Five patients were evaluated postoperatively. The authors obtained encouraging results as articular hyaline cartilage regeneration was observed at second-look arthroscopies and histological characterisation.

It is in the treatment of OA that stem cell-based therapies are most appealing [182]. In that review, it is the author’s opinion that bone marrow-stimulating techniques and ACI can improve pain relief to the patients and are superior to no treatment. Similar in their clinical outcome, they induce fibrocartilaginous repair tissue which possibly can progress to hyaline cartilage formation with time. MSCs isolated from infrapatellar fat pad have also been investigated as potential therapy [183] for treatment of knee OA. In that study, stem cell injections (n = 25; mean of 1.89 x 106 stem cells prepared with ~3.0 ml of PRP) combined with arthroscopic debridement were administered to OA patients. Results demonstrated that the mean Lysholm, Tegner activity scale and VAS scores of patients treated with stem cells improved significantly at the last follow-up, as compared to control groups (patients had undergone arthroscopic debridement and PRP injection without stem cells). Therefore, the authors found that MSC’s therapy with intra-articular injections is safe and provides assistance in reducing pain and improving function in patients with knee OA. In a recent study,
Koh et al. [177] reported once similar findings showing that MSC's injections can improve symptoms of OA knee.

Interestingly, Barry and Murphy [174] reported that 13 clinical trials addressing research on OA were ongoing in 2012. In most of the studies, MSCs isolated from bone marrow and adipose tissue are administered by intra-articular injection (1–4×10⁷ cells/injection), after in vitro expansion. In these cases, no scaffolds were used as support for cell growth and differentiation, but hyaluronan was often used as the delivery carrier.

Interestingly, preclinical studies have been exploiting combinatory strategies by means of using cell-laden hydrogels (Fig. 19.14) mimicking the extracellular matrix, which can be further loaded with micro-/nanoparticle systems for the delivery of drugs aimed at promoting cell proliferation and differentiation, at the defect site [184–186].

The pioneering work of Ohgushi et al. [187] showed that the use of MSCs isolated from the patient's iliac crest followed by seeding onto implants contributed to improve the bone-prosthesis interface, with no inflammatory reactions. These preliminary results indicated that a TE strategy using MSCs (autologous approach) can contribute for preventing aseptic loosening of the total ankle arthroplasty. Similarly, Bertram et al. [188] demonstrated the validity of matrix-assisted cell transfer for intervertebral disc cell therapy. Another report also demonstrated that BMSCs combined with porous beta-tricalcium phosphate may be beneficial in posterior spinal fusion [189].

Marcacci et al. [190] reported on a pilot study involving stem cells associated with hydroxyapatite scaffolds for the repair of critical-sized long bone defects. That study showed the long-term durability of bone regeneration achieved by a bone TE approach at 6- to 7-year follow-up.

Different works have been reporting that microfracture procedure shows comparable clinical results to those treated with ACI (autologous chondrocyte implantation) in the treatment of small cartilage defects. In addition, microfracture procedure is only able to produce fibrocartilage tissue. Thus, novel strategies based on matrix-guided stem cell implantation for treatment of chondral lesions are more appealing as compared to cellular strategies as it has the promise to improve outcomes and produce mature tissues [191]. In another preclinical study, Yamada et al. [192] reported on an investigation involving bone regeneration with stem cells isolated from several sources (e.g. deciduous teeth, extracted from puppies and grafted them into a parent canine mandible as an allograft, parent dental pulp, and bone marrow by tissue engineering and regenerative medicine technology using platelet-rich plasma as an autologous scaffold and signal molecules). In that study, it was evident that stem cells from deciduous teeth, dental pulp and bone marrow with PRP have the ability to form bones. Apparently, bone formation with puppy deciduous teeth stem cells can have the potential to produce a graft between a child and parent.

There is a general consensus that one-stage procedure is advantageous over the conventional autologous chondrocytes implantation. Girolamo et al. [193] reported on the treatment of chondral defects of the knee with one-step matrix-assisted technique improved by means of using autologous concentrated bone marrow.

In another two-case report, Kasemkijwattana et al. [178] also investigated the therapeutic effect of implanting BMSCs in cartilage defects (grade III and IV lesions of the knee joint, ICRS). Despite the need for long-term follow-up, that study corroborated the previous findings [194] that BMSC's implantation after seeding into a collagen scaffold showed a great potential for the treatment of large cartilage defects. More
recently, Richter and Zech [195] reported on the clinical evaluation of MASI procedure and 2-year follow-up in chondral defects of the foot and ankle, but no control group was included. Evaluation comprised size and location of the chondral defects, method-associated problems and the Visual Analogue Scale Foot and Ankle (VAS FA) before treatment and at follow-up. This interesting work comprised evaluation of 25 patients revealing good clinical scores and no major complications. The authors concluded that MASI is a safe and effective method for the treatment of chondral defects and presents the advantage of being a single-procedure methodology as compared to ACI and MACI.

Driven by the good preclinical results, stem cell clinical trials are still ongoing. The latter are mostly following the simpler strategy of stem cell implantation using a scaffold-free method, but the cell number and density, dosage and matrices/gels/hydrogels for cells delivery have not yet been established. In a near future however, we firmly believe that clinical trials will evolve to advanced tissue engineering strategies, i.e. making use of stem cells combined with scaffolds and possibly also supplemented with PRPs or other growth factors. Nevertheless, these will present some surgical concerns for efficient delivery and many regulatory constraints. Finally, much knowledge is still needed, namely, that related to regulation of stem cell differentiation, role of host cell recruitment, type of transplanted cells, defect-filling materials and growth factor formulations in order to help improve surgical outcomes in patients presenting large defects and showing advanced signs of disease.

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