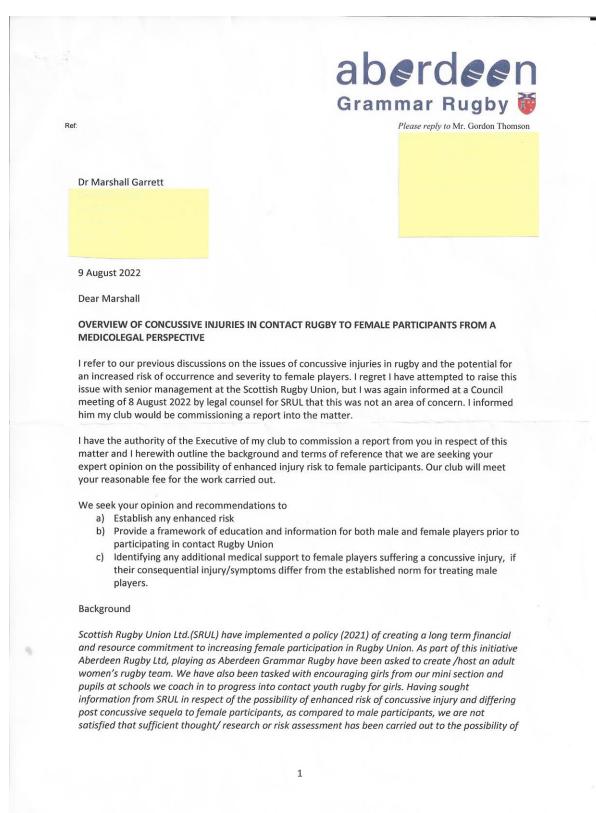
# Overview of Concussional Injuries in Female Rugby from a Medicolegal Perspective

Undertaken following instructions received, 9 August 2022, from Aberdeen Rugby Ltd.

Dr Marshall M Garrett, MBChB, L/RAMC, MIDF, MEWI Independent Medical Expert Former Honorary Clinical Senior Lecturer in Medicolegal Medicine School of Medicine and Life Sciences University of Glasgow drgarrett@garrettpartnership.co.uk

#### Appendix I

#### Letter of Instruction



increased health risks to female participants. We also do not believe the risk of litigation to clubs, and potentially their office bearers, has been given due consideration by SRUL.

#### Remit

We request that you consider published academic/medical reports on the above matter and prepare a report that either supports the view, apparently held by World Rugby and SRUL, that there is no enhanced risk to females from playing contact Rugby Union whilst also seeking information that highlights additional risk factors for female participants, if such information exists. We also ask that you use your medicolegal knowledge to assess, on a balance of probabilities, if an enhanced risk exists for female participants in respect of concussive injuries and subsequent sequela. We also seek your advice and recommendations on what actions would be required by our club in respect of information/education to be provided to both male and female players regarding concussive injuries prior to engaging in the contact Rugby Union. Any advice on additional medical support for female participants who suffer concussive injuries would also be relevant, if their treatment differs from the generic concussion procedures published by SRUL.

We will be engaging with Aberdeen University regarding the women's adult team being established at our club in late September 2022. We would require a report to be with us by no later than 30 September 2022 so we can adequately protect the club from potential risk of litigation, but more importantly have the proper education/risk management procedure in place before commencing contact rugby in this arena.

If you have any questions or require further information do not hesitate to contact me.

Yours sincerely

8

and Gordon Thomson

Director of Aberdeen Rugby Ltd & Chairman Aberdeen Grammar Rugby

2

# Appendix II Dr Marshall Garrett MB ChB L/RAMC MEWI

Graduated from University of Glasgow Medical School in 1984. After obtaining full registration in 1985 commenced working in Accident and Emergency medicine. Commissioned in the Royal Army Medical Corps in 1986 and during the following five years worked in the field of serious surgical and orthopaedic trauma, developing skills in immediate, operative and post-operative management. After leaving the RAMC worked in the NHS in Accident and Emergency at Associate Specialist level.

Full-time Medico-Legal Practitioner for the last thirty years with special expertise in:

- road traffic trauma and soft tissue orthopaedics
- industrial and domestic injuries
- slipping and tripping accidents
- injury related to Armed Forces' activities, both land-based and airborne.
- gunshot wounds and blast injuries

Medico-legal experience in provision of over 30,000 reports commissioned by plaintiff lawyers and insurance companies. Experienced in detailed investigation in medical aspects of suspected fraudulent claims.

Extremely experienced in giving medical evidence in the courts and involved in training and auditing doctors undertaking medico-legal work.

Involved in medical research regarding long-term outcomes of injury in road traffic accidents.

Former Honorary Clinical Senior Lecturer in Medicolegal Medicine at University of Glasgow Medical School, lecturing on Functional Anatomy & Medico Legal Medicine.

Honorary Senior Lecturer, Forensic Medicine Department, Glasgow University.

Medical Director of The Scottish Mock Court Initiative which covers the whole of Scotland.

Contributing author to Personal Injury and Criminal Trauma Vol.II.

Cardiff University Law School Bond Solon Civil Expert Certificate.

Member of the Expert Witness Institute.

Member of the Independent Doctors Federation.

M.D.D.U.S. Membership: M 110326 at NHS Consultant Grade.

GMC Registration Full: 2951586 1<sup>st</sup> August 1985.

# Appendix III <u>Nomenclature</u>

There is considerable disparity of nomenclature utilised to categorise head/brain injuries and specifically those involving Whiplash, Concussions, Post-concussional states, Chronic Traumatic Encephalopathy (CTE) and Second Impact Syndrome (SIS). It is critical for appreciation of the issues discussed that there is clarity, both in nomenclature usage and understanding of the precise nature of these injuries.

**Whiplash**: - This condition was first described by Professor Anthony Crowe in 1928. The precise biomechanical model reported was abrupt hyperextension of the cervical spine followed by a reflex hyperflexion (an abrupt backwards then forwards movement of the head and neck). This followed a rear impact into a stationary vehicle. Over time, the expression "whiplash" has come to be used more generally, both by the lay public and majority of non-specialist medical professionals for any abrupt head and neck movement in any plane. However, this may not reproduce the dramatic backwards then forwards displacement of the head and neck typically seen in the original whiplash mechanism but does result in abrupt head and brain movement. This may be rotational in nature which it is postulated is more associated with higher shearing stress within the brain.

"Whiplash" has been most typically associated with subsequent neck pain, primarily affecting the posterior cervical muscles and major muscles of neck support such as the trapezius. However, since the turn of the millennium a progressively increasing number of patients presenting for medicolegal assessment with whiplash type injuries have also reported an intercurrent concussion or post-concussional presentation. This is felt to be due to abrupt acceleration and deceleration of the head and neck associated with the "whiplash" mechanism. There may be no report of any direct head trauma in such instances, supporting the view that these presentations are secondary to abrupt head and neck acceleration without any direct blow to the head.

**Concussion**: - This is a type of traumatic brain injury m(TBI) caused by "a bump, blow or jolt to the head or by a hit to the body that causes the head and brain to move rapidly back and forth. This sudden movement can cause the brain to bounce around or twist within the skull creating chemical changes in the brain and sometimes stretching and damaging brain cells."

Most such injuries only produce comparatively minor symptomatology which settles rapidly, often as swiftly as 48 hours, but on occasions persisting over the first two weeks on a gradually diminishing basis. This is the type of issue experienced by most individuals suffering sports-related concussions injuries, with current estimates of incidence around 85- 90% of all concussion injuries sustained. There is no precise consensus as to a definitive timeframe when a "concussion" becomes a post-concussional state, but in practical application most medical professionals accept a period around the 14-day point.

**Persistent post concussive symptoms (post-concussion syndrome/state - PCS)**: - The Mayo Clinic defines PCS as when "concussion symptoms last beyond the expected recovery period after the initial injury. The usual recovery period is weeks to months. The symptoms may include headaches, dizziness, and problems with concentration and memory."

Despite concussion being considered a traumatic brain injury either from a direct blow or from violent shaking or movement of the head and body, individuals frequently do not lose consciousness. In fact, the risk of developing persistent post concussive symptoms does not appear to be associated with the severity of the initial injury.

In plain terms, a comparatively minor head blow may result in more prolonged and intrusive symptoms as compared to an apparently much more significant head blow with loss of consciousness, amnesia, and more significant initial clinical symptoms.

In the majority of individuals post concussive syndrome will gradually diminish over three months, but some will experience much more persistent issues for a year or more. Additionally, further concussions sustained after an initial concussion episode from which an individual has apparently made a full recovery do on average tend to show a more significant presentation, although this is not always the case.

**Chronic Traumatic Encephalopathy (CTE)**: - This is defined by the Boston University CTE centre as "a degenerative brain disease found in athletes, military veterans and other individuals with a history of repeated head trauma."

Much of the understanding of the causation of CTE comes from the research of Doctor Ann McKee at Boston University and director of the VA-BU-CLF Brain Bank who has undertaken extensive research into post-mortem changes in sufferers' brains. This has identified malfunction of Tau proteins within the brain structure. These abnormal proteins spread throughout the brain structure, killing brain cells. It is of note that symptoms do not tend to present until years after the initial pattern of repeated head traumas. Not only has this study identified the post-mortem appearances of CTE, but specific comment has been made on the incidence of CTE in the brains donated by former American Football players who developed neurological disturbances during life. The horrifying statistic is that brain changes in keeping with CTE were identified in 99% of former NFL players. The researchers also found that 48 of 53 brains of former college players showed signs of CTE as did seven of eight individuals who played professional football in Canada and 9 of 14 in semi-professional players.

These findings prompted the comment from Gil Rabinovici, a Neurologist at the University of California San Francisco that: - "I think it is increasingly difficult to deny a link between CTE and repeated traumatic brain injury, be it through contact sports or other mechanisms."

A more recent development that will require extensive future study is the hypothesis that repeated sub-concussional head injuries may also be an ultimate trigger for CTE. For clarity, these are blows to the head that are observed or reported but do not appear to cause a level of clinical symptomatology allowing a diagnosis of concussion. Investigation of this phenomenon remains in its infancy.

Chronic Traumatic Encephalopathy is a serious, progressive, and significantly debilitating condition with catastrophic long-term impacts on sufferers' cognitive function, memory, and employability. It should be noted that a similar condition was first recognised in the 1920s when research began into what was then known as "dementia pugilistica" or fist fighter's dementia following repetitive head trauma. CTE presents in four progressive and worsening stages. The first stage is one of dizziness, confusion, disorientation, and headaches. The second stage is characterised by social instability, memory loss, impulsive behaviour, and poor judgement. The third and fourth stages involve continuing deterioration with progressive dementia, communication difficulties, movement disorders, tremors, vertigo, sensory processing disorders and deafness as well as depression and suicidality.

**Second Impact Syndrome (SIS)**: - Also known as Repetitive Head Injury Syndrome, this is a condition in which an individual suffers a further concussive head injury before they have made a complete recovery from an initial concussion. This causes the brain to swell rapidly and catastrophically. The second injury may occur minutes, days, or weeks after an initial concussion and even the mildest further concussion can lead to SIS. This is often fatal and almost everyone who is not killed is severely disabled.

The precise cause of SIS is uncertain, but it is thought the brain's arterioles lose their ability to regulate their diameter and therefore lose control over cerebral blood flow, causing massive cerebral oedema (fluid-based swelling). It is of note that in this condition the initial concussion need not be severe for the second impact to cause Second Impact Syndrome. Additionally, the second impact can be minor without a direct head injury but with a jolt to the body transmitting forces of acceleration to the brain.

In SIS, the usual cause of death is herniation of the brainstem secondary to a massive increase in intracranial pressure caused by brain swelling. Whilst SIS is rare and is most frequently seen in the 16- to 19-year-old age group of senior high school, this can also affect adult athletes. Whilst a precise causation model has not yet been definitively established, it is accepted that the younger age group are up to sixty times more sensitive to metabolic chain changes within the brain after sustaining an initial head injury and hence are more susceptible to SIS. Following its initial description in 1973, cases of SIS in American athletes has resulted in regulatory changes first inducted into US law in Texas in 2007 (Will's Bill). This introduced a legal requirement that personnel involved with care and training of those participating in contact sports have a mandatory duty to be fully educated in the presentation of concussions and their management, as well as awareness of SIS and its causation. Further similar legislation enacted in Washington in 2009 has subsequently been adopted as a baseline by all states in the United States.

# OVERVIEW OF CONCUSSIONAL INJURIES IN FEMALE RUGBY FROM A MEDICOLEGAL PERSPECTIVE

Are there basic physiological, anatomical and structural differences between men and women and any difference in injury frequency, presentation, and long-term implications?

# 1. <u>ABSTRACT</u>

Objective: - To provide an evidence-based opinion as to whether concussional injuries in female rugby players occur with greater frequency than males and whether symptomatology in the female cohort is more severe and/or persistent.

Research design: - Review of current literature from complimentary disciplines to reach an evidence-based viewpoint as regards potential female versus male differences.

# 2. <u>METHODOLOGY</u>

Systematic review focusing on sex-related differences in individuals with concussion. Only articles published in peer-reviewed journals were considered for inclusion. Information has been obtained from a wide variety of sources, necessitating investigation of outcomes in comparable sports and utilisation of extensive research data that has already been undertaken in the field of human biomechanics. This allows application of evidence-based information to a human biomechanical model and to also assess peer-reviewed studies yielding data relevant to concussion injuries from around the globe.

# 3. <u>INTRODUCTION</u>

With the progressive development of women's rugby and increased numbers of participants, both elite and non-elite, there is a significant increase in media and public interest in the sport. There are now significant questions being asked in the media regarding male versus female safety in a high-energy transfer, contact sport. It should be noted that rugby is the only female team participant sport in which high-energy contact between multiple players is an integral and desirable part of the game. Interest in female rugby has increased dramatically, as has media interest in potential injuries sustained during play. Recent media coverage has focused on concussion, post-concussional states and long-term issues resulting both from individual and multiple concussions.

This review reflects on the evidence presented internationally regarding the frequency of concussion episodes between male and female contact sports participants and whether female sex increases the likelihood of a more protracted or significant post injury presentation. Given the paucity of specific studies of female rugby players, investigation has frequently necessitated assessment of comparable contact sports.

#### 4. <u>COMPARATIVE INCIDENCE OF CONCUSSION IN MALE VERSUS</u>

#### FEMALE SPORTS PARTICIPANTS

Given the comparatively recent growth in player participation in female rugby, no large-scale UK study is currently available regarding the incidence of concussion injuries in male versus female rugby. However, international studies have revealed a percentage concussion rate of 15% in female rugby players versus 8.7% in male participants(Peck *et al.*, 2013). The best comparable sports study – including the largest cohort - was undertaken by(Bretzin *et al.*, 2021). The cohort in this case consisted of 43,741 male collegiate soccer players and 39,637 female collegiate soccer players with data collected over three consecutive seasons. The total number of participants in the study was 83,378, by far the largest such study currently published. The total incidence of "sports-related concussions" in the male group was 557 and that in the female group 950. This constitutes a 1 to 1.73 male to female ratio within the examined cohort. The rugby study noted above leads to an almost identical 1 to 1.72 male to female ratio.

The published data for studies in collegiate soccer and rugby, as outlined above, suggests that women are 72 to 73% more vulnerable to sustaining concussion injuries than their male/transgender counterparts. In addition to the studies above, allowing quantitative analysis, it is widely mentioned anecdotally in numerous international papers that women have a risk of concussion injuries approximating to twice that of men. A further consideration, particularly with regard to female Rugby Union players, is that a recent study in female Rugby League found that there was an average of 14 head impacts per player per match. This compares to an average of 1 to 2 head impacts in comparable sports(King *et al.*, 2018).

This is a dramatic difference in male to female risk ratio that needs immediate recognition and appropriate action. This issue requires urgent further research and evaluation to quantify in detail and to develop further strategies mitigating injury severity and frequency in female participants. This may also have significant implications going forward for insurance rates between male and female rugby players.

#### 5. <u>SYMPTOMS OF MILD TRAUMATIC BRAIN INJURY AND CONCUSSION</u>

These are endorsed by the US Centre for Disease Control and Prevention and are, in the author's opinion, the best categorised in that potential symptoms of a concussion are broken down into physical, cognitive, social, and emotional or relating to sleep disruption, the four principal groupings within the total spectrum of potential symptoms.

5.1. Physical symptoms are categorised as follows: -

- Bothered by light or noise
- Dizziness or balance problems
- Feeling tired, no energy
- Headaches
- Nausea or vomiting (early on)
- Visual problems

#### 5.2. Cognitive issues are: -

- Attention or concentration problems
- Feeling slowed down
- "Foggy or Groggy"
- Problems with short or long-term memory
- Trouble thinking clearly

5.3. Social or Emotional issues include: -

- Anxiety or nervousness
- Irritability or easily angered
- Feeling more emotional
- Sadness

**Sleep Disruption** may be in the form of sleeping less or more than usual, or trouble falling asleep.

It has been noted that after mild traumatic brain injuries or concussion that the sufferer may not recognise or admit that they are having problems. They may not understand how the symptoms they are experiencing affect their daily activities and most significantly, issues may be overlooked by not only the sufferer, but also by family members or healthcare providers.

#### 6. <u>OUTCOMES OF SPORT-RELATED CONCUSSION</u>

This is an area where there is a significant volume of published data firmly supporting the view that females experience more significant post-concussional issues and a longer period of recovery. Females are more cognitively impaired than men by a factor of 1.7:1 and experience greater objective and subjective effects(Broshek *et al.*, 2005a). Additionally, females showed diminished performance on visual memory and total combined memory function scores after sports-related concussions(Covassin *et al.*, 2013). Recovery time is noted to be shorter for males compared to females(Gallagher *et al.*, 2018). This study additionally notes that females not taking the oral contraceptive pill had increased severity of symptomatology compared to those who were.

Specific comment regarding time differences to a return to baseline are contained within the works of (Bazarian *et al.*, 2010) and (Stone *et al.*, 2017). Bazarian notes that females experience a greater number of days post-concussion to a return to normal activities with a concomitant increase in the amount of work time missed. Stone's study specifically notes that in a cohort of 11 to 20-year-olds females it took an average of 29.1 days to return to play, as compared to males who on average took 22.7 days to return to play. Perhaps the most compelling evidence of a slower recovery pattern in females is that of (Hsu *et al.*, 2015) who identified persistent working memory impairment at 10 weeks post injury. This was not a subjective study and included evidence of noted ongoing abnormality in the female cohort when examined via functional MRI scanning. Controls and males in this study did not show similar deficits.

Given variability between both males and females and also variability in recovery times within each sex, it is not possible to define a single physiological time window for recovery after mild traumatic brain injuries(Kamins *et al.*, 2017). Published opinion is that a return to play protocol "must be objective and individual" with no attempt to impose a "one size fits all" regime(Broshek *et al.*, 2005b). Stone et al. go further, including the statement "Sex should be considered part of the decision-making process when determining a plan of care".

Further consideration must also be given to intercurrent comorbidities. These include intercurrent cervical sprain injuries more frequently seen in females than males in a contact sport context as well as pre-existing mental health status and emotional distress associated with post-traumatic complaints(Coffeng *et al.*, 2020). As the female sex typically experiences intercurrent depression at a rate twice that of males and also tends to experience a more widespread and diverse pattern of post-concussional symptoms, this is an important feature.

# 7. <u>IS THERE A GREATER RISK OF POST-CONCUSSIONAL SYNDROME IN</u>

#### **FEMALES VERSUS MALES?**

Unfortunately, the answer to this question would appear to be yes with the first study noting an increased incidence of post-concussional issues in females as long ago as 1977(Rutherford, Merrett and Mcdonali, 1977). More recent studies investigating gender differences in post-concussional syndrome in the context of sports-related injury indicate that an elevated risk exists for female participants aged 18 years or older as compared to male subjects (Preiss-Farzanegan *et al.*, 2009), but also for females in general(Mollayeva, El-Khechen-Richandi and Colantonio, 2018). Certain symptoms also appear to be more prevalent in women, particularly those of headache, dizziness, fatigue, irritability, and concentration problems at three months after sustaining a mild TBI(Covassin, Schatz and Swanik, 2007). In neurophysiological studies after sport-related brain injury it was found that at three days post-concussion, female athletes performed significantly worse on visual memory scores compared with baseline measurements than their male counterparts. They also showed a more severe decline on measures of simple and complex reaction times with respect to baseline levels(Preiss-Farzanegan *et al.*, 2009). An intriguing study once again confirmed that men demonstrated lower odds of a high post-concussional symptom score as compared to women, but noted that the increased risk in females was only apparent in childbearing years(Bazarian *et al.*, 2010). This raised the first questions regarding a possible association of increased symptoms with variations in adult female sex hormone profile.

Interestingly, despite many studies worldwide suggesting that only 10 to 15% of concussion sufferers will experience persistent difficulties beyond the initial week or two, several studies suggest a significant proportion of individuals with ongoing post-concussional symptomatology for substantially greater periods. One very recent study indicates continuing post-concussional issues in 30% of sufferers at three months(Sheldrake *et al.*, 2022). Unfortunately, this finding was not broken down into relative male versus female incidence. (Preiss-Farzanegan *et al.*, 2009) quote an incidence of post-concussional symptoms in a range of 30 to 80% three months post injury but only 15% at one year. It was, however, noted that risk of more persistent symptoms was elevated in adult women, but not in minors, as compared to men.

Findings in the post-concussional cohort were felt to be consistent across several studies indicating a worse aggregate outcome across several parameters for females as compared to males. It has been concluded that recent study findings concur with several reports in the literature of elevated risk of mild traumatic brain injury sequelae in women and highlight the need for greater awareness of this risk among physicians who evaluate and treat these patients. Once again there are calls for further research to fully investigate risk factors for prolonged recovery and resultant functional impairments and evaluate the precise causation of an elevated risk of prolonged post-concussional symptomatology in women.

#### 8. <u>DIFFERENCES IN MALE VERSUS FEMALE HEAD & NECK PHYSIOGNOMY</u>

Whilst it is obvious, even on casual inspection, that males and females display different physiognomy, there are major but disguised anatomical differences that are not frequently appreciated. Much of the definitive work in this regard was published by Doctor Anita Vasavada who after extensive biomechanical research concluded in her 2008 paper that: - "There are significant differences in head and neck geometry and neck strength in males versus females" (Vasavada, Danaraj and Siegmund, 2008).

It has been noted that on average the load bearing area of the cervical vertebrae in women is 18 to 20% smaller than that in a height matched male subject. Furthermore, excellent biomechanical research found that in a comparable height matched group, women demonstrated a 59% smaller total neck <u>muscle</u> volume in comparison to males, but a total neck volume only 27% less(Zheng *et al.*, 2013). Other studies suggest even smaller differences in average male versus female neck volume, although these did not specifically examine total neck muscle mass.

Consequently, whilst there may visually appear to be only a comparatively small difference between the neck of males and females, there is a dramatic difference in the volume and strength of the neck muscles. As the neck musculature acts as the principal dynamic supporter and stabiliser of the head, it follows that female physiognomy is less able to manage abrupt head and neck acceleration.

There have been numerous cadaver studies on the relative head mass as a percentage of total body mass with the average percentage estimated in the six principal studies between 1860(Harless) and 1975(Roebuck) as 7.76% (range 7.0-8.8%). Average head mass at the 75<sup>th</sup> centile has been selected as most likely representative of rugby players. Neck mass in isolation has been rarely studied, but can be ascertained by the differential between total head mass and total head and neck mass.

The average male neck mass is 1.66 kg with an average head mass of 5.17 kg. This gives a neck to head mass ratio of 1 to 3.11.

The average female neck mass is 1.22 kg with an average head mass of 4.68 kg. The resulting total neck to head mass ratio is 1 to 3.83.

However, when factoring in the notably lesser percentage of total <u>muscle</u> mass in the female neck, this results in a total neck muscle mass to head weight ratio of 1 to 9.36 as compared to the 1 to 3.11 ratio enjoyed by males.

Considering the lower total muscle mass composition of the female neck and the poorer neck muscle mass to head weight ratio, it is entirely reasonable to assume from mathematical modelling that the female neck is less capable of management of abrupt acceleration loads and allows greater displacement of the head and neck. This has been formally confirmed by the research of Tierney et al. published as long ago as 2005(Tierney *et al.*, 2005). This would additionally fit with the finding that females tend to experience concussion injuries at a lower neck acceleration threshold(Mollayeva, El-Khechen-Richandi and Colantonio, 2018).

As a result of the above information, which is derived from peer reviewed studies in highly respected journals, it is impossible to reach any other viewpoint than that women cannot be regarded as "small men." They demonstrate significant anatomical and physiological differences as regards head and neck function, resulting in a lower ability to withstand abrupt head blows and neck acceleration. It would therefore follow that there is a significant advantage in neck strength and head support ability between appropriately height and body weight matched males/transgender and females.

#### 9. <u>NEUROPSYCHOLOGICAL ISSUES</u>

This is an emerging area in consideration of "full" recovery following concussion type injuries. Both sexes demonstrate increased levels of psychological upset and diminished levels of quality-of-life following concussion injuries (Silver et al., 2001). Concerning quality of life after concussion injuries, females do appear to be adversely impacted with a significant increase in poor quality of life scores after concussion in contact sports. With regard to rapid return to play protocols, these may be inappropriate as in terms of neuropsychological function, 30% of concussion sufferers still show a reliable decrease from preseason values at eight days post injury(Covassin, Schatz and Swanik, 2007). This is in keeping with the opinion that a cohort of 8 to 24-year-old females shows a worse outcome on cognitive testing and report more concussion symptoms than males(Covassin et al., 2006) What is clear from the vast majority of commentators is that, as yet, extensive research into late neuropsychological sequelae of concussion injuries for females remains in its infancy. However, multiple research opinions are documented that preseason baseline testing of neurocognitive and neuropsychological function are a vital tool in management of players following concussion injuries. This is due to the fact that a prior to head injury baseline is vital to allow comparison of subsequent neurocognitive and neuropsychological scores. Even as early as 2006 Covassin states that players should not be allowed to return to participation until their neuropsychological scores are the same or better than their baseline status and their clinical symptoms have resolved" (Covassin et al., 2006). Preseason testing is also advocated by (Wunderle et al., 2014) and multiple other authors for the same reason of true baseline assessment.

Professor James Kelly (Professor of Neurology) in Denver, USA and a leading authority on traumatic brain injuries and concussions eloquently outlines the reasons for preseason testing. He emphasises the necessity to aggregate several tests to find a true baseline level without any learned response or influence of intercurrent lifestyle/illness factors in one of a series of online videos produced by Brainline.

# 10. <u>IS THERE AN INCREASED RISK OF MENTAL HEALTH ISSUES FOR</u> <u>WOMEN AFTER A CONCUSSION</u>?

Anxiety and depression are widely recognised to be more prevalent in females compared to males by a factor of approximately 2:1. This is a mean figure and has been validated across multiple studies worldwide including WHO data and is not considered contentious. 2:1 is the risk ratio prior to any head injury or traumatic brain injury(Vijayakumar, 2015). After a traumatic brain injury, approximately half of individuals will experience depression in the ensuing year with the risk of depression increasing to almost two thirds of sufferers over a seven-year timeframe. Poor mental health and depression prior to injury is widely regarded as an indicator for poorer outcomes post-concussion and a more severe pattern of post injury sequelae(Sheldrake *et al.*, 2022).

The incidence of intercurrent anxiety has been found to be 50%. It has also been found, even in those who were suffering psychiatric issues prior to any head trauma, that subsequent to a traumatic brain injury up to 65% will receive a further psychiatric diagnosis, most commonly of major depression, with anxiety the second most common feature. In up to two thirds of these individuals the diagnosis is considered to be a new feature(Whelan-Goodinson *et al.*, 2009). Consequently, the increased prevalence of anxiety and depression in females prior to injury does lead to an increased number with more significant mental health issues after mild traumatic brain injury. Depression is, unfortunately, the principal risk of subsequent suicidality(Vijayakumar, 2015).

Given the primarily subjective methodology for assessment of concussion symptomatology, issues relating to mental health are not frequently volunteered by sufferers and not examined in depth or compared to a prior to injury baseline. This is an area where increased depressive and anxiety symptoms in the female cohort undoubtedly require heightened awareness and consideration by health care providers.

Once again, there is a clear indication of gender difference from current studies, but much further research is required to evaluate the precise causation of sex-specific depression rates following mild traumatic brain injuries in detail.

#### 11. SUICIDE RISKS

After a concussion injury, an extensive study including a cohort of 235,000 adults confirmed a three times greater prevalence of suicide as compared to the background population(Fralick *et al.*, 2016). A broadly similar 2.23:1 ratio was noted after traumatic brain injuries in Taiwan(Lu *et al.*, 2020). The risk was also statistically increased by a further third in those who had sustained their injury at a weekend, leading to the hypothesis that the risk appeared increased in those involved in recreational sporting pursuits(Fralick *et al.*, 2016). No gender specific comment between males and females has been offered in this study, although it is of note that available WHO data confirms a male to female general suicide ratio of 3.2 to 1 in the United Kingdom with a concussion-related suicide risk of 2.03:1 compared to the background population. This is the one area identified in which there appears to be an increase in risk after concussion injuries that is equal between the two sexes.

Specific comitant risks identified for suicide in those suffering from minor traumatic brain injuries are intercurrent psychological conditions and psychosocial disadvantages. Intriguingly, incidence of suicide in females appears highest when circulating oestrogen levels are at their lowest in the late luteal phase of the menstrual cycle(Vijayakumar, 2015).

Once more, current research on the subject has not yet been able to precisely identify a reliable cascade of events leading to suicide following a concussion injury, but does suggest that higher vigilance and psychosocial monitoring subsequent to concussion injuries is necessary. Given the possible hormonal link, female centric questioning would be appropriate.

This is likely to save lives from early identification of suicidal thoughts and swift provision of appropriate support. It is, however, clear from the research that a previous suicide attempt is a much higher indicator of a future similar attempt and potential fatality(Rojas *et al.*, 2019).

# 12. <u>THE INFLUENCE OF HORMONAL FACTORS IN CONCUSSION</u>

### **INCIDENCE AND THE "REBOUND PHENOMENON."**

There is excellent developing evidence of hormonal influence on outcome after traumatic brain injury. Studies have revealed that whilst there is little difference in male versus female outcome in age groups prior to puberty and after menopause, there is a notable difference in concussion severity in women during their years of menstruation(Bazarian *et al.*, 2010).

Prior research on hormonal factors has already led to use of progesterone in the treatment of those with severe traumatic brain injuries, as progesterone is felt to be neuroprotective. In the menstrual cycle there is significant fluctuation of background progesterone levels. These are much higher in the luteal phase, normally between 14 and 28 days of the average menstrual cycle. It is widely accepted that traumatic brain injuries are associated with an abrupt drop in progesterone levels. A significant diminution is therefore only possible during the luteal phase of the menstrual cycle whilst progesterone levels are at their peak, allowing a much greater difference between peak progesterone and post head injury progesterone levels. This is known as the Rebound Phenomenon.

Whilst males also have circulating progesterone, this is at a very much lower background level and hence any notable change post head injury is not possible. Similarly, women whose progesterone is artificially maintained utilising the contraceptive pill do not appear to suffer dramatic progesterone level changes post head injury or similar negative outcomes. Obviously, prepubertal and postmenopausal females do not have such marked fluctuation of sex hormones compared to those of childbearing years. Those women who suffer a mTBI during the luteal phase of their ovulatory cycle demonstrate more significant postconcussional symptomatology that is not demonstrated in females who are prepubertal, taking the contraceptive pill or postmenopausal(Wunderle et al., 2014). This variance is not noted in males who do not demonstrate any significant change in their baseline progesterone levels mimicking the female menstrual cycle. It is postulated that for females up to two thirds of concussion incidents are suffered in the late luteal phase with a significantly poorer quality of life as measured one month after injury in comparison to females who do not sustained their injury in the late luteal phase. Other studies relating to sport injuries, but not focused on head injuries or minor traumatic brain injuries, have also noticed hormonal cycle variance in injury occurrence and severity, particularly in the field of anterior cruciate ligament injury. It is of note that a number of elite athletes in non-contact sports have recently attributed fluctuating performance levels to the timing of competitive events within their ovulatory cycle, a further subject currently receiving media attention. Once again, further in-depth study of this phenomenon is required.

#### 13. FEMALE NEUROANATOMY CONSIDERATIONS

Very little consideration has historically been given to basic neuroanatomical differences between male and female brains. However, this is likely to cause significant differences in outcome for females versus males. Computational models of concussion impacts indicate greater strain at the Corpus Callosum, the area of the brain responsible for interhemispheric nerve signal connections. It follows that disruption in this area of the white matter results in a difference of perceived symptoms between the male and female as females utilise both hemispheres for the majority of tasks, necessitating increased use of cross hemispherical connections, whereas males tend to use a single hemisphere more exclusively(Solomito, Reuman and Wang, 2019).

Furthermore, female axons particularly in the white matter tend to be smaller with fewer microtubules and consequently axons are more likely to be damaged than those of men at the same force application level(Dollé *et al.*, 2018). Diminished average diameter of female axons was confirmed via neuroimaging by Alexander et al. in 2010(Alexander *et al.*, 2010). This would be in keeping with the finding that women tend to experience concussion injuries at a lower average impact threshold(Sayre *et al.*, 2019),(Mollayeva, El-Khechen-Richandi and Colantonio, 2018). Diminished average axon diameter would result in less ultimate axon resilience, particularly with application of an abrupt shear or longitudinal load in a head impact.

# 14. <u>CURRENT INVESTIGATION METHODOLOGIES</u>

Setting aside the subjective initial assessment of potential minor traumatic brain injury sufferers, there would appear to be poor understanding of the reasons for objective investigation of individuals who have suffered a "head injury." The majority who have suffered such injuries will normally anticipate investigation via x-ray, CT scanning or MRI scanning. It should be understood that, following head injuries, these investigations are primarily to exclude intercurrent pathology such as skull fractures or intracranial bleeding. These are extremely useful tools in the identification of bony injury to the skull and are vital investigations to exclude intracranial bleeding which may or may not require surgical intervention to alleviate pressure on the brain structures.

What is not appreciated is that X-rays, CT (Computerised Tomography) scans and MRI (Magnetic Resonance Imaging) scans are poor at visualising brain changes after mild traumatic brain injuries. Emerging technologies however, including functional MRI scans, PET (positron emission tomography) and Neuroencephalography, measuring the electrical activity of the brain, have shown considerable promise in identification of functional changes consistent with post-traumatic brain injury. As previously noted, a recent controlled trial in Taipei(Hsu *et al.*, 2015) was able to visualise evidence of changes consistent with post-traumatic brain injury using functional MRI scans. These showed a slower functional recovery for women as compared to men. An increased level of white matter changes in females as compared to males has also been noted on MRI scans(Rubin *et al.*, 2018).

This study followed investigation of brain changes after repetitive heading of a football in male and female groups.

There can be no doubt that further refinement of investigative technology is likely to allow visualisation of the subtle imaging changes of minor traumatic brain injury. Similarly, further investigation into white matter changes after concussion injury may well lead to a situation where conclusive proof of a mild traumatic brain can be obtained via appropriate imaging. As yet this technology is still emerging and cannot be relied upon.

At present, progress of, or recovery from many diseases is gauged using blood biomarkers. This presents an easy and minimally invasive method that can accurately and quickly assess disease presence or severity. Until recently, no reliable biochemical test for traumatic brain injury was available, but in 2018 Banyan Biomedical presented a new biomarker assay for FDA approval in the United States. This identifies specific biomarkers released by damaged brain and glial cells after head injury and is effective if the test is performed within 12 hours(Mendoza *et al.*, 2020). After rigorous scrutiny, FDA approval was granted, and it is thought likely that this may well become an extremely useful investigative tool to assist in accurate diagnosis of minor traumatic brain injury and design of return to play protocols.

Similarly a 2021 study of hormonal biomarkers following mild traumatic brain confirmed that an older female cohort aged 35 to 49 did worse than a younger cohort of 17 to 35-yearolds and a control cohort with only orthopaedic injuries. This related specifically to increased cognitive and somatic symptoms(Anto-Ocrah, Mannix and Bazarian, 2021). Further reference to the potential benefit of biomarkers for brain injury is included in the work of(Shahim *et al.*, 2014) who suggest that plasma T-tau, which has high central nervous system specificity, is a promising biomarker for post-concussional diagnosis and has potential use in management of return to play protocols. This minimally invasive assessment using blood or saliva samples only may in future help definitively confirm evidence of brain cell injury and assist in assessing when a full recovery has been made and a return to play is appropriate.

#### 15. <u>SECOND IMPACT SYNDROME</u>

Whilst the vast majority of research documentation examined related primarily to intersex differences in mTBI, it is important to consider this rarer but extremely significant possible complication of concussion injuries. Second impact syndrome results, almost exclusively, from a second episode of head trauma after a previous minor traumatic brain injury has been sustained, especially if a full recovery has not been made. This results in catastrophic failure of brain blood supply regulation resulting in gross brain swelling and subsequent brain ischaemia from compression against areas of bony prominence on the inside of the skull but more typically causing downward herniation of the brainstem and ultimately resulting in death. This condition primarily occurs in school-age children and must therefore be regarded as a significant risk factor in young rugby players.

As the female sex is twice as likely to sustain a concussion during play, this is of particular concern in female youth rugby, especially when attempts are being made to increase female player participation at a young age.

#### 16. <u>CHRONIC TRAUMATIC ENCEPHALOPATHY</u>

This is an extremely topical subject at present given the emergence of significant cohorts of symptomatic retired rugby players both in Scotland and England. Numbers in each cohort do appear to show close numerical similarity to the relative populations of both countries. Unfortunately, there has been virtually zero research relating to this presentation in women and at present only two brains held in the brain bank at Boston University show evidence of chronic traumatic encephalopathy. One of these brains was donated by a sufferer of repeated domestic violence who had sustained multiple head blows over a lifetime and the other was from an individual with developmental issues who had habitually indulged in head-banging behaviour. All other brains had been donated by individuals who experienced neurological issues in life and a clinical pattern indicating a potential neurodegenerative disorder. It has been found that 99% of previous NFL players do demonstrate neuropathology in keeping with CTE and with notably high CTE presentations in multiple players participating at a less elite level. Similar findings with a notable increase in CTE neuropathology have been demonstrated in retired football (soccer) players in the United Kingdom. This work has been undertaken by Professor Willie Stewart and forms part of the findings of the "FIELD" trial. This has revealed that repetitive concussive or sub-concussive injuries results in a 3.5 times risk of neurodegenerative disease generally, a five times increased risk of Alzheimer's disease and a risk of Parkinson's disease at twice the rate of the background population(Russell et al., 2019).

The significant question that cannot be definitively answered as yet is whether after expansion of the female game there will be a significant cohort of female rugby players who present with CTE. Unfortunately, the condition can only be definitively diagnosed post-mortem after neuropathological examination of the affected individual's brain. However, it is already acknowledged by the Alzheimer's Society that women are differentially affected twice as frequently as males and tend to have a more rapid rate of brain cell death than their male counterparts. Consequently, if a further risk factor such as repeated head trauma is introduced to the equation, it would appear highly probable that over time a significant female cohort of CTE will emerge. This view is supported by Professor Robert Stern, Professor of Neurology at Boston University. As regards whether immediate action should be taken concerning the risk of CTE in female sports participants, it is Professor Stern's opinion that: - "We cannot wait another thirty to sixty years for whole life studies. We must combine common sense with the growing body of evidence".

The relative risk of either sex developing CTE after contact sport participation has yet to be elucidated accurately and further studies are desperately needed. The journal Science did

however estimate the risk of CTE development in NFL players between 1963 and 2008 as being between 10 and 90%. It would appear from subsequent neuropathology studies that in elite sport at the highest level that the risk is significant. Consequently any future studies must take into account a potentially emerging female cohort and any differences in formation of the causative Tau protein within the brains of females as compared to males should be highlighted, hopefully opening the way for further specifically directed research.

Given the close relationship between differing neurodegenerative disorders it may well be that genetic markers for increased risk may become apparent from the research in associated fields into Alzheimer's and Parkinson's and researchers into CTE must remain vigilant regarding any potential advances of benefit in these areas.

# 17. <u>IOC CONCUSSION IN SPORT STUDIES</u>

Prior to the Covid 19 pandemic, specific conferences regarding concussion in sport had been undertaken under the aegis of the IOC on a four yearly basis. Examination of the findings at successive meetings shows that following the meeting in Zurich in 2012, it was not felt that a unanimous consensus could be reached as to whether the available research showed a significant gender bias between male and female. At that time, evidence was deemed "not conclusive enough." At the following and last such meeting in Berlin in 2016, female-centric research is not mentioned at all within the summary of meeting findings. There was, in fact, no specific mention of female athletes apart from acceptance that female high school athletes show a higher incidence of concussion injuries than their male counterparts. It is unclear why there was no further female specific consideration of research evidence at that time. Unfortunately, due to the Covid 19 pandemic, there has been no such further conference since 2016, although further consideration of concussions in sport is due in the late autumn of 2022. Consequently, there has been no further consideration of a potential difference in female versus male concussion rates and outcomes despite the aggregation of a further 10 years of academic research. The reasons for this are unclear.

#### 18. <u>CONCLUSIONS</u>

Considering the medicolegal position, the aim is to reach an opinion based on the balance of probabilities. This is secondary to investigation of the causation of a specific injury and its anticipated outcome when compared to a matched group cohort.

Regarding mild traumatic brain injuries or "concussions," there is no doubt that these occur following direct blows to the head or following non-direct bodily impacts causing abrupt head and neck acceleration. This applies to both males and females.

In this case the question focuses on whether injuries are more frequent in female participants and result in a different pattern of presentation and more protracted symptoms.

Applying these criteria, it is the author's view that there is undoubtedly a greater risk to female rugby players of sustaining a concussional injury during rugby participation. This has been statistically confirmed by numerous studies of sports-related concussions worldwide. It should be noted that this is not a minor difference in frequency as compared to males but constitutes at minimum a 75% increased risk from the data available.

There is also excellent and compelling biomechanical evidence supporting marked differences in physiognomy, muscle mass and head and neck acceleration resistance between males and females with the biodynamic model confirming a significantly increased risk to women. Post-concussional syndrome frequency is higher for female participants and there would appear to be a higher risk of late mental health issues after a concussion. Additionally, suicide rates after sustaining a concussion are some three times higher than the background population. In this final area there does not appear to be a notable male versus female bias.

Perhaps the greatest area of concern is the increasing body of evidence indicating a link to the severe neurodegenerative disorder CTE (Chronic Traumatic Encephalopathy) in those sustaining multiple episodes of head trauma. This is primarily seen in the sporting arena and specifically affects those participating in contact/collision sports. There is already noteworthy media coverage of this phenomenon as regards retired elite male rugby players. At present, women's rugby remains an "emerging sport," but with an anticipated significant expansion in player participation in coming years. As yet, large numbers of women who have played rugby over a significant timeframe and consequently been subject to repeated head trauma have not been studied. However, given the evidence from investigation of retired and deceased male players, it would seem highly probable that there will, over time, be an emerging cohort of female players with neurodegenerative disorders whose condition was as a consequence of multiple head traumas sustained whilst playing.

Having undertaken this review, the author would consider that the balance of probability <u>has</u> been met as regards whether females playing rugby are at a higher risk of concussion injuries and that these may result in more prolonged recoveries and serious long-term sequelae.

The implications of this opinion remain to be tested in a court of law. However, given the findings outlined above and when considering current players' welfare and long-term "brain health," the medicolegal viewpoint would be that there is already sufficient proof of differences in injury frequency and longevity/seriousness of symptoms between male and female rugby participants. Consequently, females should be made aware of this increased risk. This would allow them to make an informed decision as to whether they choose to take up the sport or continue to participate having considered this risk factor. It would not be good enough currently to delay making a decision on the subject over an extended period whilst awaiting the outcome of yet more academic research.

In plain English, medicolegal litigation seeks to achieve a balance of probabilities consensus rather than the "beyond reasonable doubt" standard of criminal litigation. This threshold has been met.

# **19.** <u>ACTIONS RECOMMENDED</u>

Accepting that the balance of probability criteria have been met regarding an increased risk of traumatic brain injury and potentially longer and more significant sequelae for female rugby players, the following recommendations are made: -

a) New or current female players at a club should require formal notification that they are subject to increased risk in comparison to men of sustaining a minor traumatic brain injury. This should be acknowledged in writing. Ideally this should be presented in conjunction with formal education regarding concussion type injuries, their potentially serious implications, the importance of player reporting of suggestive symptoms and acknowledgement of the current world rugby directives on return to play protocols.

b) It should be the responsibility of Senior Club Management to inform players in their care of the increased risk of head injury when considering males v females. Their welfare is the direct responsibility of Club Officers, and the club structure and actions would be the first area of focus for any subsequent medicolegal litigation. Prior written acknowledgement of potential future risks by any player would form a strong defence basis.

c) Foster an environment in which reporting of subjective symptoms, which may be related to a concussion, by all players is encouraged and reported for appropriate action. This forms the basis of informed monitoring of player welfare under the club's care.

d) At all times treat potential concussions as a serious issue, with no gender bias and equal access to expert medical assessment and any further indicated investigations.

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