Nutritional support to maintain proper immune status of athletes during intense training

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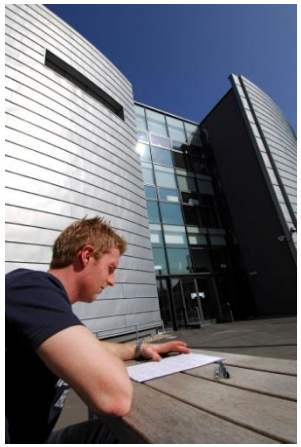
TEAM GB

The Official Preparation Camp Headquarters for Team GB

Summary

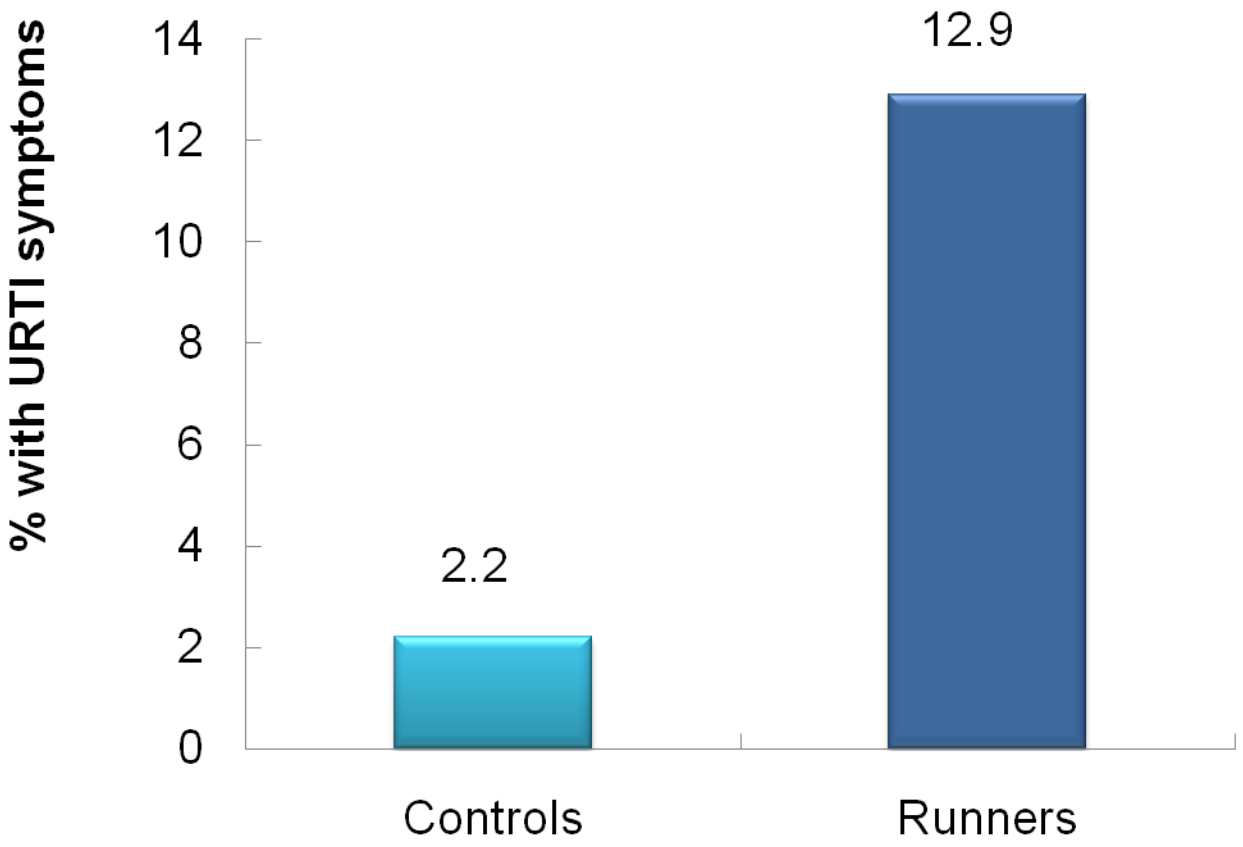
- Effects of exercise stress on the immune system
- Nutrition and the immune system
- Nutritional interventions for immune system support in athletes involved in intense training






Marathon running and upper respiratory tract infection (URTI)

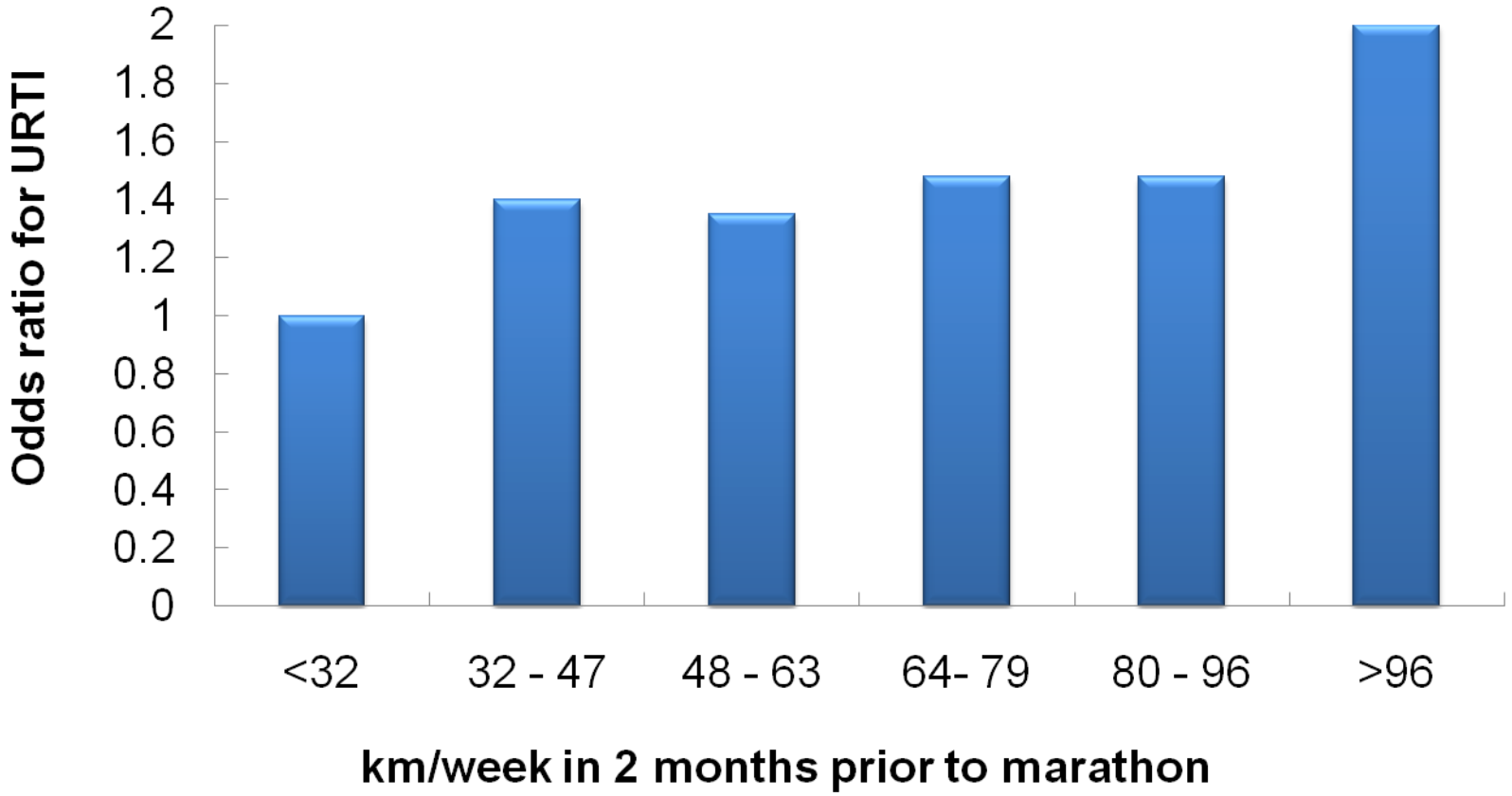
2,311 runners surveyed 1 week after the 1987 LA marathon



Nieman et al 1990 J Sports Med Phys Fitness 30: 316-328

Training volume and URTI relative risk in the 2 months prior to the marathon

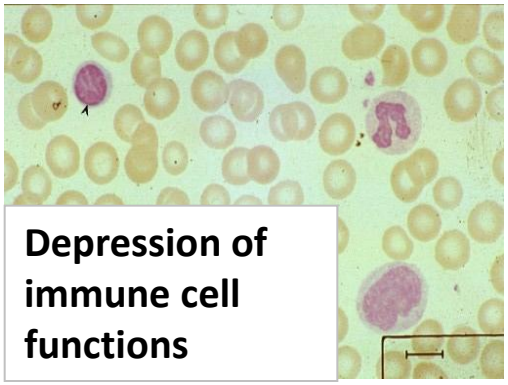
40% of the runners had at least one URTI episode in this 2-month period



Nieman et al 1990 J Sports Med Phys Fitness 30: 316-328

Prolonged (> 90 minutes) hard bouts of exercise depress immune function

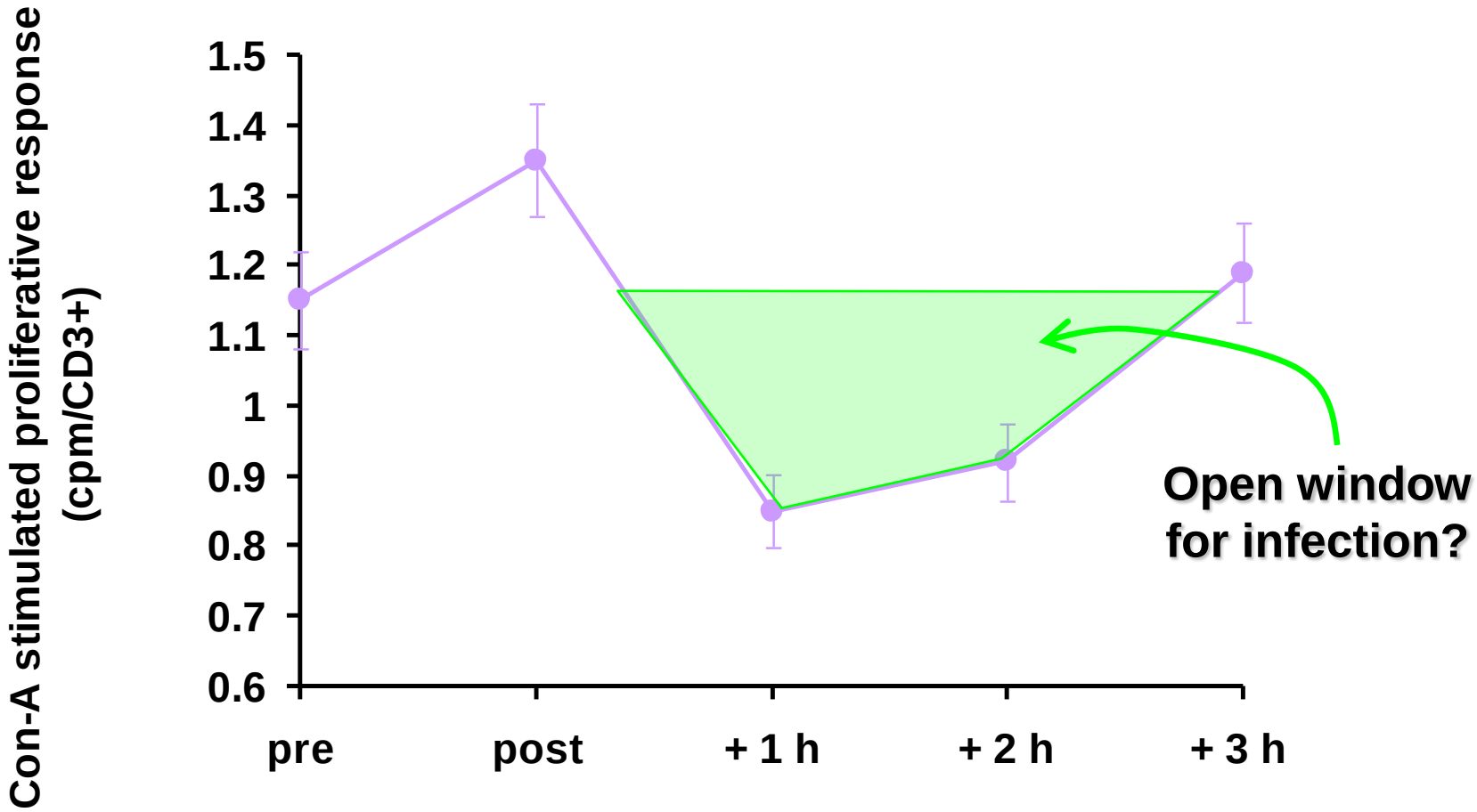
↓ Blood glucose
↓ Muscle glycogen
↑ IL-6 & IL-10
↑ Stress hormones
↑ Free radicals



Depression of immune cell functions

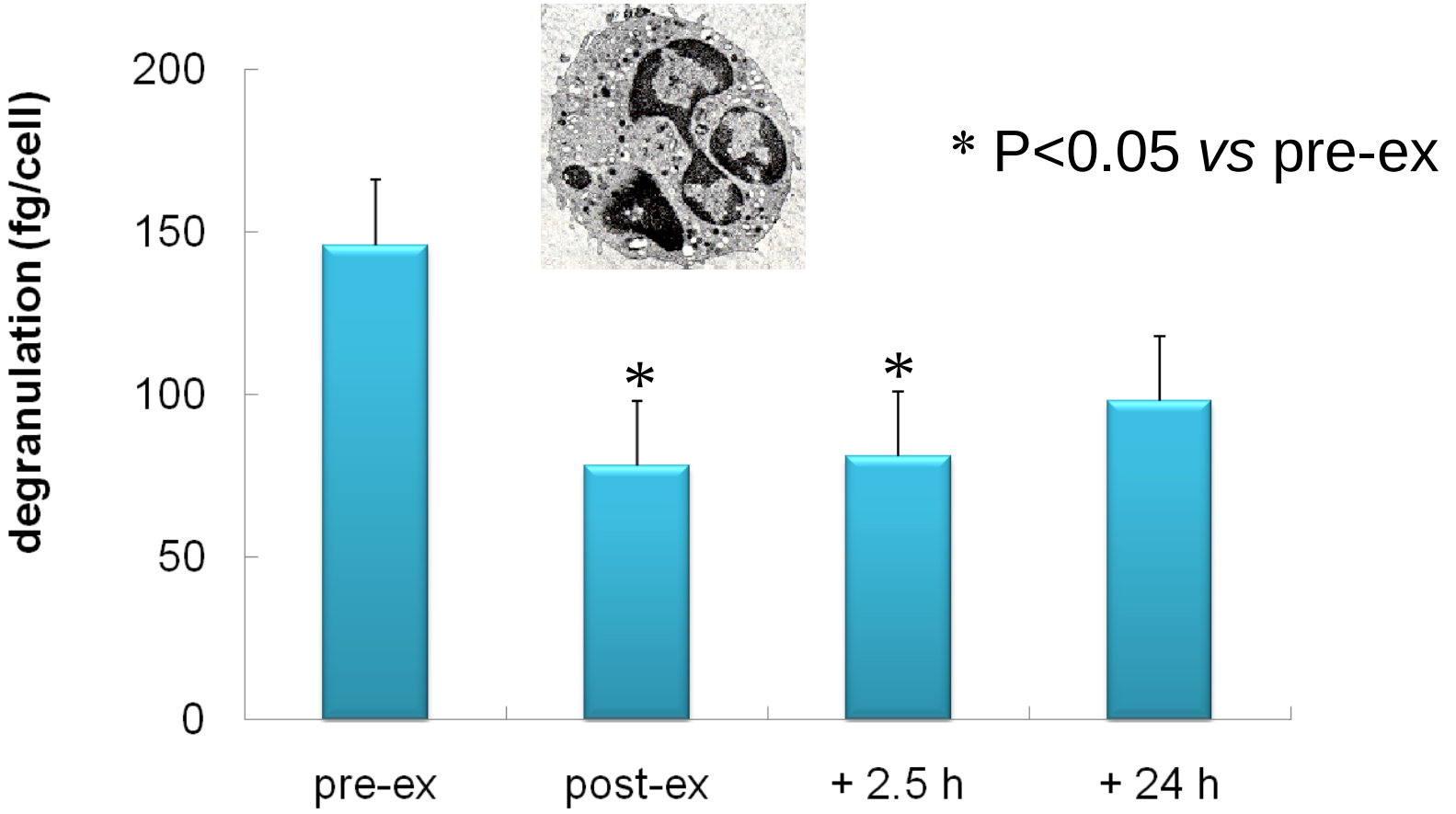
Increased infection risk

Acute prolonged intense exercise and mitogen stimulated T cell proliferation



Nieman et al 1994 Int J Sports Med 15: 199-206

Neutrophil function following 3 h cycling @ 55% VO_2max (n=18)

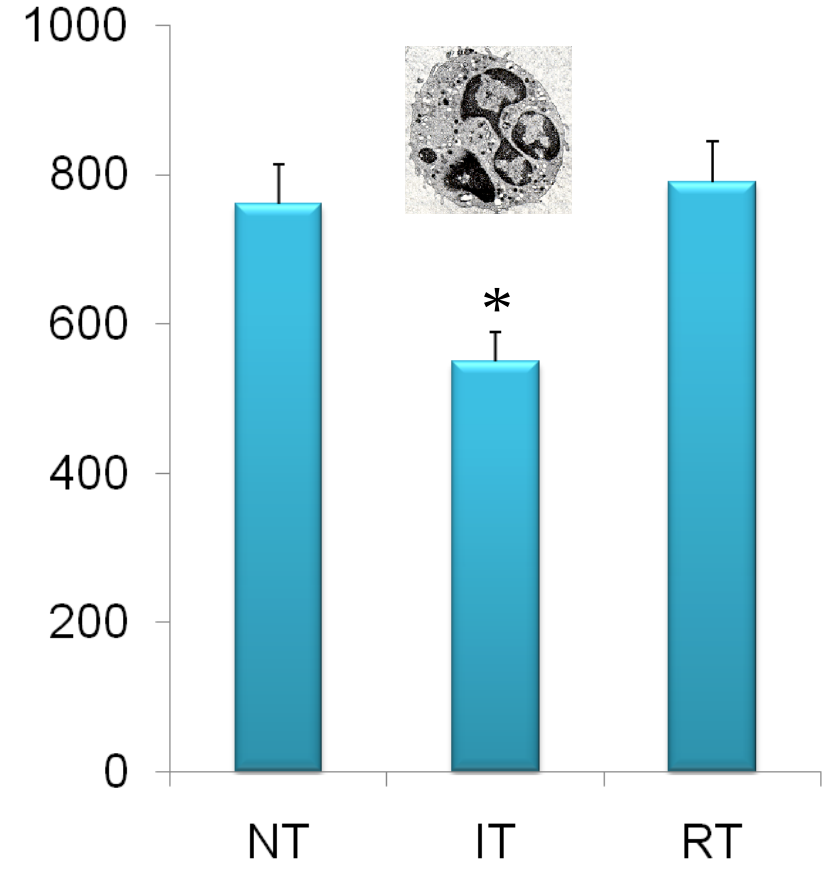


Robson et al 1999 Int J Sports Med 20: 128-135

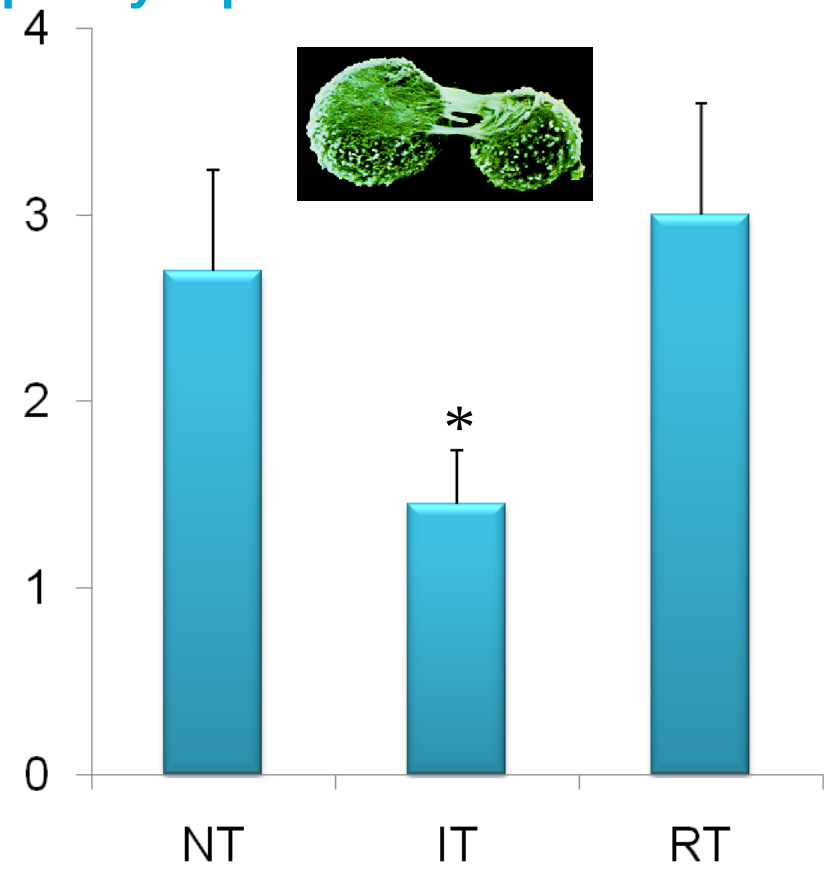
Effect of training load on resting immune cell functions

NT = normal training, IT = intensified training, RT = recovery training

Neutrophil oxidative burst

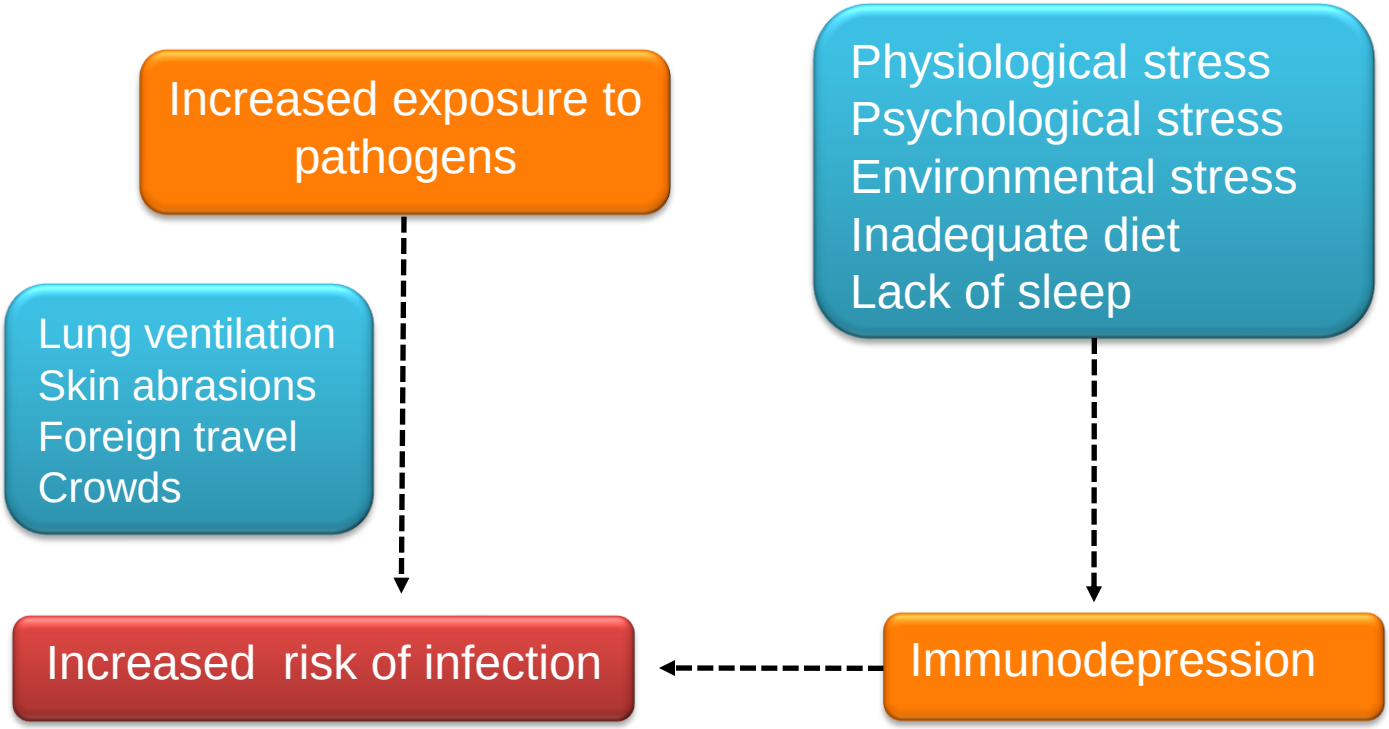


Lymphocyte proliferation index



Lancaster et al 2004 Exerc Immunol Rev 10: 91-106

Causes of increased infection in athletes



Effect of nutrient deficiencies on immune function

Nutrient Deficiency	Effects on Immune Function
Protein-Energy	↓ Thymus weight
Vitamin A	↓ T-lymphocyte number
Iron	↓ Lymphocyte proliferation
Zinc	↓ IL-2 and IFN-γ production
Copper	↓ Cell-mediated immunity
Selenium	↓ Antibody production

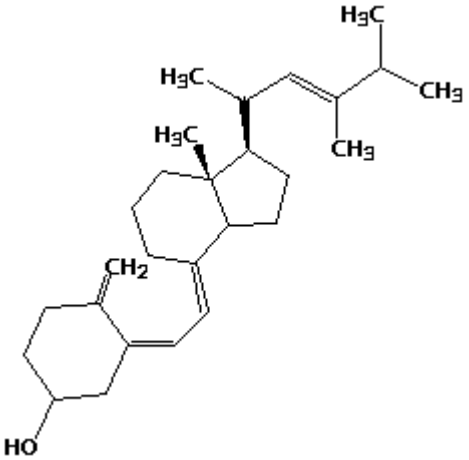
Nothing depresses immunity more than Protein-Energy Malnutrition
Almost all nutrients in the diet play a role in maintaining optimal immune function

Keusch 2003 J Nutr 133: 336S-340S

Vitamin D - a newly recognised role in immunity

Vitamin D upregulates anti-microbial peptides and has direct effects on T-lymphocyte activation and the function of antigen-presenting cells

Kamen & Tangpricha 2010 J Mol Med 88(5): 441-450

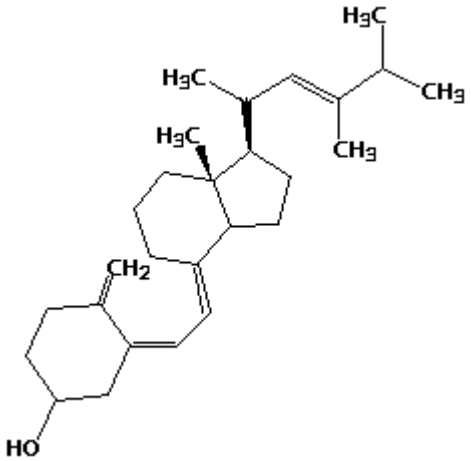


Vitamin D deficiency (serum concentration of 25(OH)D <30 nmol/L) is common in athletes (especially if training indoors; during winter months; in countries with limited sunlight)

Constantini et al 2010 Clin J Sport Med 20(5): 368-371
Larson-Meyer & Willis 2010 Curr Sports Med Rep 9: 220-226
Close et al 2012 J Sports Sci (in press)

Vitamin D – what level is adequate or optimal?

Vitamin D is important for bone health, muscle function and immune function



Classification of Vitamin D status

Serum Total 25(OH)D	**Status**
<12 nmol/L	Severely deficient
12-30 nmol/L	Deficient
30-50 nmol/L	Inadequate
>50 nmol/L	Adequate
120-225 nmol/L	Optimal

Close & Fraser (2012) The Sport & Exercise Scientist 33: 24-25

Nutritional strategy #1

Avoid deficiencies of essential micronutrients

Take a daily multivitamin tablet
Check blood for insufficiency of Vitamin D, Iron, Zinc
Consider weekly Vitamin D supplement (20,000 - 40,000 IU/week) to reach adequate (>50 nmol/L) or optimal (>120 nmol/L) serum 25(OH)D level

AND
Avoid deficiencies of protein and energy

Nutritional strategy #2

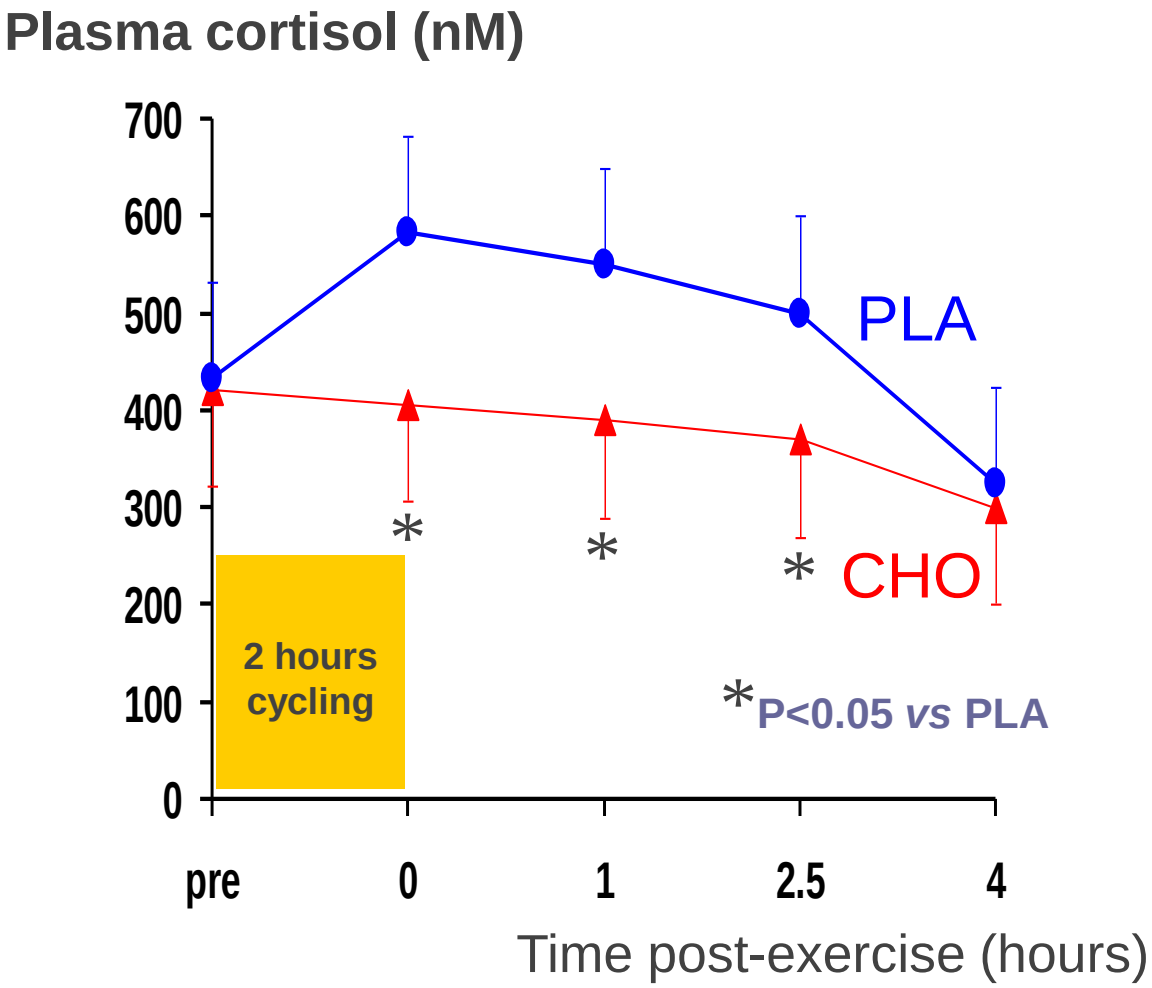
Ingest 30-60 g of carbohydrate per hour during prolonged exercise bouts

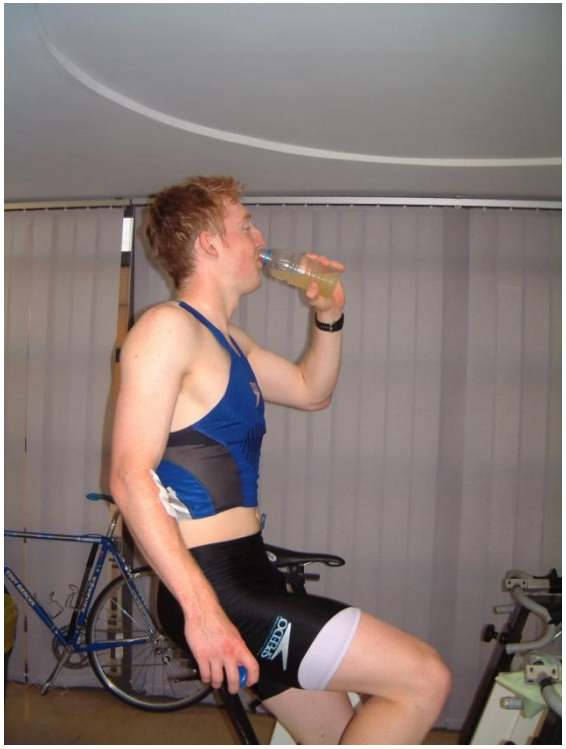
Carbohydrate and the immunoendocrine response to exercise

Carbohydrate (CHO) feeding during exercise prevents the fall in blood sugar and reduces the magnitude of rises in anti-inflammatory cytokines and stress hormones and thus helps to prevent exercise-induced immune function depression

Gleeson et al 2004 J Sport Sci 22(1): 115-125

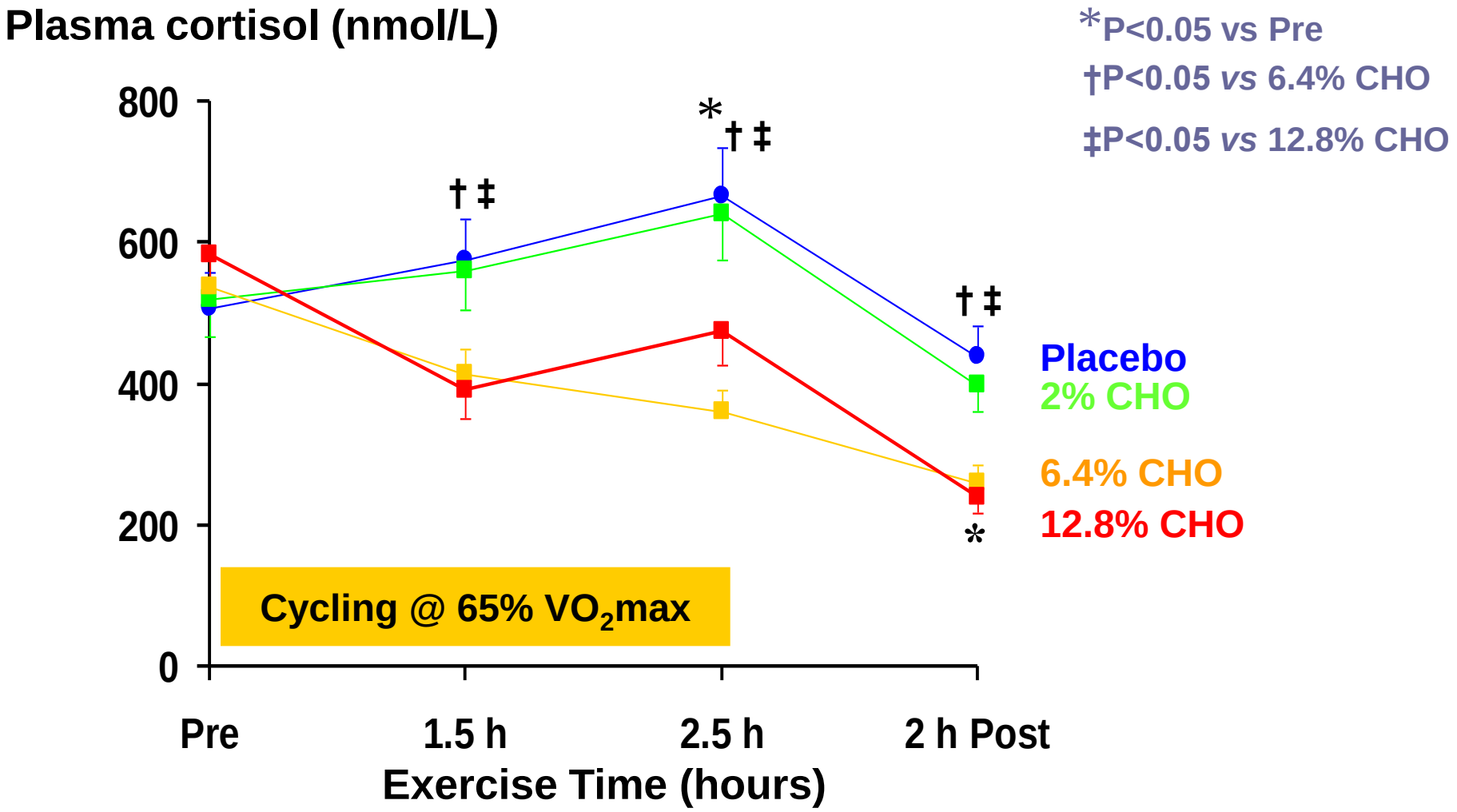
CHO intake during exercise attenuates plasma cortisol





Bishop et al 1999 J Sports Sci 17: 26-27

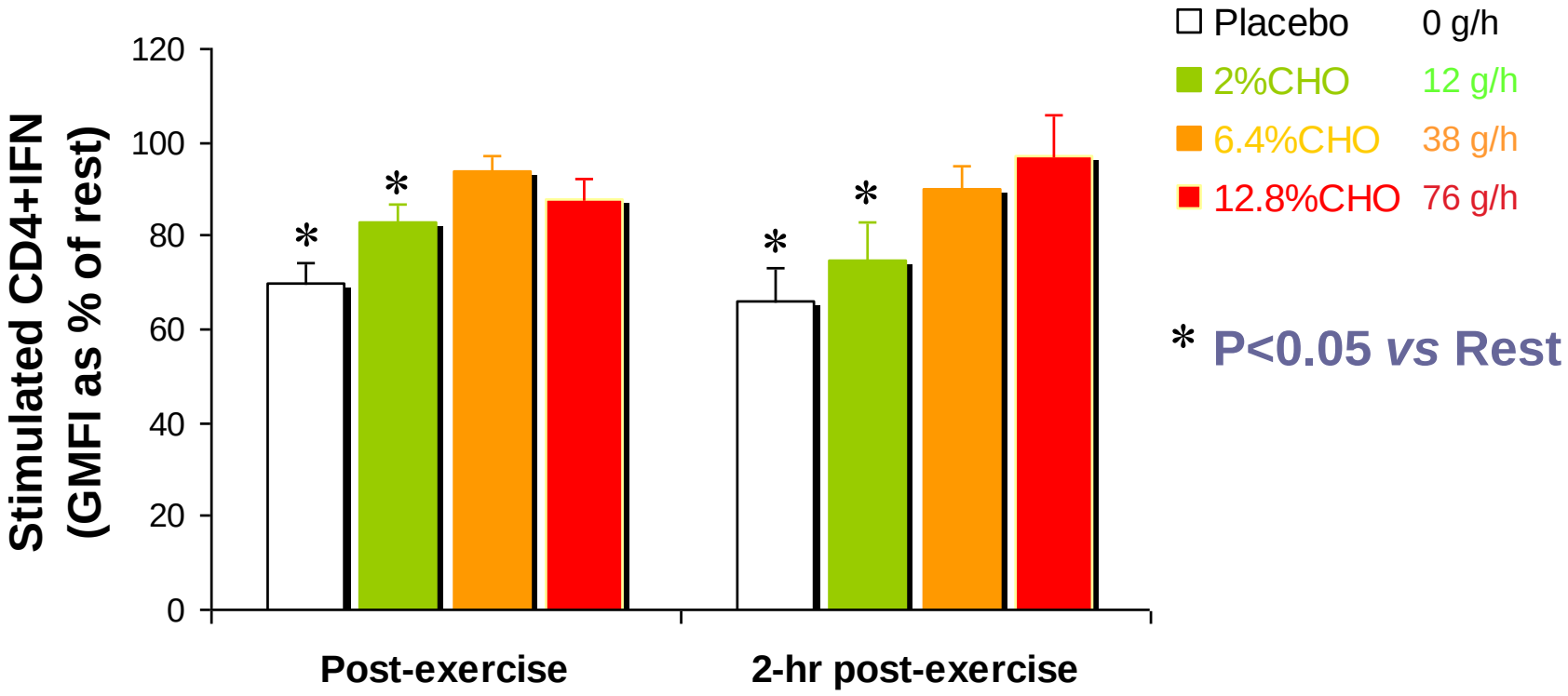
Effect of CHO dosage during prolonged exercise on plasma cortisol



Lancaster et al 2005 J Appl Physiol 98: 565-571

Effect of CHO dosage on IFN-γ production by T-lymphocytes

IFN-γ production by T-lymphocytes after 2.5 h cycling at 65% VO_2max



Immune function was maintained by feeding 38-76 g CHO per hour

Lancaster et al 2005 J Appl Physiol 98: 565-571

CHO drinks to prevent exercise-induced immunodepression

- CHO drinks help to maintain plasma glucose and reduce stress hormone responses to exercise limiting some aspects of immunodepression (e.g. neutrophil functions, T cell cytokine production, proliferation and migration)
- However…falls in some aspects of immune function with exercise (e.g. NK cell cytolytic activity, B cell function, salivary IgA) are not prevented by CHO ingestion
- Thus, CHO is only a partial countermeasure

Antioxidants

Several studies have examined the effects of short-term and long-term antioxidant supplementation on hormonal, cytokine and immune responses to prolonged strenuous exercise and/or URTI incidence

High dose Vitamin C

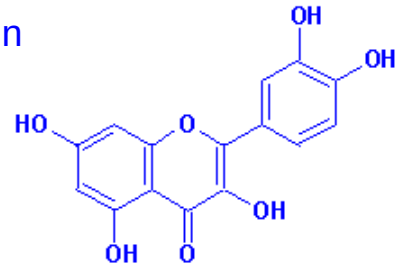
Vitamin C + Vitamin E

Flavonoids / Polyphenols

(e.g. Quercetin, Epicatechin)

in green tea, red grapes, cocoa products, beer

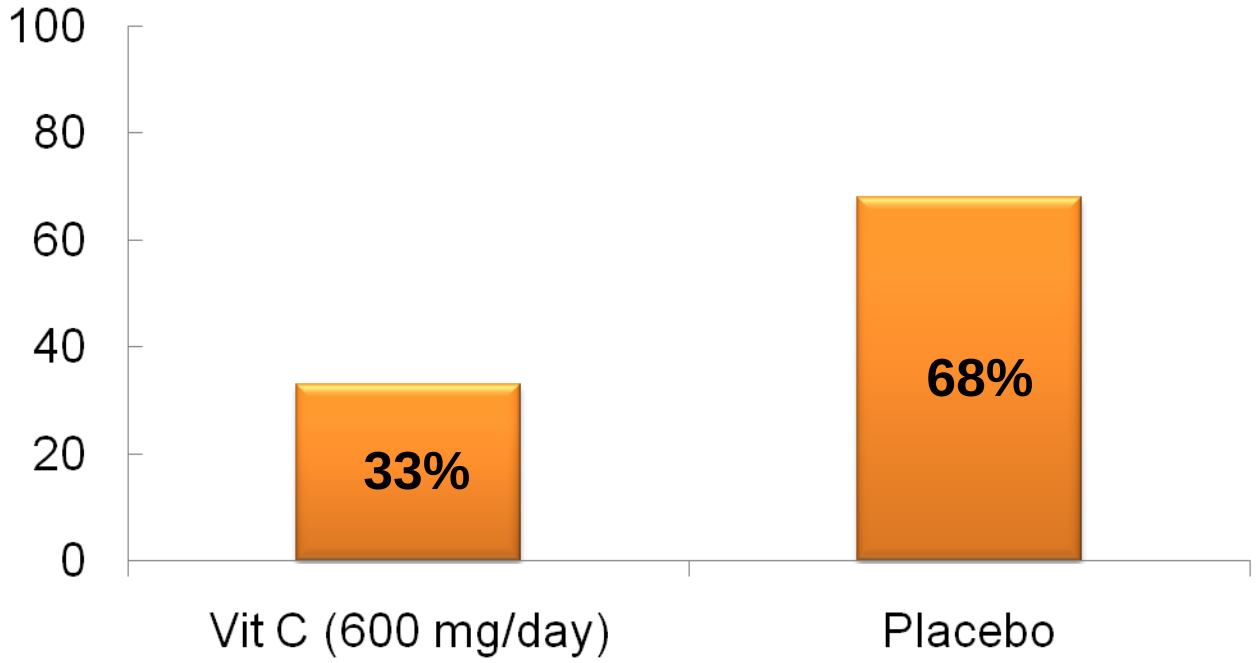
Quercetin



All are antioxidants and some may also have anti-inflammatory, antipathogenic and cancer-preventive influences

Vitamin C supplementation and post-race incidence of URTI

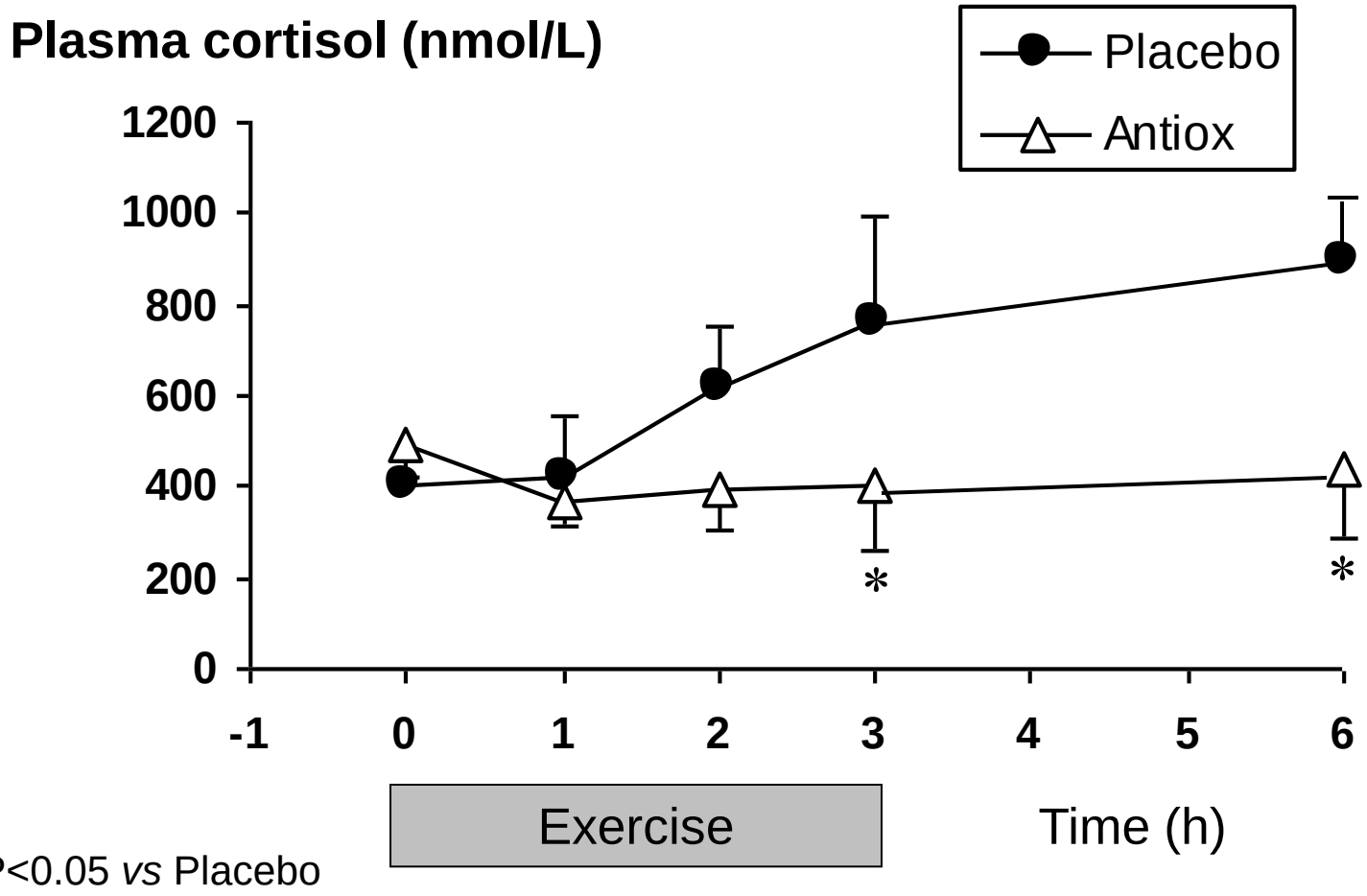
% of participants reporting symptoms of URTI within 14 days of an ultramarathon race



Peters et al 1993 Am J Clin Nutr 57: 170-174

Smaller cortisol response to exercise with antioxidant supplementation

4 weeks daily Vit C & E supplements OR Placebo followed by 3 h knee extensor exercise



*P<0.05 *vs* Placebo

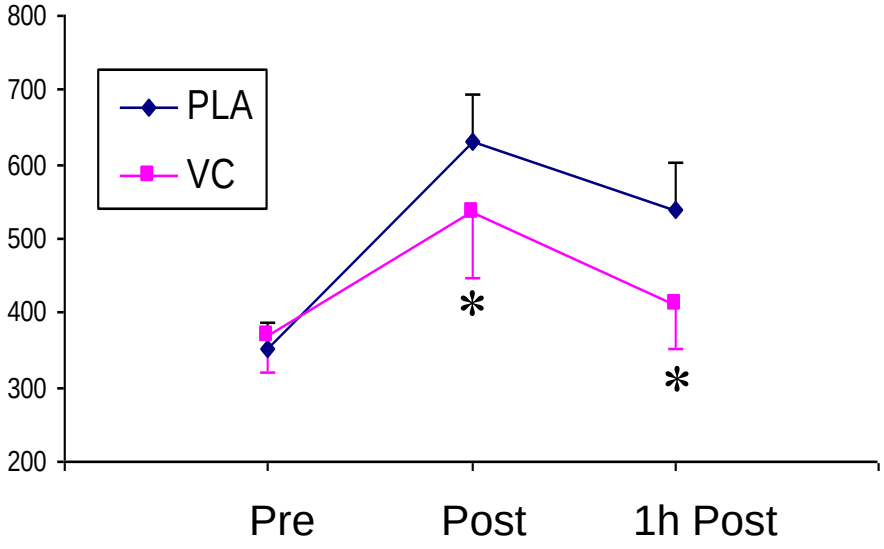
Fischer et al 2004 J Physiol 558(2): 633-645

Vitamin C supplements and the immunoendocrine response to exercise

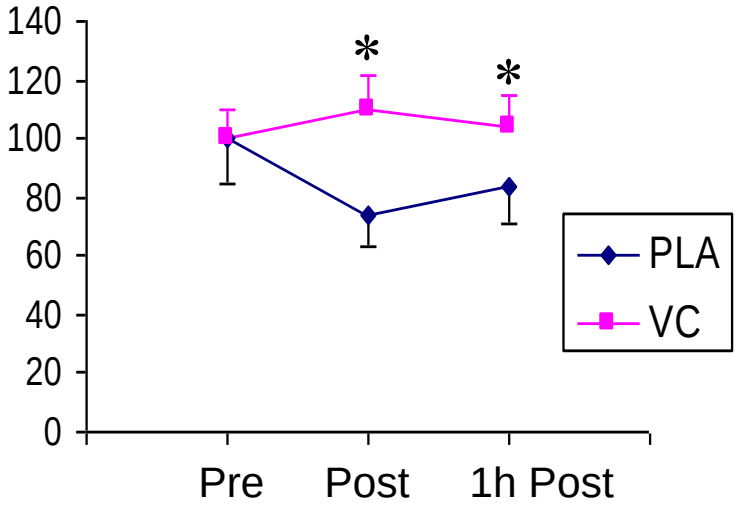
Randomised placebo-controlled paired crossover study followed by 2.5 h cycling

Reduced cortisol response to 2.5 h cycling at 60% VO_2max and maintenance o neutrophil function with 1 g/day Vitamin C for 2 weeks

Cortisol nmol/L



Neutrophil Function (% Pre-ex OBA)



Davison & Gleeson 2006 Eur J Appl Physiol 97(4): 454-461

Summary: Anti-oxidants, exercise and immune function

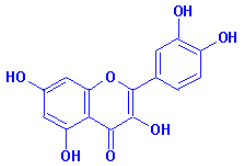
- Chronic supplementation with Vitamin C (but not other anti-oxidants) is associated with a lower incidence of URTI following an ultramarathon (Peters et al 1993, 1996)
- Chronic supplementation with Vitamin C increases plasma antioxidant capacity and attenuates the cortisol response to exercise (Fischer et al 2004, Davison & Gleeson 2006)
- Possible beneficial effects of more potent antioxidants?
  - quercetin
  - polyphenols in grape juice
  - green tea
  - dark chocolate
  - beer

Bad news ladies…no effect of acute or chronic dark chocolate ingestion on immunoendocrine responses to exercise

- Davison G, Cooper K, Callister R & Gleeson M. (2012). The effect of acute pre-exercise dark chocolate consumption on plasma antioxidant status, oxidative stress, and immunoendocrine responses to prolonged exercise. *Eur J Nutr* **51**(1): 69-79.

- Allgrove JE, Farrell E, Gleeson M, Williamson G & Cooper K. (2011). Regular dark chocolate consumption's reduction of oxidative stress and increase of free-fatty-acid mobilization in response to prolonged cycling. *Int J Sport Nutr Exerc Metab* **21**(2):113-23.

Quercetin reduces illness but not immune pertubations after intensive exercise



Supplement with Quercetin (1 g/day) n=20 or Placebo n=20

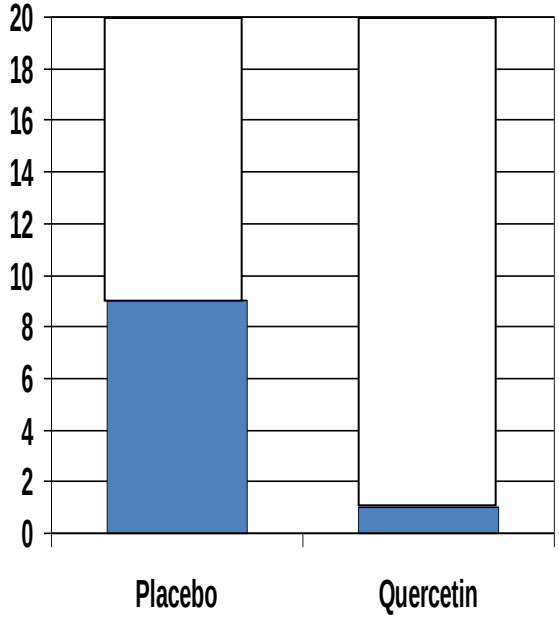
3 weeks | 3 days | 2 weeks

ITP

Normal training (1.5 h/day) | Normal training

Record URTI symptoms throughout

Number of URTI episodes in the 2-weeks post ITP



ITP = Intensified training period: 3 h cycling at 68% VO_2max per day for 3 days (with pre- and post-exercise blood for immune measures)

Nieman et al 2007 Med Sci Sports Exerc 39(9): 1561-1569

Non-alcoholic beer reduces inflammation and incidence of URTI following a marathon race

Supplement with NAB (1-1.5 L/day) or Placebo (n=277, age 42±9 y)

3 weeks | Race | 2 weeks

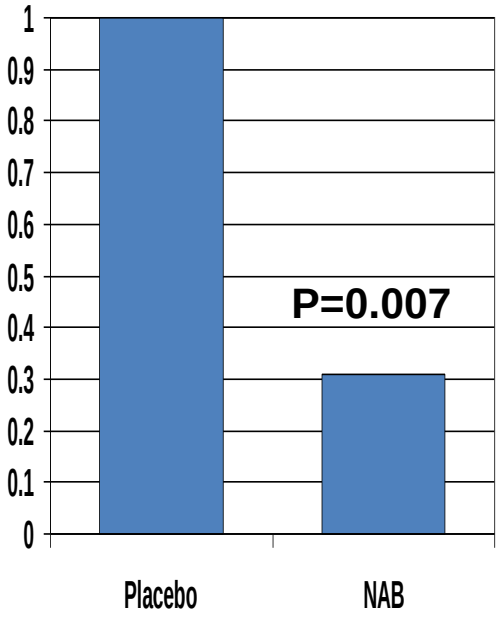
Munich Marathon

Normal training | Normal training

Record URTI symptoms

Post-marathon changes in Plasma IL-6 and WBC counts were ~20% lower with NAB compared with placebo. URTI incidence was 3.25 lower on NAB

Relative risk of URTI in the 2-weeks post-marathon



Scherr et al 2012 Med Sci Sports Exerc 44(1): 18-26

Nutritional strategy #3

Eat plenty of fruits and vegetables to ensure a high intake of natural dietary antioxidants. High fruit intake is known to be associated with a lower risk of URTI (*Nieman et al 2010*)

Consider taking vitamin C supplements (200 -1000 mg/day)

Consider taking polyphenol antioxidant supplements (e.g. Quercetin 1 g / day) or foods/beverages that contain high amounts of plant polyphenols (e.g. nonalcoholic beer; green tea)

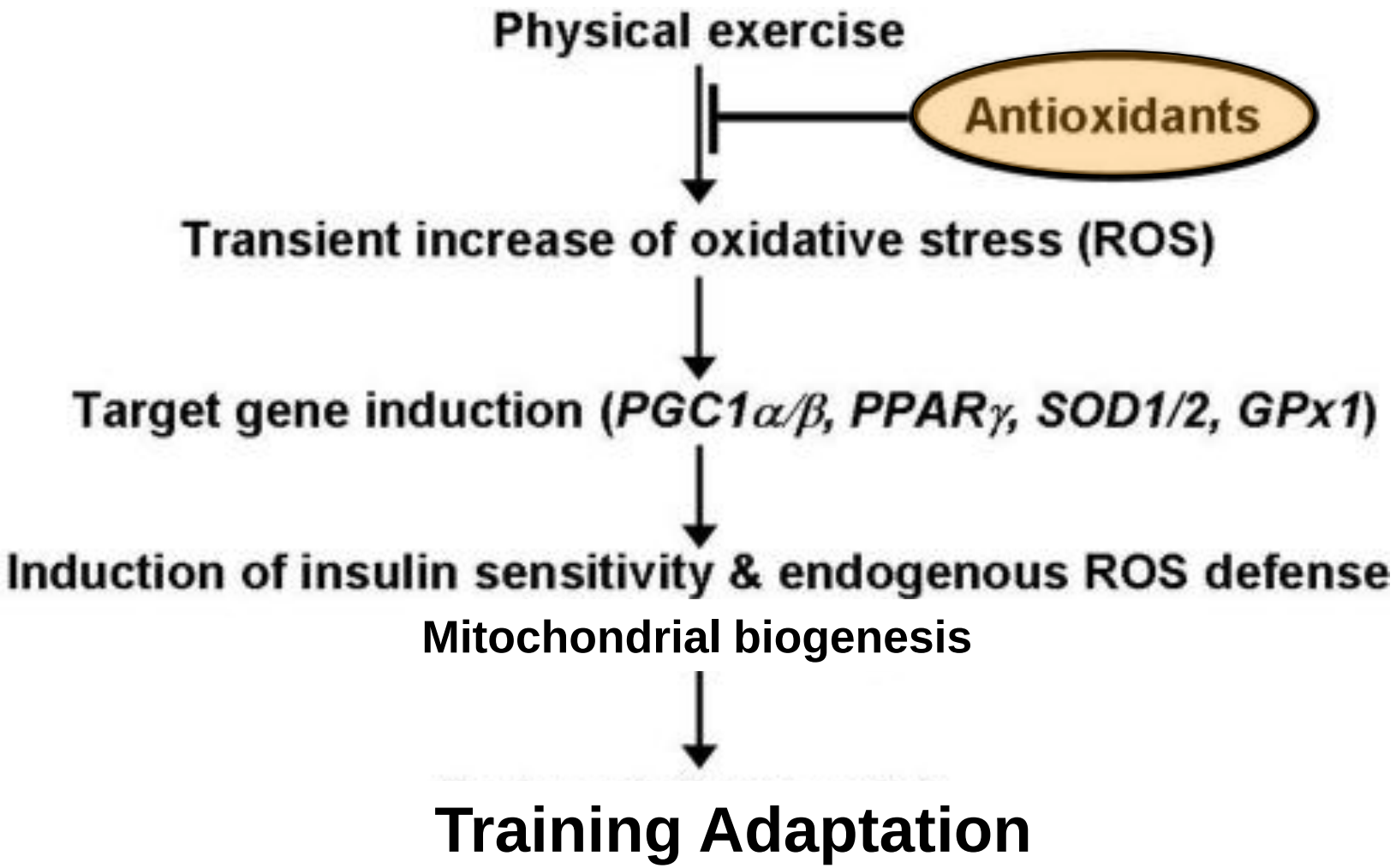
A possible disadvantage of high dose antioxidant supplementation

Antioxidant supplementation impedes exercise-induced adaptations in humans

Gomez-Cabera et al. 2008 Am J Clin Nutr 87: 142-149

Ristow et al. 2009 Proc Nat Acad Sci 106(21): 8665-8670

Is oxidative stress needed as a stimulus for adaptation to training?



Adapted from Ristow et al. 2009 Proc Nat Acad Sci 106(21): 8665-8670

Is oxidative stress needed as a stimulus for adaptation to training?

Not supported for high dose Vitamin C supplementation – no effect of high daily dose of Vitamin C on performance gains with endurance training in human athletes

Roberts et al. (2011) **Vitamin C consumption does not impair training-induced improvements in exercise performance**
Int J Sports Physiol Perform 6(1):58-69

Yfanti et al. (2010) **Antioxidant supplementation does not alter endurance training adaptation**
Med Sci Sports Exerc 42(7):1388-1395

Other dietary immunostimulants

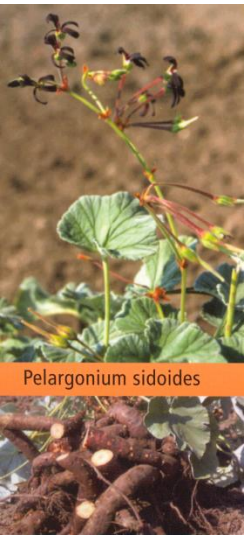
- **Herbals (e.g. Echinacea, Kaloba) – no strong support in human studies for reduced infection incidence but may shorten duration of symptoms when coming down with a cold**
- **Zinc – may reduce cold symptom duration (*Singh & Das 2011*)**
- **Bovine Colostrum – mixed results for saliva IgA levels in athletes; some evidence of decreased URTI episodes though mechanism is not clear (*Crooks et al 2006; 2010*)**
- **Glutamine – not responsible for exercise-induced immunodepression (*Hiscock & Pedersen 2002*)**
- **β-Glucan – evidence of effectiveness in reducing exercise-stress associated viral infection in mice (*Davis et al 2004*) but not in humans (*Nieman et al 2008*)**

Everyone uses herbals so they must work…mustn't they?

The evidence for Echinacea as an effective immunostimulant:

- Its been used as a herbal remedy in Asia for many years
  – doesn't mean it prevents infections; may reduce illness symptom duration but so do many other cold remedies
- *In vitro* studies indicate that echinacea extracts stimulate NK cell, neutrophil and macrophage antibactericidal actions and monocyte cytokine production – great; but so do lots of other things…*in vitro*
- Similar effects *in vivo* are not seen with oral Echinacea
  – so bioavailability may be a problem
- Some studies show positive benefits (e.g. reduced infections with oral Echinacea) in athletes – were they large scale, placebo-controlled , randomised studies, over several months? No.
- *Turner et al 2005 New Engl J Med 353(4): 341-348:*
  437 volunteers randomly assigned to echinacea or placebo 7 days before rhinovirus challenge and at time of challenge
  RESULTS: No statistically significant effects of three oral echinacea extracts on rates of infection or severity of symptoms

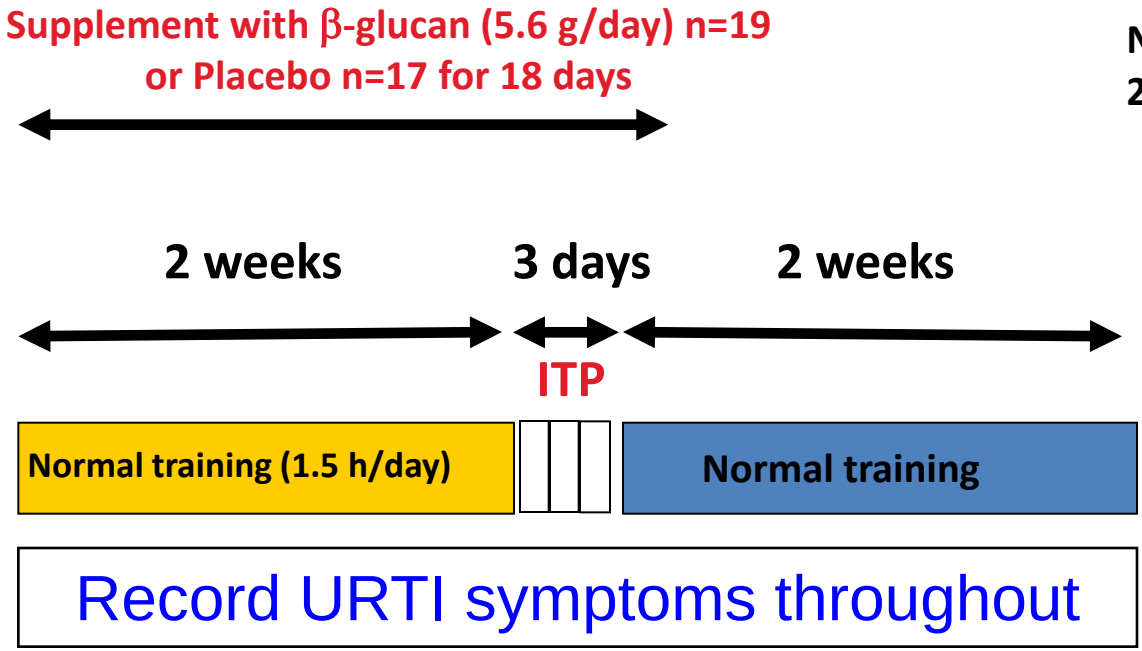
Better evidence for some other herbals: EPs®7630 (Kaloba®)



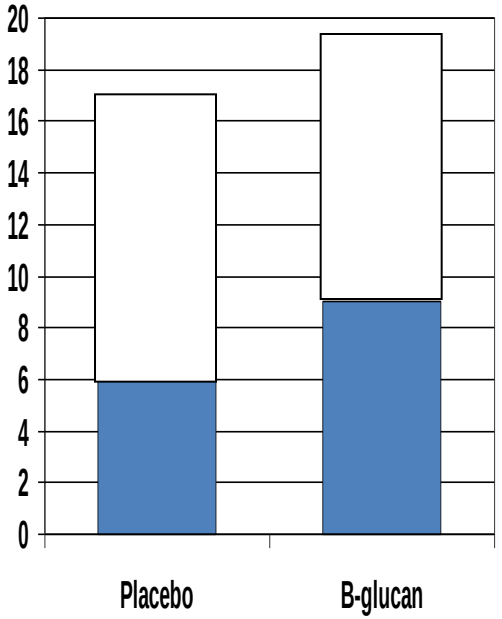
EPs®7630 (Kaloba®) is an extract of the roots of the South African plant *Pelargonium sidoides*

- **Contains polyphenols (e.g. catechins and quercetin) and coumarins. Daily dose is 3 x 1.5 ml**
- ***In vitro* studies indicate that EPs®7630 stimulates neutrophil and macrophage antimicrobial actions *(Conrad et al 2007)*, interferon production *(Koch et al 2002)*, ciliary beat frequency of airway epithelia *(Neugebauer et al 2005)* and inhibits bacterial adhesion to healthy mucosal cells *(Conrad et al 2007)***
- **Some studies show reduced symptom severity and duration in acute bronchitis, sinusitis and common cold in adults and children – mostly large scale (n = 100-400), randomised, double-blind, placebo-controlled studies *(Cuchalin et al 2005, Lizogub et al 2007, Bachert et al 2009)***
- ***Timmer et al 2008 Cochrane Database of Systematic Reviews CD006323:* Meta-analysis of 8 studies of EPs®7630 *vs* placebo: CONCLUSION: "EPs®7630 may be effective in relieving symptoms in acute brochitis, rhinosinusitis and the common cold"**

β-glucan does not alter immune pertubations or URTI after intensive exercise



Number of URTI episodes in the 2-weeks post ITP



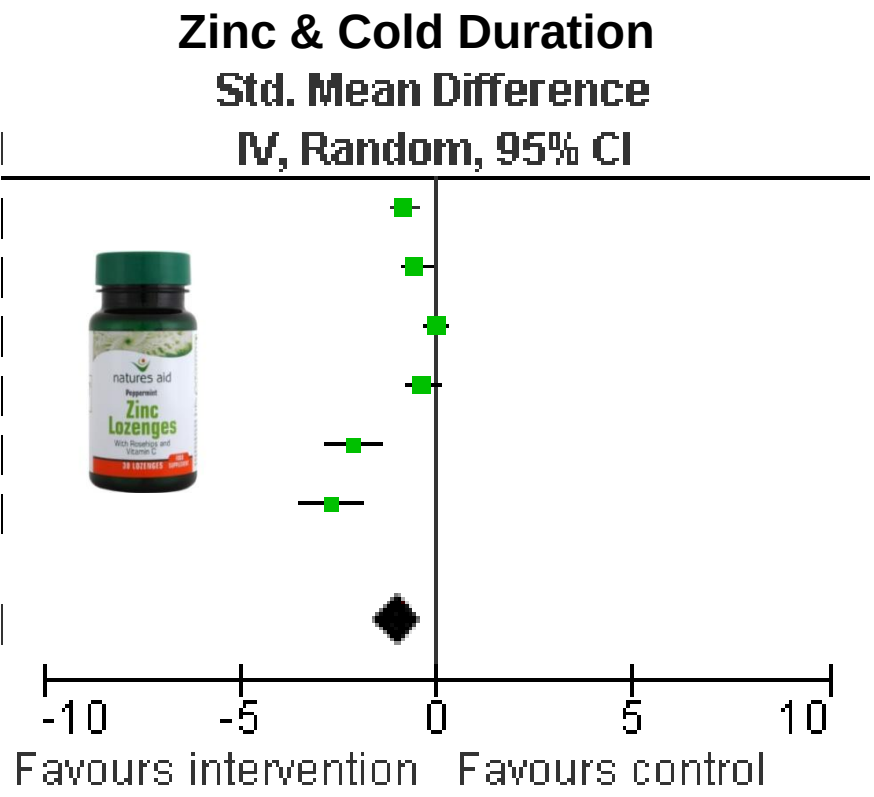
ITP = Intensified training period: 3 h cycling at 68% VO_2max per day for 3 days (with pre- and post-exercise blood for immune measures)

Nieman et al 2008 Med Sci Sports Exerc 40(8): 1463-1471

Evidence for zinc reducing the burden of the common cold

2011 Cochrane Systematic Review

15 trials involving 1360 people aged 1-64



- **Zinc inhibits rhinoviral replication**
- **Zinc syrup, lozenges or tablets taken within a day of the onset of cold symptoms reduce the severity and length of illness (by one day)**
- **Children who took zinc syrup or lozenges for 5 months or longer caught fewer colds and took less time off school**
- **Zinc also reduced antibiotic use in children**

Singh & Das 2011 Cochrane database of Systematic Reviews 2011, Issue 2: CD001364

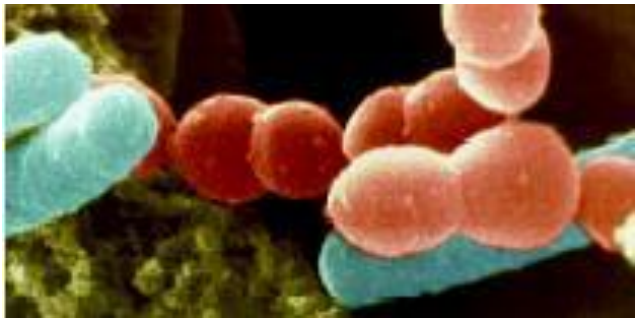
Nutritional strategy #4

Don’t waste money on supplements that claim to boost immunity but don’t have a strong scientific evidence base

Consider taking herbals (e.g. Kaloba) and zinc lozenges (high in ionic zinc, 75 mg/day) just before competition periods (to reduce severity/duration of symptoms) in anticipation of the unfortunate event of picking up a cold

Probiotics

Probiotics – may reduce incidence and severity of respiratory infections (*Gleeson & Thomas 2008, Cox et al 2010; Gleeson et al 2011; West et al 2011*)



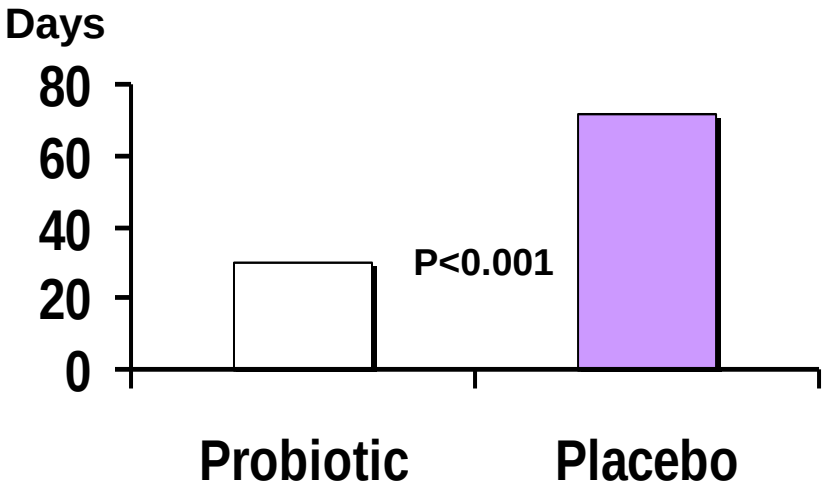
Probiotics are live microorganisms which, when administered in adequate amounts, confer a health benefit on the host (FAO/WHO 2001)

Probiotics modify the gut microbiota and have been shown to increase some aspects of mucosal and systemic immunity in healthy humans

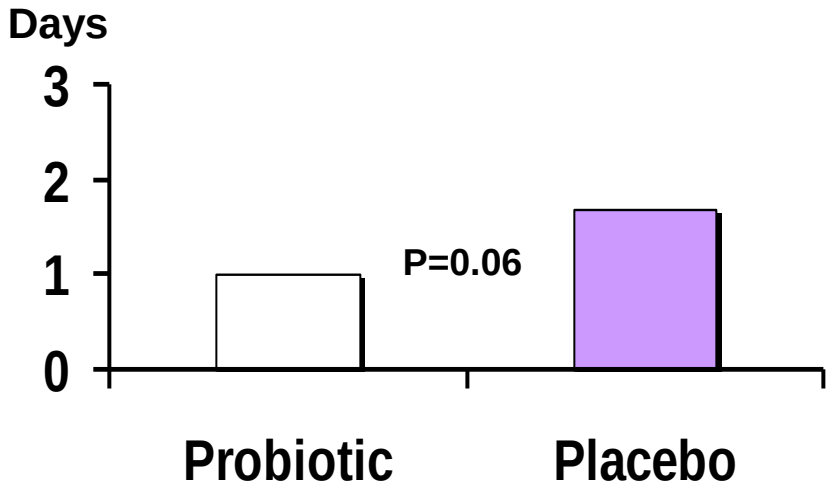
Oral probiotic and mucosal immunity in endurance athletes

- 20 healthy elite male distance runners
- 1.2 x 10^{10} CFU *Lactobacillus fermentum* VRI-003 or placebo during 4 weeks of winter training. Double-blind, crossover design with 4 weeks washout
- Fewer days with illness symptoms and lower symptom severity

Number of days of illness symptoms



Severity of illness symptoms

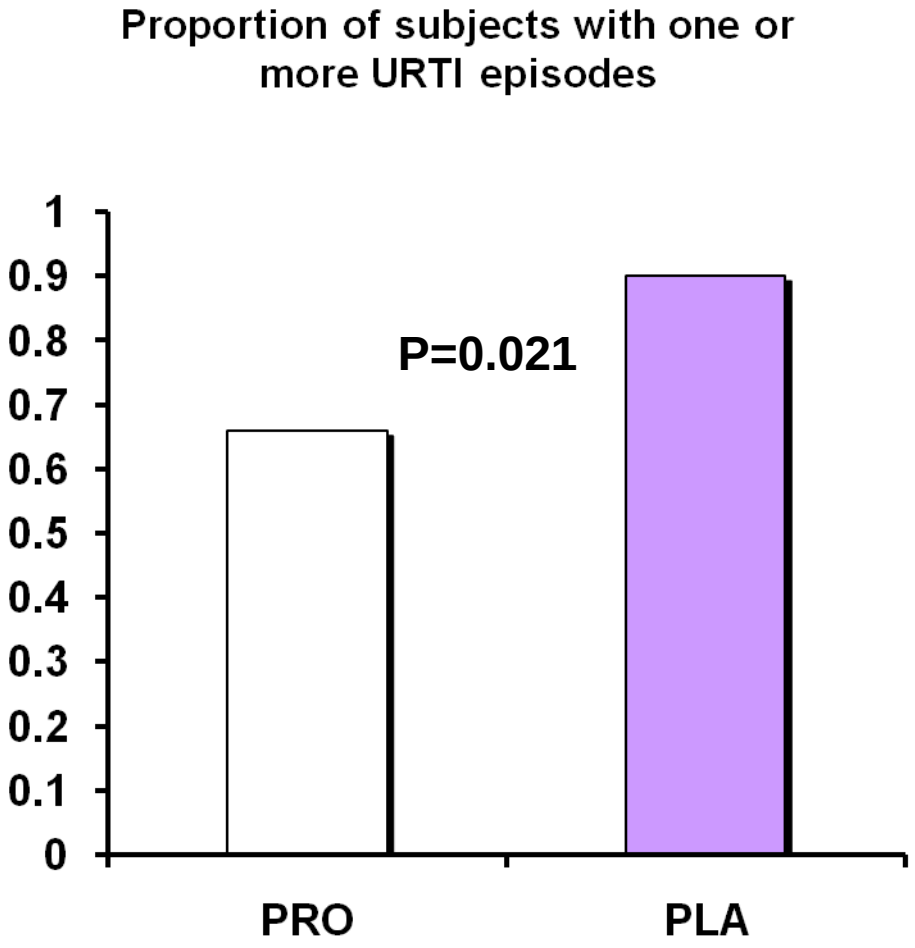


Cox et al 2010 Br J Sports Med 44(4): 222-226

Effect of probiotic on URTI incidence in an athlete cohort (N=58)

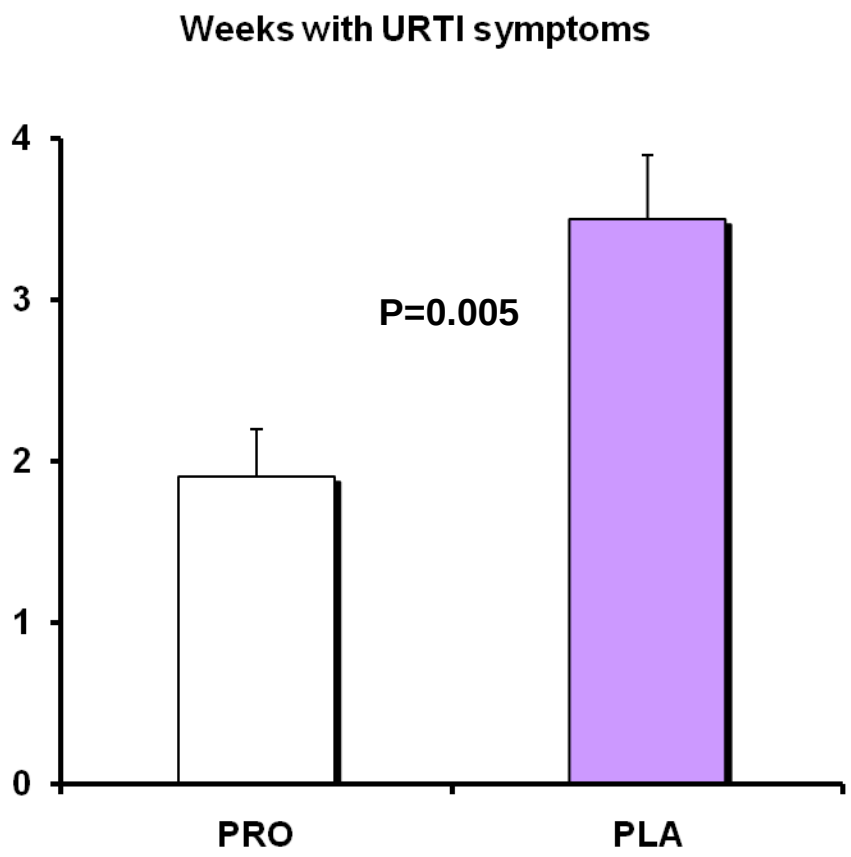
Daily probiotic drink or placebo for 16 weeks during winter training in endurance athletes

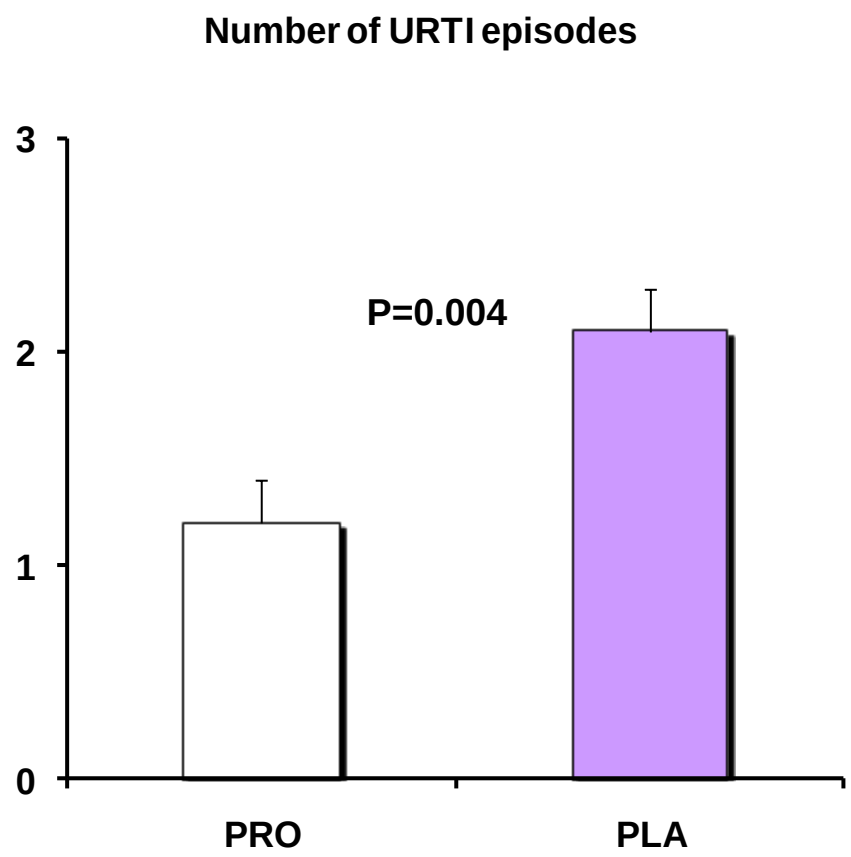
Randomised, double-blind study



Gleeson et al 2011 Int J Sport Nutr Exerc Metab 21: 55-64

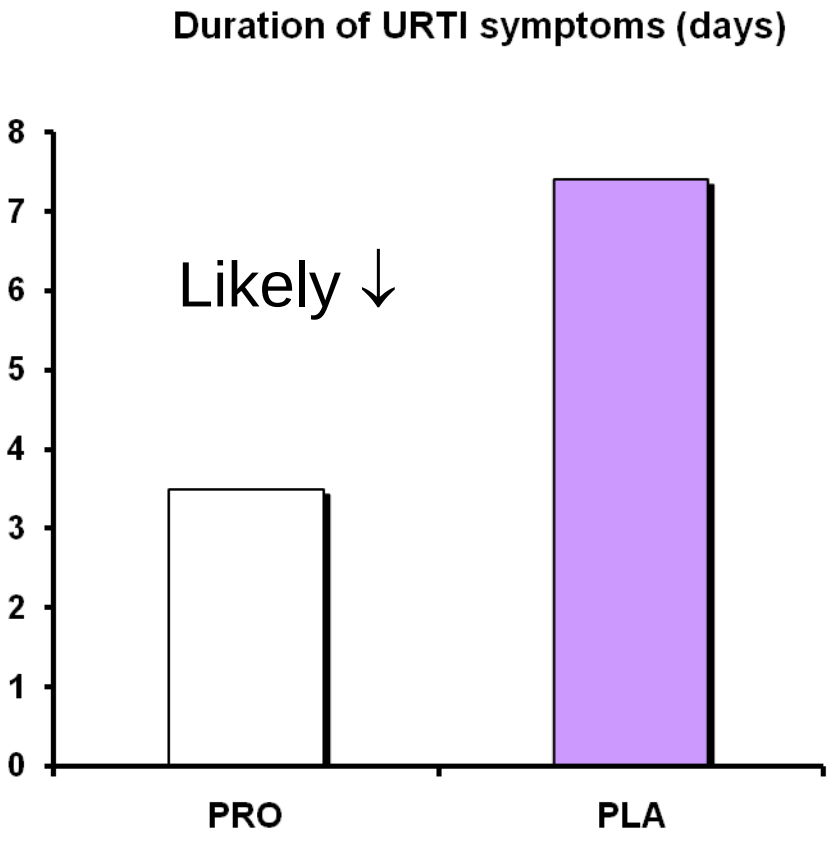
Effect of probiotic on URTI incidence in an athlete cohort (N=58)

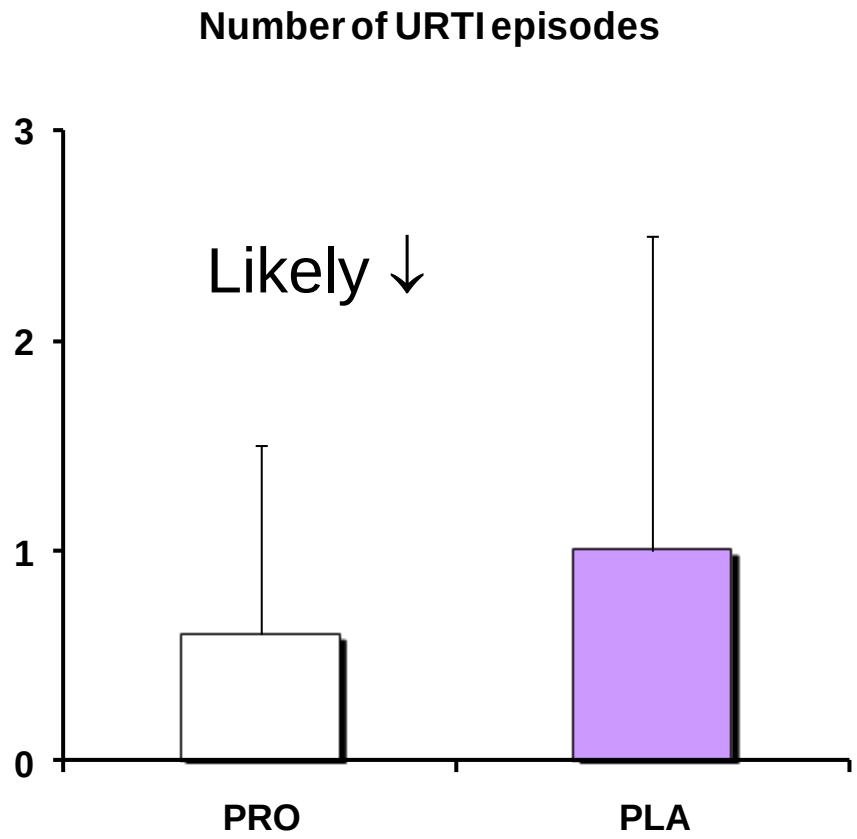




Gleeson et al 2011 Int J Sport Nutr Exerc Metab 21: 55-64

Effect of *L. fermentum* on URTI incidence in male cyclists (N=62) during 11 weeks of winter training





West et al 2011 Nutr J 10: 30

Evidence for probiotics preventing acute URTI (the common cold)

2011 Cochrane Systematic Review

10 trials involving 3451 people (infants, children, adults)

Probiotic intervention better than placebo:

Odds ratio for number of participants experiencing at least one URTI episode: 0.58 (0.36 – 0.92; 95% CI)

three URTI episodes: 0.53 (0.36 – 0.80)

Rate ratio of URTI episodes: 0.88 (0.81 – 0.96)

Antibiotic prescription: 0.67 (0.45 – 0.98)

No difference from placebo:

Mean duration of URTI episode: -0.29 (-3.71 – 3.13)

CONCLUSION: Benefit in using probiotics to prevent acute URTIs

Hao et al 2011 Cochrane database of Systematic Reviews 2011, Issue 9: CD006895

Nutritional strategy #5

Take a daily *Lactobacillus* probiotic

According to manufacturer's recommendations but should contain ~10^{10} live bacteria

Possible benefit, no harm and low cost so no reason why athletes should not take probiotics, especially if travelling abroad or illness-prone

May also defend against gastrointestinal problems

Nutritional strategies to maintain immunity and minimise stress

- Ensure energy balance and adequate carbohydrate and protein intake
- Avoid micronutrient deficiencies (daily multivitamin tablet)
- Avoid dehydration and a dry mouth (drink plenty)
- Ingest carbohydrate during exercise (30-60 g/hour)
- High antioxidant intake (lots of fruit & veg)
- Dietary immunostimulants that *might* work for athletes: -
  Flavonoids/Polyphenols ~1 g/day from foods, beverages, supplements
  Vitamin C and D supplements?
  Lactobacillus Probiotics (daily according to recommendation)
  Herbals (Kaloba/EPs®7630) and zinc before competition

And…Nutrition is only one factor in illness prevention

Other practical strategies to minimise illness risk

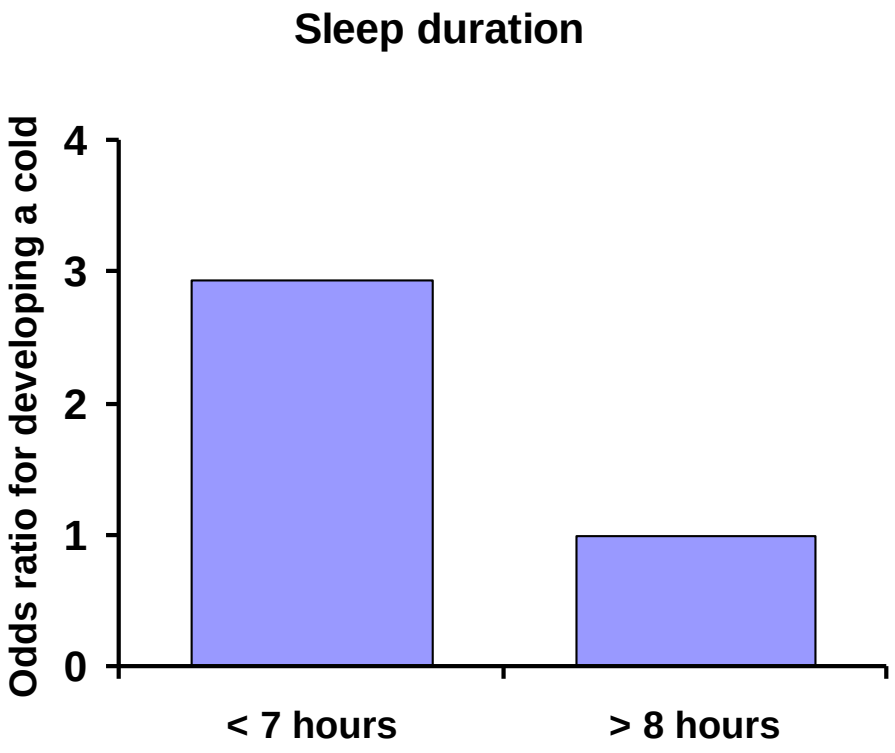
Minimise the chances of immunodepression:-

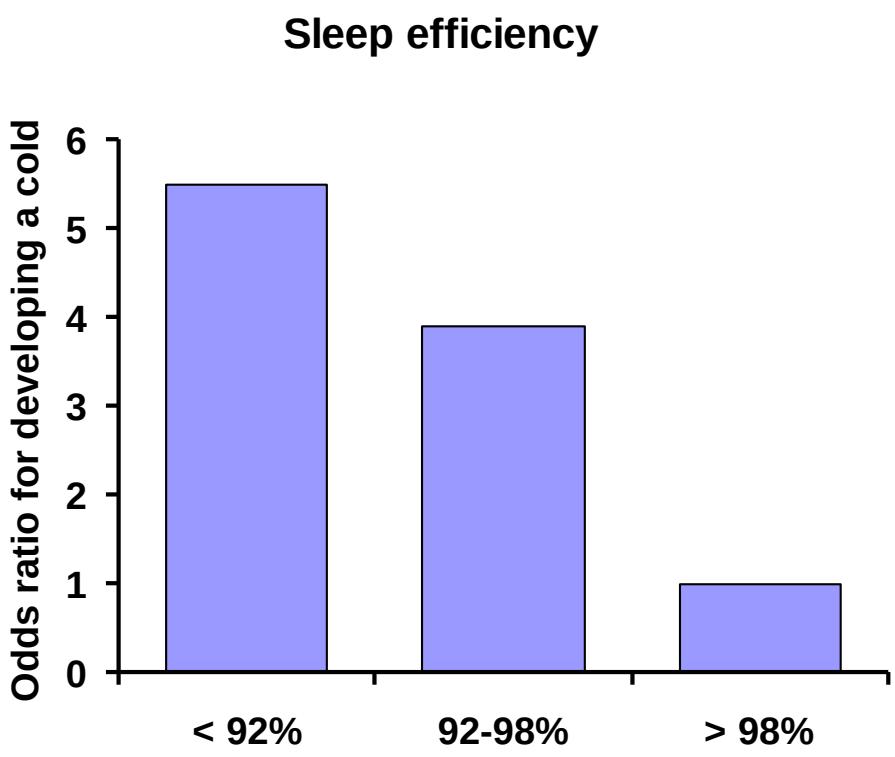
- Avoid very prolonged training sessions (> 2 hours), overtraining and chronic fatigue
- Keep other life stresses to a minimum
- Get adequate sleep (at least 7 hours)
- Avoid rapid weight loss
- Vaccinate against influenza if competing in the winter

Minimise the potential for transmission of infectious agents:-

- Avoid sick people and large crowds in enclosed spaces if possible
- Good personal hygiene (wash hands and brush teeth regularly)
- Never share drink bottles, cutlery, towels etc
- Avoid putting hands to eyes and nose (a major route of viral self-inoculation)
- Good food hygiene

Sleep quality affects susceptibility to the common cold





Lower sleep duration and efficiency (% of time in bed asleep) are associated with increased risk of developing a cold following rhinovirus exposure

Cohen et al 2009 Arch Int Med 169(1): 62-67

Possible confounding factors influencing sleep quantity and quality
#1 Who you sleep with…

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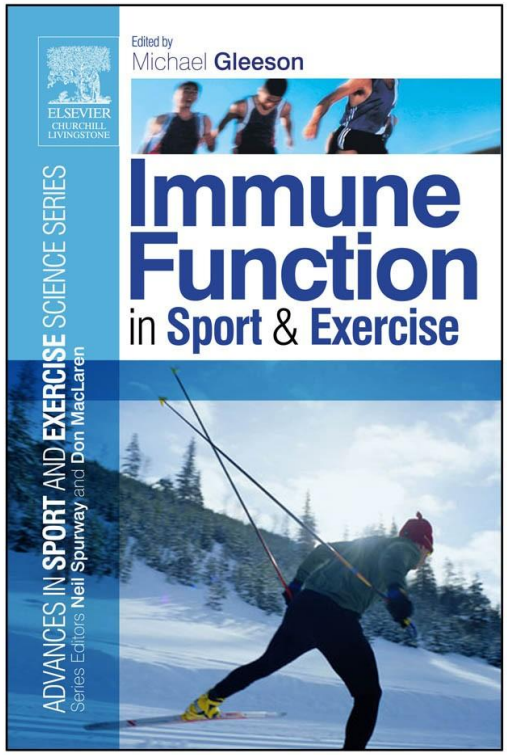
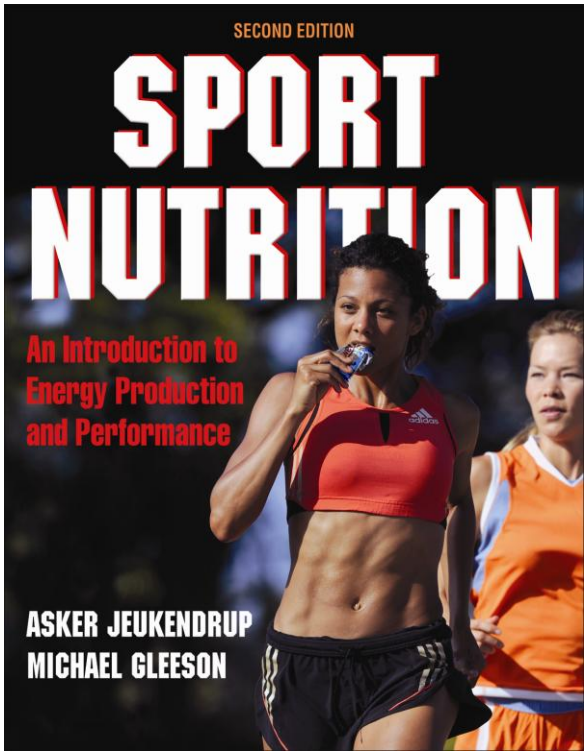


Elsevier, Nov 2005
ISBN 0-443-10118-3



Human Kinetics, Jan 2010
ISBN 978-0-7360-7962-4

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