

本文章已註冊DOI數位物件識別碼

► Exercise and Salivary IgA Response

運動與唾液免疫球蛋白A之反應

doi:10.6127/JEPF.2007.06.04

運動生理暨體能學報, (6), 2007

Journal of Exercise Physiology and Fitness, (6), 2007

作者/Author：李再立(Tzai-Li Li)

頁數/Page：35-49

出版日期/Publication Date：2007/08

引用本篇文獻時，請提供DOI資訊，並透過DOI永久網址取得最正確的書目資訊。

To cite this Article, please include the DOI name in your reference data.

請使用本篇文獻DOI永久網址進行連結:

To link to this Article:

<http://dx.doi.org/10.6127/JEPF.2007.06.04>



DOI Enhanced

DOI是數位物件識別碼（Digital Object Identifier, DOI）的簡稱，是這篇文章在網路上的唯一識別碼，用於永久連結及引用該篇文章。

若想得知更多DOI使用資訊，

請參考 <http://doi.airiti.com>

For more information,

Please see: <http://doi.airiti.com>

請往下捲動至下一頁，開始閱讀本篇文獻

PLEASE SCROLL DOWN FOR ARTICLE



運動與唾液免疫球蛋白 A 之反應

李再立

國立東華大學運動與休閒學系

摘要

唾液免疫球蛋白 A (salivary immunoglobulin A; sIgA) 已被採用為評估壓力對體液性免疫功能影響之指標。本篇綜評旨在討論下列課題：(1)sIgA 分泌之調節機制(2)sIgA 和運動引發之上呼吸道感染 (upper respiratory tract infection; URTI) (3)sIgA 反應和運動之關係(4)營養補充和運動引發之 sIgA 反應(5)單日重複性運動和 sIgA 反應。統整分析相關文獻後，獲致下列結語：(1)sIgA 分泌和功能同時受到交感神經系統 (sympathetic nervous system; SNS) 和丘腦下部-腦垂體-腎上腺軸 (hypothalamic-pituitary-adrenal-axis; HPA-axis) 之調節；(2)因運動激活之 SNS 和 HPA 可能急性地減少唾液流量，並抑制 sIgA 之分泌；(3)較低之 sIgA 濃度可能削弱免疫功能，運動訓練或比賽所引發之壓力，可能暫時性地抑制呼吸道之免疫功能，致使優秀運動員在訓練或比賽後二週內有較高之 URTI 罹患率；(4)碳水化合物和維他命 C 攝取不影響耐力性運動後之 sIgA 反應；(5)不同時段運動不影響 sIgA 反應；(6)相較於第一次運動，單日重複第二次耐力性運動不會進一步減弱口腔免疫功能，在單日重複性運動之任何時段補充碳水化合物不會影響 sIgA 之反應。

關鍵詞：唾液免疫球蛋白 A、運動、交感神經系統、丘腦下部-腦垂體-腎上腺軸

連絡作者：李再立

聯絡電話：(03)8632611

投稿日期：96 年 03 月

通訊地址：花蓮縣 97401 壽豐鄉志學村大學路二段一號

E-mail：leej@mail.ndhu.edu.tw

接受日期：96 年 05 月

Introduction

Saliva is normally a colourless liquid with a density ranging from 1.002 to 1.012 g·mL⁻¹, consisting of inorganic and organic constituents and usually more than 99% water. The secretory volume of saliva each day through the salivary glands approaches 750 mL, which represents a rate of approximately 0.5 mL·min⁻¹ arising from the submandibular glands (65%), parotid glands (23%), minor mucous glands (8%) and sublingual glands (4%) (Crawford, Taubman, & Smith, 1975).

Immunity against microorganisms at remote sites, such as the nasal cavity, oral cavity, respiratory tract, digestive tract and gut, is primarily due to secretory immunoglobulin A (IgA), which has been considered as the first line of defence to infection in the lumen of the respiratory tract and gut (Quan, Berneman, Pires, Avrameas, & Bouvet, 1997). Secretory IgA is produced by local plasma cells and function as a multi-layered mucosal defence. For example, IgA prevents antigens and microbes from adhering to and penetrating the epithelium (immune exclusion), interrupts replication of intracellular pathogens during transcytosis through epithelial cells (intracellular neutralization), and binds antigens in the lamina propria facilitating their excretion through the epithelium back into the lumen (immune excretion) (Lamm, 1998).

Hence, salivary IgA (sIgA) has been used to be a key indicator in determining the effect of different forms of stress on mucosal immunity. Previous studies could not provide an

agreement of how exercise stress affects sIgA and upper respiratory tract infection (URTI) (Gleeson, 2000). Therefore, this review was focused to discuss the following topics: (1) the modulation of sIgA secretion; (2) salivary IgA and exercise-induced URTI; (3) salivary IgA response and exercise; (4) nutritional supplementation and exercise-induced salivary IgA responses; (5) repeated bouts of exercise and salivary IgA responses.

Modulation of salivary IgA secretion

Salivary IgA is produced in the submucosa of salivary glands and then binds to a receptor (polymeric immunoglobulin receptor) located on the mucosal epithelium. Subsequently, the complex is transported across the mucosal epithelium and released into the saliva as IgA (Brandtzaeg, 1998; Mostove, 1994). The modification of sIgA secretion is regulated via the rate of syntheses (days) (Goodrich & McGee, 1998; Toellner, Luther, Sze, Choy, Taylor, MacLennan *et al.*, 1998) or transcytosis (minutes) (Kugler, 1999). Therefore, the acute alteration induced by exercise is likely through the modulation of the trans-epithelial secretory process rather than B lymphocyte activation.

Nervous Control

The salivary glands are innervated by both parasympathetic nerves and sympathetic nerves (Busch, Sterin-Borda, & Borda, 2002; Chicharro,

Lucia, Perez, Vaquero, & Urena, 1998). Parasympathetic stimulation induces a marked elevation in regional blood flow to salivary glands by vasodilation, resulting in a higher saliva flow rate with a relatively low protein concentration; whereas the sympathetic stimulation causes vasoconstriction, resulting a lower saliva flow rate but rich in protein (Anderson & Garrett, 1998; Chicharro *et al.*, 1998; Garrett, 1987).

Glucocorticoids

Cortisol has been suggested to play an important role in inhibiting sIgA mobilization (Hucklebridge, Clow, & Evans, 1998). Wira *et al.* (1990) reported a decline in sIgA level at 24 h after a single injection of dexamethasone, which preceded a rise in serum IgA concentration detected 24 h after the second hormone treatment and suggested that IgA increased in serum and decreased in salivary secretions due to a redistribution of polymeric IgA from mucosal surfaces to the circulation controlled by glucocorticoids. A subsequent study (Alverdy & Aoys, 1991) showed a fall of 77% in IgA concentration, an augmentation in bacterial adherence (2.4-fold), and an increased incidence of bacterial translocation to the mesenteric lymph nodes (60% vs 0%) observed after 2 days in dexamethasone-treated rats. The levels of polymeric IgA and antigen-specific IgA antibody in serum were also reported to be elevated after dexamethasone treatment (Wira & Rossoll, 1991); however, the sIgA level and antigen-specific IgA production after oral antigenic challenge was markedly inhibited. These data suggested that glucocorticoids

might impair mucosal IgA synthesis, secretion and function and promote bacterial translocation (Moyer, Cerra, Chenier, Peters, Oswald, & Watson *et al.*, 1981).

In summary, the substantial evidences of previous studies suggested that the sIgA secretion and functions are regulated both by the stimulation of sympathetic nervous system (SNS) and hypothalamic-pituitary-adrenal-(HPA)-axis.

Salivary IgA and exercise-induced URTI

Measurement of sIgA is thought to be an indicator of the functional status of the entire mucosal immune system (Mestecky, 1993). Local production of sIgA provides adaptive immunologic protection to mucosal surfaces (Johansen, Braathen, & Brandtzaeg, 2001). The low sIgA levels or chronic sIgA deficiency appeared to facilitate the adherence and entrance of pathogens through the epithelial surface (Alverdy & Aoys, 1991; Ostergaard, 1977), increasing frequency of URTI episodes (Gleeson, McDonald, Pyne, Cripps, Francis, Fricker *et al.*, 1999), recurrent URTI (Isaacs, Webster, & Valman, 1984), or reduced protection against certain epithelial infections (Asahi, Yoshikawa, Watanabe, Iwasaki, Hasegawa, Sato *et al.*, 2002). In a meta-analysis of nine studies, Jemmott and McClelland (1989) concluded that low local levels of sIgA could compromise immune resistance to respiratory infections.

Mucosal immunity and susceptibility to URTI are likely related to exercise stress because various aspects of immune function are temporarily changed following exercise (Mackinnon, 1999). Epidemiological studies have indicated that intensive prolonged training or competition is associated with an elevated incidence of URTI, placing athletes at a higher risk of URTI than control groups during and after competition or training (Douglas & Hanson, 1978; Heath, Ford, Craven, Macera, Jacson, & Pate, 1991; Nieman, Johanssen, Lee, & Arabatzis, 1990; Peters & Bateman, 1983). Peters and Bateman (1983) reported the runners who completed an ultramarathon (35 miles) had more than 2-fold incidence of URTI within 2 weeks after the race compared

with the matched controls. The running mileage for a year appeared to be an influential factor for developing URTI according to Heath *et al.* (1991) who showed that individuals who ran more than 3.8 miles per day, on average, had a 2-fold higher incidence of URTI than those who ran less than 1.3 miles per day. Nieman *et al.* (1990) also reported that the risk of an infectious episode was 5-fold higher for marathon runners in the week after a race compared with runners who trained but did not compete in the race. Subsequently, Nieman (1994) hypothesised the relationship between susceptibility to URTI and exercise workload as a J-shaped curve (Figure 1).

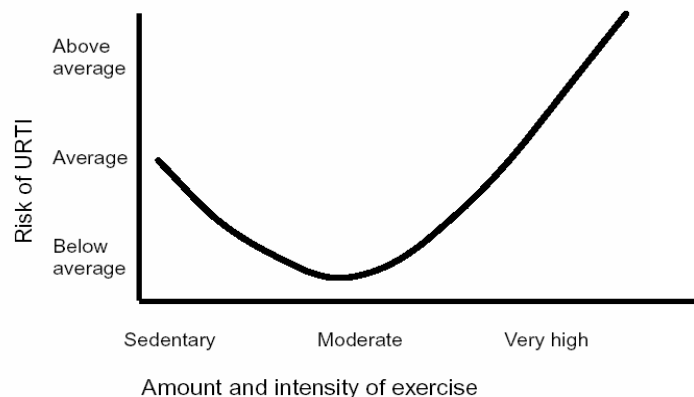


Figure 1 J-shaped model of the relationship between exercise and URTI risk (Modified from Nieman, D. C. (1994). *International Journal of Sports Medicine*, 15, S131-S141)

This J-shaped curve model predicts that individuals who exercise moderately are at less risk of infection, whereas those who exercise heavily are more at risk compared with

sedentary counterparts. If the model is effectively mediated by sIgA, then the alteration in sIgA concentration and/or output should be inversely associated with the incidence of

URTI. Preliminary support has been provided by many previous studies (Gleeson *et al.*, 1999; Mackinnon, Ginn, & Seymour, 1993; Reid, Mackinnon, & Drummond, 2001). Mackinnon *et al.* (1991) described that eleven of twelve URTI episodes were preceded within 2 days by a 22% decrease in sIgA levels. Later a study from the same lab supported this idea by reporting that hockey and squash players developed symptoms of URTI had reductions in sIgA of 22% and 23% with 2 days of symptom onset, whereas those players who remained healthy, sIgA either increased slightly or was unchanged (Mackinnon *et al.*, 1993).

In summary, previous findings consistently supported that the lower levels of sIgA under a threshold may compromise immune resistance to infections in mucosal surfaces and physiological and psychological stresses induced by heavy training or stressful competition would temporarily impair oral immunity, placing elite athletes at a higher risk of URTI than control groups within 2 weeks after competition or training.

Salivary IgA response and exercise

Many studies have been done to examine how exercise affects the sIgA alteration. However, the results have been inconsistent. The following paragraphs were to discuss the relationships between exercise and saliva flow rate, sIgA concentration, and sIgA secretion rate.

Saliva flow rate

A decreased saliva flow rate has been consistently observed following strenuous exercise (Blannin, Robson, Walsh, Clark, Glennon, & Gleeson, 1998; Steerenberg, van Asperen, van Nieuw Amerongen, Biewenga, Mol, & Medema, 1997; Walsh, Bishop, Blackwell, Wierzbicki, & Montague, 2002). A steady blood flow to salivary glands is required for maintenance of adequate salivation because the water of saliva is from the plasma (Smaje, 1998). Anderson and Garrett (1998) demonstrated that the α -adrenergic receptor activation causes vasoconstriction, whereas the β -adrenergic activity induces vasodilation in rat submandibular glands. Further, recent studies have shown that α_1 -adrenergic blockade by doxazosin and β -adrenergic blockade by propranolol have no effect on saliva flow rate after 8-min submaximal cycling at 50W (Ring, Harrison, Winzer, Carroll, Drayson, & Kendall, 2000; Winzer, Ring, Carroll, Willemssen, Drayson, & Kendall, 1999). However, α_2 -adrenoceptor agonist dexmedetomidine infusion induces vasoconstriction in men (Talke, Lobo, & Brown, 2003). This suggests that the α_2 -adrenergic receptors may be the play an important role in the exercise-induced decrease of saliva flow rate.

Rantonen and Meurman (2000) suggested that the saliva flow rate was likely to be the single salivary defensive factor which significantly affected oral health. This notion was supported by recent studies, which showed the absence of caries in children with familial

dysautonomia was associated with a higher saliva flow rate (Mass, Gadoth, Harell, & Wolff, 2002), and the increased incidence of oral candidal infections in HIV-infected patients (Lin, Johnson, Patterson, Wu, Lu, Shi *et al.*, 2001) was related to a lower saliva flow rate. Fox *et al.* (1985) also suggested individuals who suffered from dry mouth syndrome had an increased incidence of URTI.

Salivary IgA concentration

Previous studies have shown paradoxical results in sIgA concentration immediately after exercise; some reported increased (Bishop, Blannin, Walsh, Armstrong, Rickman, & Gleeson, 2000; Dimitriou, Sharp, & Doherty, 2002), unaffected (Housh, Johnson, Housh, Evans, & Tharp, 1991; McDowell, Chaloa, Housh, Tharp, & Johnson, 1991), or decreased sIgA concentration (Krzykowski, Petersen, Ostrowski, Link-Amater, Boza, Halkjaer-Kristensen *et al.*, 2001; Tharp & Barnes, 1990). A few studies have demonstrated a delayed effect of exercise on the saliva IgA response. Mackinnon and her colleagues reported a significant decrease in sIgA level occurred between 2 to 24 h after intense prolonged exercise (Mackinnon, Chick, Van As, & Tomasi, 1987) or on the second and third consecutive days of moderate intensity exercise, but not on the first day (Mackinnon & Hooper, 1994).

Salivary IgA secretion rate

The protective effect of sIgA in the respiratory tract is dependent on both sIgA con-

centration and saliva flow rate – the total amount of sIgA covering the mucosal surface (Mackinnon & Hooper, 1994). In vitro, sIgA is secreted by both acinar and ductal units under the stimulation of α - and β -adrenoreceptors and peptidergic receptor. The secretion rate of sIgA is relatively constant for each agonist across a range of doses (Proctor & Carpenter, 2002). The α -adrenoreceptor agonist phenylephrine has been demonstrated to stimulate the secretion of IgA and protein via β -adrenoreceptor-dependent pathway with a manner of dose-independent above a certain threshold (Proctor, Garrett, Carpenter, & Ebersole, 2003). However, Ring *et al.* (2000) suggested that the acute decrease in sIgA secretion rate was mediated by α 1-adrenergic mechanisms. Furthermore, prolonged stimulation of β -adrenoreceptor agonist isoprenaline appeared to reduce the replenishment of IgA into the glandular pool (Proctor *et al.*, 2003).

Several studies showed no alteration in sIgA secretion rate after tennis drill (Nieman, Kernodle, Henson, Sonnenfeld, & Davis, 2000), soccer play (Bishop, Blannin, Robson, Walsh, & Gleeson, 1999) or cycling (Blannin *et al.*, 1998). On the other hand, other studies reported a decrease in sIgA secretion rate following Olympic-distance triathlon race (Steerenberg *et al.*, 1997), competitive marathon race (Nieman, Henson, Fagoaga, Utter, Vinci, Davis *et al.*, 2002) and 2 h cycling (Krzykowski *et al.*, 2001). Recovery of sIgA to pre-exercise levels usually occurs within 24 h. However, in elite athletes undertaking mul-

tiple exercise sessions in a single day and/or habitual intensive training, the recovery will be affected by the intensity of the training sessions. The recovery rate may prove to be a key indicator of the long-term consequences of accumulative mucosal immunodepression in high performance athletes (Gleeson, 2000).

In summary, the results of abovementioned studies indicated that the stressed exercise would either stimulate SNS, which might elicit immediate effects of decreasing saliva

flow rate by constricting the blood supply to saliva glands, temporarily increasing sIgA secretion via elevated transcytosis from the glandular IgA pool, and depleting sIgA pool after long-term stimulation, or activate HPA, which possibly evokes delayed effect of inhibiting sIgA secretion and antigen-specific IgA production after 24 hour. The possible mechanisms involved in the regulation of saliva IgA secretion during prolonged exercise are illustrated with Figure 2.

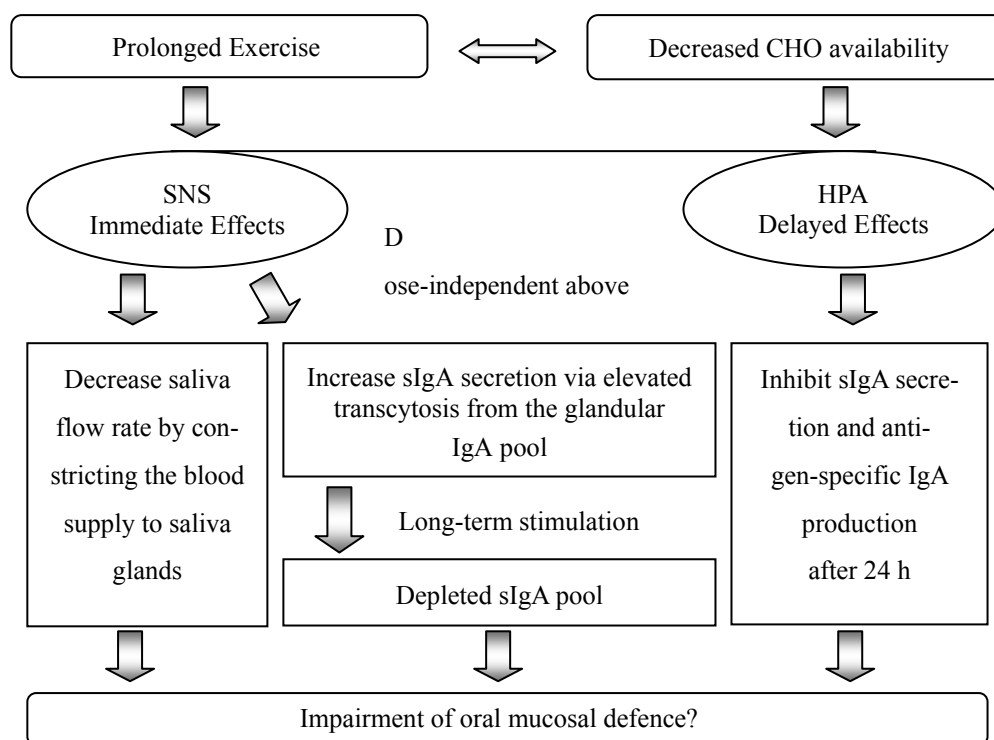


Figure 2 The possible mechanisms involved in the regulation of saliva IgA secretion during prolonged exercise. CHO: carbohydrate [Li, T. L. (2004). *The effects of repeated bouts of prolonged cycling and carbohydrate supplementation on immunoendocrine responses in man*. Unpublished doctoral thesis, Loughborough University, United Kingdom.]

Nutritional supplementation and exercise-induced sIgA responses

Dietary intake of nutrients has been suggested to potentially affect immune system function since most nutrients are involved in the synthesis and regulation of immune factors (Gleeson, Lancaster, & Bishop, 2001). To date, some studies have been conducted to look at the effects of nutritional intervention on salivary IgA responses as described below.

Carbohydrate ingestion and exercise-induced sIgA responses

Because exercise influences saliva flow

rate and composition via the activation of SNS and HPA-axis, the blunt responses of stress hormones after carbohydrate (CHO) ingestion may attenuate the effect on oral immunity (Chicharro *et al.*, 1998). However, CHO ingestion appears not to affect sIgA concentration (Nehlsen-Cannarella, Nieman, Fagoaga, Kelln, Henson, Shannon *et al.*, 2000; Nieman *et al.*, 2002), secretion rate (Nehlsen-Cannarella *et al.*, 2000; Nieman *et al.*, 2002) and saliva flow rate (Bishop *et al.*, 2000) following a single bout of prolonged exercise compared with a placebo (PLA) trial (Table 1).

Table 1 Summary of carbohydrate ingestion and exercise-induced saliva IgA responses

Reference	Experimental Design	Subject	Main Findings
(Nieman <i>et al.</i> , 2002)	Marathon race. Exercise volume was ~4.4 h at 83% HR max.	CHO: 48 PLA: 50	Saliva IgA secretion rate decreased 34% compared with pre-race level; however, there was no difference between CHO and PLA.
(Bishop <i>et al.</i> , 2000)	Three trials: CHO, PLA and restricted fluid intake (RFI). 2 h cycling at 60% VO ₂ max	15 males	CHO feeding better maintained plasma glucose concentration compared with PLA and RFI. Saliva flow rate and sIgA concentration in CHO was higher than RFI but not different to PLA.
(Nehlsen-Cannarella <i>et al.</i> , 2000)	2 h rowing consisted of a 3-min rest every 15 min. Subjects drank a 6% CHO or placebo beverage for 12 and 4 mL·kg ⁻¹ body mass before and every 15 min during rowing, respectively.	15 female rowers	CHO ingestion had no effect on saliva flow rate and sIgA concentration and secretion rate compared with PLA.
(Bishop <i>et al.</i> , 1999)	90 min soccer-specific exercise protocol. Subjects drank 400 mL of a 6% CHO or placebo beverage at 10 min before the start of each 45 min of exercise and 150 mL at 14 and 29.5 min into each period of exercise.	8 males	CHO ingestion had no effect on saliva flow rate and sIgA concentration and secretion rate compared with PLA.

The saliva samples of all studies in this table were from the unstimulated whole-mixed saliva and the sIgA concentration was measured using ELISA.

Vitamin C supplementation and exercise-induced sIgA responses

Vitamin C supplementation before exercise has been proven to attenuate the increases of plasma cortisol and adrenaline, which were

regarded as possible depressor of immunity, following prolonged exercise (Peters, Anderson, Nieman, Fick, & Jogessar, 2001). Therefore, it was logical to assume that vitamin C supplementation might positively attenuate the impact of prolonged exercise on sIgA re-

sponses. However, the results of a previous study indicated that ingestion of 1500 mg vitamin C per day for 7 days prior to the race did not influence saliva flow rate, sIgA concentration, sIgA secretion rate, and the ratio of sIgA and saliva protein compared with PLA following an ultramarathon (Palmer, Nieman, Henson, McAulty, McAulty, Swick *et al.*, 2003).

In summary, the ingestion of CHO and vitamin C appeared to attenuate the activation of HPA and SNS; however, it was not found to affect sIgA response following prolonged exercise.

Repeated bouts of exercise and salivary IgA responses

Many athletes train more than once each day and repeated bouts of prolonged exercise have become part of routine training programmes for elite endurance athletes. However, only few studies have investigated the effect of repeated bouts of prolonged exercise or time of day on saliva flow rate and sIgA responses.

Circadian variation

Most components of the immune system show rhythmic changes (Shephard & Shek, 1996). Gleeson *et al.* (2001) showed that there was a diurnal variation in sIgA concentration, which was highest in the early morning, followed by a decline during the morning and then was stable from around noon onwards.

This finding was supported by recent studies, which showed a higher sIgA concentration but a lower saliva flow rate and sIgA secretion rate in the morning compared with afternoon (Dimitriou *et al.*, 2002; Li & Gleeson, 2004b). The observation supports the notion that the diurnal variation must be considered when the aim of a study is to compare the effect of exercise performed at different times of day on the aforementioned parameters.

Different times of day

Li and Gleeson (2004a) first published a study regarding this topic and showed that performing an identical bout of prolonged cycling in the morning or in the afternoon did not differently affect the salivary responses in terms of oral mucosal immunity. This finding was further proven by a very recent study which reported that the different times of day did not affect both sIgA concentration and secretion rate following a 90-min soccer-specific intermittent exercise bout (Sari-Sarraf, Reilly, Doran, & Atkinson, 2007).

The first vs. the second of two repeated bouts of prolonged exercise

Recent studies reported that a second exercise bout on the same day induced a larger neuroendocrine response than the first exercise bout (Li & Gleeson, 2004b; Ronsén, Haug, Pedersen, & Bahr, 2001; Ronsén, Pedersen, Oritsland, Bahr, & Kjeldsen-Kragh, 2001). Thus, it was hypothesised that the salivary composition might be affected during

two bouts of prolonged exercise. However, it was surprisingly found that a second prolonged exercise bout did not appear to further compromise the oral immunity although it elicited a greater stress hormone response compared to the first identical exercise bout (Li & Gleeson, 2004a; Sari-Sarraf *et al.*, 2007).

Carbohydrate ingestion during two bouts of prolonged exercise

Ingestion of CHO compared with PLA during the first or the second bout of exercise appeared consistently to better maintain the plasma glucose concentration, attenuate the activation of SNS and HPA, and blunt the increase in blood numbers of leukocytes (Li & Gleeson, 2005a; Li & Gleeson, 2005b). However, CHO ingestion during any period of two prolonged exercise bouts did not induce different effects on oral immunity as compared with PLA trial (Li & Gleeson, 2005a).

In summary, there is a diurnal variation in sIgA concentration, which suggests that it must be considered when the aim of a study is to compare the effect of exercise performed at different times of day. However, the different times of day did not influence sIgA response to exercise. Even though a second exercise bout on the same day induced a larger neuro-endocrine response than the first exercise bout and CHO ingestion attenuated the perturbation of SNS, HPA, and leukocytes mobilisation, it was surprisingly learnt that the second exercise bout did not appear to further compromise the oral immunity compared to the first identical

exercise bout and CHO ingestion during any period of two prolonged exercise bouts seemed not to induce different effects on oral immunity compared with PLA.

Summary

Saliva function is important to oral health both by flushing microorganisms and their products into the gut and by continuously supplying both non-immune and immune factors into the mouth. Therefore, salivary diagnosis is increasingly used in the fields of exercise and sport sciences, dentistry, internal medicine, endocrinology, paediatrics, immunology, clinical pathology, and psychology because many antibodies, hormones, drugs, and proteins can be detected in saliva, which is a safe, convenient, non-invasive, and practical diagnostic implement compared to blood analysis. In this review the current knowledge of the salivary IgA responses to exercise was depicted and summaries were concluded: (1) the sIgA secretion and functions are regulated both by the stimulation of SNS and HPA-axis; (2) the lower levels of sIgA under a threshold may compromise immune resistance to infections in mucosal surfaces and physiological and psychological stresses induced by heavy training or stressful competition would temporarily impair oral immunity, placing elite athletes at a higher risk of URTI than control groups within 2 weeks after competition or training; (3) the stressed exercise would either stimulate SNS or activate HPA, which might

decrease saliva flow rate immediately and inhibit sIgA secretion and antigen-specific IgA production over a long period of time; (4) the ingestion of CHO and vitamin C appeared not to affect sIgA response following prolonged exercise; (5) the different times of day did not influence sIgA response to exercise; (6) the second exercise bout did not appear to further compromise the oral immunity compared to the first identical exercise bout and CHO ingestion during any period of two prolonged exercise bouts did not induce different effects on oral immunity compared with PLA trial.

References

- Alverdy, J., & Aoy, E. (1991). The effect of glucocorticoid administration on bacterial translocation. Evidence for an acquired mucosal immunodeficient state. *Annals of Surgery*, 214(6), 719-723.
- Anderson, L. C., & Garrett, J. R. (1998). Neural regulation of blood flow in the rat submandibular gland. *European Journal of Morphology*, 36(Suppl.), 213-218.
- Asahi, Y., Yoshikawa, T., Watanabe, I., Iwasaki, T., Hasegawa, H., Sato, Y., Shimada, S., Nanno, M., Matsuoka, Y., Ohwaki, M., Iwakura, Y., Suzuki, Y., Aizawa, C., Sata, T., Kurata, T., & Tamura, S. (2002). Protection against influenza virus infection in polymeric Ig receptor knockout mice immunized intranasally with adjuvant-combined vaccines. *Journal of Immunology*, 168, 2930-2938.
- Bishop, N. C., Blannin, A. K., Robson, P. J., Walsh, N. P., & Gleeson, M. (1999). The effects of carbohydrate supplementation on immune responses to a soccer-specific exercise protocol. *Journal of Sports Sciences*, 17, 787-796.
- Bishop, N. C., Blannin, A. K., Walsh, N. P., Armstrong, E., Rickman, M., & Gleeson, M. (2000). Carbohydrate and fluid intake affect the saliva flow rate and IgA response to cycling. *Medicine & Science in Sports & Exercise*, 32(12), 2046-2051.
- Blannin, A. K., Robson, P. J., Walsh, N. P., Clark, A. M., Glennon, L., & Gleeson, M. (1998). The effect of exercising to exhaustion at different intensities on saliva immunoglobulin A, protein and electrolyte secretion. *International Journal of Sports Medicine*, 19, 547-552.
- Brandtzaeg, P. (1998). Synthesis and secretion of human salivary immunoglobulins. In J. R. Garrett, J. Ekstrom & L. C. Anderson (Eds.), *Glandular mechanisms of salivary secretion* (Vol. 10, pp. 167-199). London: Basel, Karger.
- Busch, L., Sterin-Borda, L., & Borda, E. (2002). Differences in the regulatory mechanism of amylase release by rat parotid and submandibular glands. *Archives of Oral Biology*, 47, 717-722.
- Chicharro, J. L., Lucia, A., Perez, M., Vaquero, A. F., & Urena, R. (1998). Saliva composition and exercise. *Sports Medicine*, 26(1), 17-27.
- Crawford, J. M., Taubman, M. A., & Smith, D. J. (1975). Minor salivary glands as a major source of secretory immunoglobulin a in the human oral cavity. *Science*, 190(4220), 1206-1209.
- Dimitriou, L., Sharp, N. C., & Doherty, M. (2002). Circadian effects on the acute responses of salivary cortisol and IgA in well trained swimmers. *British Journal of Sports Medicine*, 36(4), 260-264.
- Douglas, D. J., & Hanson, P. G. (1978). Upper respiratory infections in the conditioned athlete. *Medicine & Science in Sports & Exercise*, 10, 55.
- Fox, P. C., van der Ven, P. F., Sonies, B. C., Weiffenbach, J. M., & Baum, B. J. (1985). Xerostomia evaluation of a symptom with increasing significance. *Journal of American Diet Association*, 110, 519-525.
- Garrett, J. R. (1987). The proper role of nerves in salivary secretion: A review. *Journal of Dental Research*, 66(2), 387-397.
- Gleeson, M. (2000). Mucosal immune response and risk of respiratory illness in elite athletes. *Exercise Immunology Review*, 6, 5-42.
- Gleeson, M., Bishop, N. C., Sterne, V. L., & Hawkin, A. J. (2001). Diurnal variation in saliva immunoglobulin A concentration and the effect of a previous day of heavy exercise. *Medicine & Science in Sports & Exercise*, 33, Supplement, ISEI abstract 54.
- Gleeson, M., Lancaster, G. I., & Bishop, N. C. (2001). Nutritional strategies to minimise exer-

- cise-induced immunosuppression in athletes. *Canadian Journal of Applied Physiology*, 26(Suppl.), S23-S35.
- Gleeson, M., McDonald, W. A., Pyne, D. B., Cripps, A. W., Francis, J. L., Fricker, P. A., & Clancy, R. (1999). Salivary IgA levels and infection risk in elite swimmers. *Medicine & Science in Sports & Exercise*, 31, 67-73.
- Goodrich, M. E., & McGee, D. W. (1998). Regulation of mucosal B cell immunoglobulin secretion by intestinal epithelial cell-derived cytokines. *Cytokine*, 10(12), 948-955.
- Heath, G. W., Ford, E. S., Craven, T. E., Macera, C. A., Jacson, K. L., & Pate, R. R. (1991). Exercise and the incidence of upper respiratory tract infections. *Medicine & Science in Sports & Exercise*, 23, 152-157.
- Housh, T. J., Johnson, G. O., Housh, D. J., Evans, S. L., & Tharp, G. D. (1991). The effect of exercise at various temperatures on salivary levels of immunoglobulin A. *International Journal Sports Medicine*, 12(5), 498-500.
- Hucklebridge, F., Clow, A., & Evans, P. (1998). The relationship between salivary secretory immunoglobulin A and cortisol: Neuroendocrine response to awakening and the diurnal cycle. *International Journal of psychophysiology*, 31, 69-76.
- Isaacs, D., Webster, A. D. B., & Valman, H. B. (1984). Immunoglobulin levels and function in preschool children with recurrent respiratory infections. *Clinical Experimental Immunology*, 58, 335-340.
- Jemmott, J. B., & McClelland, D. C. (1989). Secretory IgA as a measure of resistance to infectious disease: Comment on stone, cox, valdimarsdottir, and neale. *Behavioral Medicine*, 15, 63-71.
- Johansen, F.-E., Braathen, R., & Brandtzaeg, P. (2001). The J chain is essential for polymeric Ig receptor-mediated epithelial transport of IgA. *The Journal of Immunology*, 167, 5185-5192.
- Krzykowski, K., Petersen, E. W., Ostrowski, K., Link-Amater, H. J. H., Boza, J., Halkjaer-Kristensen, J., & Pedersen, B. K. (2001). Effect of glutamine and protein supplementation on exercise-induced decreases in salivary IgA. *Journal of Applied Physiology*, 91, 832-838.
- Kugler, J. (1999). Biobehavioral influences on respiratory immunity. In M. Schedlowski & U. Tewes (Eds.), *Psychoneuroimmunology: An interdisciplinary introduction* (pp. 359-371). New York: Kluwer Academic/Plenum Publishers.
- Lamm, M. E. (1998). Current concepts in mucosal immunity iv. How epithelial transport of IgA antibodies relates to host defense. *American Journal of Physiology*, 274, G614-G617.
- Li, T.-L., & Gleeson, M. (2004a). The effect of single and repeated bouts of prolonged cycling and circadian variation on saliva flow rate, immunoglobulin A and α -amylase responses. *Journal of Sport Sciences*, 22(11-12), 1015-1024.
- Li, T.-L., & Gleeson, M. (2004b). The effect of single and repeated bouts of prolonged cycling on leukocyte redistribution, neutrophil degranulation, IL-6 and plasma stress hormone responses. *International Journal of Sport Nutrition and Exercise Metabolism*, 14(5), 501-516.
- Li, T.-L., & Gleeson, M. (2005a). The effects of carbohydrate supplementation during repeated bouts of prolonged exercise on saliva flow rate and immunoglobulin A. *Journal of Sport Sciences*, 23(7), 713-722.
- Li, T. L., & Gleeson, M. (2005b). The effects of carbohydrate supplementation during the second of two prolonged cycling bouts on immunoenocrine responses. *European Journal of Applied Physiology*, 95(5-6), 391-399.
- Lin, A. L., Johnson, D. A., Patterson, T. F., Wu, Y., Lu, D. L., Shi, Q., & Yeh, C. K. (2001). Salivary anticandidal activity and saliva composition in an HIV-infected cohort. *Oral Microbiology and Immunology*, 16(5), 270-278.
- Mackinnon, L. T. (1999). *Advances in exercise immunology*. Champaign IL: Human Kinetics.
- Mackinnon, L. T., Chick, T. W., Van As, A., & Tomasi, T. B. (1987). The effect of exercise on secretory and natural immunity. *Advanced Experiment in Medical Biology*, 216A, 869-876.
- Mackinnon, L. T., Ginn, E., & Seymour, G. (1991). Temporal relationship between exercise-induced decreases in salivary IgA concentration and subsequent appearance of upper respiratory illness in elite athletes. *Medicine & Science in Sports & Exercise*, 23, S45.
- Mackinnon, L. T., Ginn, E., & Seymour, G. J. (1993). Temporal relationship between decreased salivary IgA and upper respiratory track infection in elite athletes. *The Australian Journal of Science and Medicine in Sport*, 25(4), 94-99.
- Mackinnon, L. T., & Hooper, S. (1994). Mucosal (secretory) immune system responses to exercise

- of varying intensity and during overtraining. *International Journal Sports Medicine*, 15, S179-S183.
- Mass, E., Gadoth, N., Harell, D., & Wolff, A. (2002). Can salivary composition and high flow rate explain the low caries rate in children with familial dysautonomia? *Pediatric Dentary*, 24(6), 581-586.
- McDowell, S. L., Chaloa, K., Housh, T. J., Tharp, G. D., & Johnson, G. O. (1991). The effect of exercise intensity and duration on salivary immunoglobulin A. *European Journal of Applied Physiology*, 63, 108-111.
- Mestecky, J. (1993). Saliva as a manifestation of the common mucosal immune system. *Annals of the New York Academy of Sciences*, 694, 184-194.
- Mostov, K. E. (1994). Transepithelial transport of immunoglobulins. *Annual Review of Immunology*, 12, 63-84.
- Moyer, E., Cerra, F., Chenier, R., Peters, D., Oswald, G., Watson, F., Yu, L., McMenamy, R. H., & Border, J. R. (1981). Multiple systems organ failure: Vi. Death predictors in the trauma-septic state--the most critical determinants. *Journal of Trauma*, 21(10), 862-869.
- Nehlsen-Cannarella, S. L., Nieman, D. C., Fagoaga, O. R., Kelln, W. J., Henson, D. A., Shannon, M., & Davis, J. M. (2000). Saliva immunoglobulins in elite women rowers. *European Journal of Applied Physiology*, 81, 222-228.
- Nieman, D. C. (1994). Exercise, infection, and immunity. *International Journal of Sports Medicine*, 15, S131-S141.
- Nieman, D. C., Henson, D. A., Fagoaga, O. R., Utter, A. C., Vinci, D. M., Davis, I. M., & Nehlsen-Cannarella, S. L. (2002). Change in salivary IgA following a competitive marathon race. *International Journal of Sports Medicine*, 23, 69-75.
- Nieman, D. C., Johanssen, L. M., Lee, J. W., & Arabatzis, K. (1990). Infectious episodes in runners before and after the Los Angeles marathon. *Journal of Sports Medicine and Physical Fitness*, 30, 316-328.
- Nieman, D. C., Kernodle, M. W., Henson, D. A., Sonnenfeld, G., & Davis, J. M. (2000). Acute immune responses to tennis drills in adolescent athletes. *Research Quarterly of Exercise and Sport*, 71, 403-408.
- Ostergaard, P. A. (1977). IgA levels, bacterial carrier rate, and the development of bronchial asthma in children. *Acta Pathology and Microbiology Scandinavia*, 85(3), 187-195.
- Palmer, F. M., Nieman, D. C., Henson, D. A., McAnulty, S. R., McAnulty, L., Swick, N. S., Utter, A., Vinci, D. M., & Morrow, J. D. (2003). Influence of vitamin C supplementation on oxidative and salivary IgA changes following an ultramarathon. *European Journal of Applied Physiology*, 89, 100-107.
- Peters, E. M., Anderson, A., Nieman, D. C., Fick, H., & Jogessar, V. (2001). Vitamin C supplementation attenuates the increase in circulation cortisol, adrenaline and anti-inflammatory polypeptides following ultramarathon running. *International Journal of Sports Medicine*, 22, 537-543.
- Peters, E. M., & Bateman, E. D. (1983). Ultramarathon running and upper respiratory tract infections. An epidemiological survey. *South African Medical Journal*, 64(15), 582-584.
- Proctor, G. B., & Carpenter, G. H. (2002). Neural control of salivary secretion. In A. Clow & F. Hucklebridge (Eds.), *International review of neurobiology* (Vol. 52, pp. 187-212). London: Academic Press.
- Proctor, G. B., Garrett, J. R., Carpenter, G. H., & Ebersole, L. E. (2003). Salivary secretion of immunoglobulin A by submandibular glands in response to autonomic infusions in anaesthetized rats. *Journal of Neuroimmunology*, 136, 17-24.
- Quan, C. P., Berneman, A., Pires, R., Avrameas, S., & Bouvet, J. (1997). Natural polyreactive secretory immunoglobulin A autoantibodies as a possible barrier to infection in human. *Infection and immunity*, 65(10), 3997-4004.
- Rantonen, P. J. F., & Meurman, J. H. (2000). Correlations between total protein, lysozyme, immunoglobulins, amylase, and albumin in stimulated whole saliva during daytime. *Acta Odontologica Scandinavica*, 58, 160-165.
- Reid, M. R., Mackinnon, L. T., & Drummond, P. D. (2001). The effects of stress management on symptoms of upper respiratory tract infection, secretory immunoglobulin A, and mood in young adults. *Journal of Psychosomatic Research*, 51, 721-728.
- Ring, C., Harrison, L., Winzer, A., Carroll, D., Drayson, M., & Kendall, M. (2000). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic, cold pressor, and exercise: Effects of alpha-adrenergic blockade. *Psychophysiology*, 37, 634-643.

- Ronsen, O., Haug, E., Pedersen, B. K., & Bahr, R. (2001). Increased neuroendocrine response to a repeated bout of endurance exercise. *Med. Sci. Sports Exerc.*, 33(4), 568-575.
- Ronsen, O., Pedersen, B. K., Oritsland, T. R., Bahr, R., & Kjeldsen-Kragh, J. (2001). Leukocyte counts and lymphocyte responsiveness associated with repeated bouts of strenuous endurance exercise. *Journal of Applied Physiology*, 91, 425-434.
- Sari-Sarraf, V., Reilly, T., Doran, D. A., & Atkinson, G. (In Press). The effects of single and repeated bouts of soccer-specific exercise on salivary IgA. *Archive of Oral Biology*.
- Shephard, R. J., & Shek, P. N. (1996). Interactions between sleep, other body rhythms, immune responses, and exercise. *Canadian Journal of Applied Physiology*, 22(2), 95-116.
- Smaje, L. H. (1998). Capillary dynamics in salivary glands. In J. R. Garrett, J. Ekstrom & L. C. Anderson (Eds.), *Glandular mechanisms of salivary secretion* (Vol. 10, pp. 118-131). Basel: Karger.
- Steerenberg, P. A., van Asperen, I. A., van Nieuw Amerongen, A., Biewenga, A., Mol, D., & Medema, G. J. (1997). Salivary levels of immunoglobulin A in triathletes. *European Journal of Oral Science*, 105(4), 305-309.
- Talke, P., Lobo, E., & Brown, R. (2003). Systemically administered alpha2-agonist-induced peripheral vasoconstriction in human. *Anesthesiology*, 99(1), 65-70.
- Tharp, G. D., & Barnes, M. W. (1990). Reduction of saliva immunoglobulin levels by swim training. *European Journal of Applied Physiology*, 60, 61-64.
- Toellner, K.-M., Luther, S. A., Sze, D. M.-Y., Choy, R. K.-W., Taylor, D. R., MacLennan, C. M., & Acha-Orbea, H. (1998). T helper 1 (Th1) and Th2 characteristics start to develop during T cell priming and are associated with an immediate ability to induce immunoglobulin class switching. *Journal of Experimental Medicine*, 8, 1193-1204.
- Walsh, N. P., Bishop, N. C., Blackwell, J., Wierzbicki, S. G., & Montague, J. C. (2002). Salivary IgA response to prolonged exercise in a cold environment in trained cyclists. *Medicine & Science in Sports & Exercise*, 34(10), 1632-1637.
- Winzer, A., Ring, C., Carroll, D., Willemsen, G., Drayson, M., & Kendall, M. (1999). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic, cold pressor, and exercise: Effect of beta-adrenergic blockade. *Psychophysiology*, 36, 591-601.
- Wira, C. R., & Rossoll, R. M. (1991). Glucocorticoid regulation of humoral immune system. Dexamethason stimulation of secretory component in serum, saliva, and bile. *Endocrinology*, 128(2), 835-842.
- Wira, C. R., Sandoe, C. P., & Steele, M. G. (1990). Glucocorticoid regulation of the humoral immune system. I. In vivo effects of dexamethasone on IgA and IgG in serum and at mucosal surfaces. *Journal of Immunology*, 144, 142-146.

Exercise and Salivary IgA Response

Tzai-Li Li

National Dong Hwa University

Abstract

Salivary IgA (sIgA) has been used to be a key indicator in determining the effect of different forms of stress on mucosal immunity. This review was focused to discuss the following topics: (1) the modulation of sIgA secretion; (2) sIgA and exercise-induced upper respiratory tract infection (URTI); (3) sIgA response and exercise; (4) nutritional supplementation and exercise-induced sIgA responses; (5) repeated bouts of exercise and sIgA responses. Summaries were concluded in this review according to the current knowledge of the sIgA responses to exercise: (1) sIgA secretion and functions are regulated both by the stimulation of sympathetic nervous system (SNS) and hypothalamic-pituitary- adrenal-(HPA)-axis; (2) activated SNS and/or HPA induced by exercise might decrease saliva flow rate immediately and inhibit sIgA secretion and antigen-specific IgA production chronically; (3) the lower levels of sIgA may compromise immunity in mucosal surfaces and stresses induced by training and/or competition would temporarily impair oral immunity, placing elite athletes at a higher risk of URTI within 2 weeks after exercise; (4) the ingestion of carbohydrate and vitamin C appeared not to affect sIgA response following prolonged exercise; (5) the different times of day did not influence sIgA response to exercise; (6) the second exercise bout did not appear to further compromise the oral immunity compared with the first identical exercise bout and carbohydrate ingestion during any period of two repeated prolonged exercise bouts did not to induce different effects on oral immunity compared with placebo trials.

Key words: salivary IgA, exercise, SNS, HPA