Institution: Loughborough University

Unit of Assessment: C26 Sport and Exercise Sciences, Leisure and Tourism

Title of case study: Development of strategies to monitor stress and help avoid infections in athletes and games players

1. Summary of the impact (indicative maximum 100 words)

The impact of the research by Professor Gleeson on immune responses to exercise and predictors of infection risk in athletes has altered practice of sport science support personnel, coaches and athletes in several areas including: immunoendocrine monitoring procedures, training prescription and the use of nutritional interventions to reduce exercise stress responses and minimize risk of infection. In this way, the research conducted during 2008-2013 at Loughborough University has impacted internationally upon the ways in which sports scientists operate, and athletes and games players are prepared for competition.

2. Underpinning research (indicative maximum 500 words)

The research described below concerns the work of Professor Mike Gleeson (Professor of Exercise Biochemistry 2002-2013) (with Dr Lettie Bishop, senior lecturer 2000-2013) who have developed research focused on the impact of exercise and training on immune function and infection risk in athletes. A series of studies that began in 2000 at Loughborough University has demonstrated that immune perturbations (e.g. depression of lymphocyte cytokine production) could be prevented by an appropriate dose (30-60 g/hour) of carbohydrate ingestion during prolonged exercise via an attenuation of the exercise cortisol response **[3.1]** and that chronic (daily high dose vitamin C and E supplementation for 4 weeks), but not acute, high-dose antioxidant vitamin supplementation could also reduce the cortisol response to exercise and so reduce the inhibitory effect of exercise on some aspects of immune function **[3.2]**. Further studies initiated in 2009 at Loughborough University have established that regular ingestion of Lactobacillus probiotics can reduce common cold or upper respiratory tract infection (URTI) risk in athletes; for example, the paper published in 2011 **[3.3]** described the first study to show that daily ingestion of a probiotic supplement could reduce respiratory infection risk in a large student cohort of endurance athletes and games players.

Research at Loughborough University has also established the value of immunoendocrine monitoring as a practical tool to identify athletes who are not responding well to stress **[3.4, 3.5]** and are therefore at an increased risk of infection. For example, a study on Americas Cup yachtsmen in 2008 (with Dr Jonathan Folland, senior lecturer, 2004-2013), established that weekly measurement of salivary immunoglobulin A (IgA) was a good predictor of URTI risk **[3.4]**. Falls in salivary IgA of 40% or more below normal healthy baseline concentration indicated a one in two chance of contracting an URTI within 3 weeks. These findings have important implications for athletes and coaches in identifying periods of high URTI risk. Other studies since 2008 have established which aspects of altered immune function predispose an athlete to URTI and predict illness risk. For example, papers published in 2011 and 2012 **[3.5, 3.6]** showed that illness-prone athletes had lower salivary IgA secretion and a higher anti-inflammatory cytokine production to antigen challenge than athletes who remained illness-free during 4 months of winter training, thus establishing two markers that can be used to evaluate infection risk in athletes. Furthermore, both anti-inflammatory cytokine production to antigen challenge and infection incidence were higher in athletes with high training loads compared with athletes who had low-moderate training loads.

Gleeson has published over 60 relevant papers since 2000 with an H-index of 36. The six exemplar research outputs listed in section 3 are separated into: (A) those which changed practice in elite sport by providing evidence for the potential benefit of certain practical or nutritional interventions to minimize immune impairment and infection risk and (B) those focusing on advancing sports science immunoendocrine monitoring procedures. The number of citations to these articles and the journal impact factor (IF) are also provided, where relevant.

3. References to the research (indicative maximum of six references)

All of these outputs exceed the threshold of 2-star quality because they represent novel research and were published in high-quality, peer-reviewed journals. Further evidence of quality is that the research was funded, in part, by grants awarded to Gleeson by UK Sport, GlaxoSmithKline, Nestle and Yakult. The co-authors were mostly PhD students, though Jeukendrup and Drayson were collaborating colleagues from the University of Birmingham, Wallace was a scientist from GlaxoSmithKline and Tauler was a visiting scientist on sabbatical from the University of The Balearic Islands.

A. Nutritional Interventions

3.1. Lancaster, G.I., Khan, Q., Drysdale, P.T., Wallace, F., Jeukendrup, A.E., Drayson, M.T. and Gleeson, M. (2005). Effect of prolonged strenuous exercise and carbohydrate ingestion on type 1 and type 2 T lymphocyte distribution and intracellular cytokine production in humans. *Journal of Applied Physiology* 98: 565-571. DOI: 10.1152/japplphysiol.00754.2004 (46 citations; IF = 4.2).

3.2. Davison, G., Gleeson, M. and Phillips, S. (2007). Antioxidant supplementation and immunoendocrine responses to prolonged exercise. *Medicine and Science in Sports and Exercise* 39(4): 645-652. DOI: 10.1249/mss.0b013e318031303d (38 citations; IF = 4.1).

3.3. Gleeson, M., Bishop, N.C., Oliveira, M. and Tauler, P.J. (2011). Daily probiotic's (*Lactobacillus casei* Shirota) reduction of infection incidence in athletes. *International Journal of Sport Nutrition and Exercise Metabolism* 21: 55-64. PubMed PMID: 21411836 (this journal does not supply a DOI). (32 citations; IF = 2.2).

B. Immunoendocrine Monitoring

3.4. Neville, V., Gleeson, M. and Folland, J.P. (2008). Salivary IgA as a risk factor for upper respiratory infections in elite professional athletes. *Medicine and Science in Sports and Exercise* 40(7): 1228-1236. DOI: 10.1249/MSS.0b013e31816be9c3 (76 citations; IF = 4.1).

3.5. Gleeson, M., Bishop, N.C., Oliveira, M., McCauley, T. and Tauler, P. (2013). Influence of training load on upper respiratory tract infection incidence and antigen-stimulated cytokine production. *Scandinavian Journal of Medicine and Science in Sports.* 23: 451-457. DOI: 10.1111/j.1600-0838.2011.01422.x (3 citations; IF = 2.8).

3.6. Gleeson, M., Bishop, N.C., Oliveira, M., McCauley, T., Tauler, P. and Muhamad, A.S. (2012). Respiratory infection risk in athletes: association with antigen-stimulated IL-10 production and salivary IgA secretion. *Scandinavian Journal of Medicine and Science in Sports* 22: 410-417. DOI: 10.1111/j.1600-0838.2010.01272.x (18 citations; IF = 2.8).

Underpinning research was funded through a range of sponsored projects awarded to Prof Michael Gleeson (PI); Co-I: Dr Nicolette Bishop including:

G3.1. Grant title: 'Effects of Yakult probiotic on mucosal immunity and infection risk in an athletic population'. Sponsor: Yakult Honsha. Period of the grant: 1 year: Dec 2008-Sept 2009. Value: £69,400.

G3.2. Grant title: 'Effects of a probiotic intervention on infection, cold symptom duration/severity and mucosal immunity in endurance athletes'. Sponsor: GlaxoSmithKline. Period of the grant: 1 year: Dec 2008-Sept 2009. Value: £49,300.

G3.3. Grant title: 'Effects of a Lactobacillus probiotic on cold symptom duration/severity and mucosal immunity in endurance athletes'. Sponsor: Yakult Honsha. Period of the grant: 1 year: Nov 2011-Oct 2012. Value: £188,000.

4. Details of the impact (indicative maximum 750 words)

The guidelines developed by Gleeson for immunoendocrine monitoring of athletes and strategies to minimize risk of overtraining and infection were commissioned by UK Sport and have since been updated as an expert position statement (with a previous PhD student, Prof Neil Walsh, Bangor University: Gleeson M and Walsh N. The British Association of Sport and Exercise Sciences (BASES) Expert Statement on Exercise, Immunity and Infection. *Journal of Sports Sciences* 30(3):

321-324, 2012) endorsed by BASES and are employed throughout the UK and beyond. For example, the regular monitoring of salivary IgA and nutritional and lifestyle strategies to limit stress and minimize infection risk are currently recommended by BASES, the English Institute of Sport (EIS) **[5.1]**, the Australian Institute of Sport (AIS) **[5.2]**, the European College of Sport Science (ECSS) and the International Society of Exercise and Immunology (ISEI). Gleeson's guidelines were adopted by the recent programme of infection prevention strategies that were developed in 2011-2012 by a medic working for UK Sport/EIS **[5.3]**. Thus, the research has both wide reach to applied sport scientists, athletes and coaches and significance by altering nutrition and monitoring practices leading to reduced infection risk for athletes.

The Loughborough University-based research 2008-2013 has led to an appreciation of the importance of monitoring salivary IgA as a non-invasive marker of immune function and predictor of illness risk in athletes and the monitoring of salivary cortisol and testosterone as hormonal markers of stress **[5.4]** in both able and spinal cord injured athletes. With Gleeson's assistance, saliva monitoring has been used to assess training/competition stress in several professional football and rugby clubs including Chelsea FC, Manchester City FC, Manchester United FC **[5.4]**, Leicester City FC and Leicester Tigers RFC and the England rugby union squad. Gleeson has been instrumental in setting up these initiatives with these clubs in the period 2004-2010, initially by providing assistance with the analysis of saliva samples and guidance on sample collection methods and the timing of collections and the appropriate interpretation of the results of the analysis **[5.4]**.

Loughborough University's research **[3.1-3.3]** on the most effective nutritional interventions to boost immunity and reduce infection risk is being applied in the world of sport. For example, probiotic supplementation is presently being used to support training and/or competition performances by UK Athletics, British Cycling Federation, British Rowing, British Canoe Union, British Triathlon Federation, British Swimming, the Rugby Football Union, the Welsh and Scottish Rugby Football Unions, and other professional athletes **[5.1, 5.2, 5.5]**. The Lactobacillus probiotic product that Gleeson's research demonstrated to be effective in reducing incidence of URTI in athletes was used by GB athletes in the lead up to and during the most recent 2010 Commonwealth, and 2012 Olympic and Paralympic Games following discussions with the Head of Performance Nutrition of the EIS **[5.1]** and via advice disseminated to Sport Dietitians UK. The Loughborough University research has also widened the market of probiotics to the sporting population **[5.5, 5.6]**.

The research findings have been communicated in conversation with key individuals within the EIS **[5.1, 5.3]**, AIS **[5.2]**, International Olympic Committee (IOC) etc and also through invited presentations in the UK since 2008 (e.g. EIS Strength and Conditioning conference; EIS Nutrition conference; EIS Unwell Athlete workshop; UKA Coaches conference, Sport Dietitians UK Workshops, Royal Society of Medicine Symposia) and abroad (e.g. IOC Offices, Switzerland; Nestle Nutrition Institute Symposia in Zurich and Mallorca). Moreover, for wider impact, Gleeson occasionally contributes articles aimed at practicing sport scientists, coaches and athletes (e.g. *The Sport and Exercise Scientist, Strength and Conditioning, UEFA Direct*) and lay people (*SportEX Health, Peak Performance, Men's Health, Runners World, Cycling Weekly*) as well as disseminating translation of the research to the national press, radio and television, both home and abroad. This ensures that the research findings inform not only the elite, but also the wider general public who engage in regular exercise for fun and health.

The example outputs **[3.1-3.6]**, along with other related outputs, have contributed to the development of nutritional support protocols and guidelines documents for monitoring of athletes as part of physiological support services to athletes **[5.1-5.3]**. These documents have been published as review articles in academic journals (e.g. An ECSS/ACSM position statement on prevention, diagnosis and treatment of the overtraining syndrome in *European Journal of Sport Sciences* 2013, two ISEI position statements on exercise and immune function and maintaining immune health in *Exercise Immunology Review* 2011, a BASES expert statement in *Journal of Sports Sciences* 2012). Loughborough University has developed a strong reputation for high quality original research in this area as evidenced by Gleeson's tenure as vice president (2005-2007) and president (2007-2009) of the ISEI.

5. Sources to corroborate the impact (indicative maximum of 10 references)

The following senior, external sources are available to corroborate the impact points made in this case:

5.1. Letter from previous Head of Performance Nutrition, English Institute of Sport (now working for High Performance Sport New Zealand) – will corroborate the international impact that Gleeson's research has had in the fields of exercise physiology, immunology and sports nutrition.

5.2. Letter from Head of Sports Nutrition, Australian Institute of Sport – will corroborate the international impact that Gleeson's research has had in the fields of exercise physiology, immunology and sports nutrition.

5.3. Letter from lead medic with the English Institute of Sport (now based at Claremont Sport Medicine and Performance Centre, UK) – will corroborate the impact that Gleeson's research has had on current recommendations to British athletes and coaches, on practice within the EIS and in the wider world of elite sport.

5.4. Letter from Head of Strength and Conditioning, Manchester United FC – will corroborate the impact that Gleeson's research has had in elite football.

5.5. Copy of Probiotic Bulletin 2012 – Sport Special Edition (pdf) provides evidence of increased use of probiotics in sport in recent years.

5.6. Letter from the UK Science Director of Yakult corroborate the impact that Gleeson's research has had on the probiotics industry.