

ANTIOXIDANTS AND RESPIRATORY INFECTIONS IN PHYSICALLY STRESSED PEOPLE

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**For a summary of recommendations by Gary Moller for vitamin C intake for
physically stressed people arising from consideration of these findings and
discussions go [here](#)**

Vitamin C

In 1996, I pooled the findings of three randomized placebo-controlled double-blind trials with participants under heavy acute physical stress: with **marathon runners**, Canadian troops in winter exercise, and school children in a skiing camp in the Swiss Alps. The incidence of the common cold was highly significantly lower in the vitamin C groups: pooled RR = 0.50 (95% CI 0.35-0.69) (Paper 1).

In 2004, we updated the meta-analysis by adding three newer trials, **all with marathon runners**. The estimated benefit did not change at all, but the confidence interval became narrower: RR = 0.50 (95% CI: 0.38-0.66; P = 0.000,001) (Papers 2 to 4).

Furthermore, vitamin C reduced the incidence of pneumonia in three controlled trials, one of which was carried out with military recruits under recruit training period (Papers 5 to 7).

In the general population, vitamin C has no effect on common cold incidence (Papers 2 and 3 and 8 to 10).

Regularly administered vitamin C has quite consistently shortened the duration (by 5 to 30%) and alleviated the symptoms of the common cold (Papers 2 and 3 and 9 to 16). The practical significance of this effect is not yet clear.

In the early 1970's Linus Pauling proposed that vitamin C might be beneficial against the common cold (Papers 17a and 17b). It is worth noting that Pauling based his conclusions primarily on Ritzel's (1961) trial with school children in a skiing camp in the Swiss Alps (Paper 17c). The Ritzel trial is one of the six trials with participants under heavy acute physical stress (Papers 1 to 4). Thus, it seems that Pauling was correct in his conclusion that the vitamin shortens the colds and reduces common cold incidence in some population groups, although he was overoptimistic as to the practical importance of these effects (Papers 17 and 18).

While placebo-controlled trials quite consistently shown that vitamin C alleviates common cold symptoms, it is quite strange that major medical textbooks have stated for decades that vitamin C has no effect on colds. I have shown that the most influential reviews on vitamin C and the common cold cited in the major textbooks

contain numerous erroneous statements, and present data inconsistent with the original study reports (Papers 14 to 16 and 18).

In a brief letter, I recently pointed out that small trials with surrogate endpoints may give uninformative results (paper 19), however, small studies with surrogate endpoints are very popular.

1

Hemilä H

Vitamin C and common cold incidence: a review of studies with subjects under heavy physical stress

Int J Sports Med 1996;17:379-83

<http://www.ltdk.helsinki.fi/users/hemila/H4.pdf>

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Douglas RM, Hemilä H, D'Souza R, Chalker EB, Treacy B

Vitamin C for preventing and treating the common cold

Cochrane Database for Systematic Reviews

<http://dx.doi.org/10.1002/14651858.CD000980.pub2>

entire text (version 2004;4):

[http://medicine.plosjournals.org/archive/1549-](http://medicine.plosjournals.org/archive/1549-1676/2/6/supinfo/10.1371_journal.pmed.0020168.sd001.pdf)

[1676/2/6/supinfo/10.1371_journal.pmed.0020168.sd001.pdf](http://medicine.plosjournals.org/archive/1549-1676/2/6/supinfo/10.1371_journal.pmed.0020168.sd001.pdf)

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Douglas RM, Hemilä H

Vitamin C for preventing and treating the common cold

PLoS Medicine 2005;2:e168

<http://dx.doi.org/10.1371/journal.pmed.0020168>

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Hemilä H

Do vitamins C and E affect respiratory infections? p. 48-50

Thesis, University of Helsinki, 2006

<http://ethesis.helsinki.fi/julkaisut/laa/kansa/vk/hemila/>

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Hemilä H

Vitamin C intake and susceptibility to pneumonia

Pediatr Infect Dis J 1997;16:836-7

<http://dx.doi.org/10.1097/00006454-199709000-00003>

<http://www.ltdk.helsinki.fi/users/hemila/H6.pdf>

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Hemilä H, Louhiala P.

Vitamin C for preventing and treating pneumonia

Cochrane Database for Systematic Reviews

<http://www.cochrane.org/reviews/en/ab005532.html>

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Hemilä H

Vitamin C supplementation and respiratory infections: a systematic review

Military Medicine 2004;169:920-5

<http://www.ingentaconnect.com/content/amsus/zmm/2004/00000169/00000011/art00026>

http://www.findarticles.com/p/articles/mi_qa3912/is_200411/ai_n9469932

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Hemilä H

Vitamin C intake and susceptibility to the common cold

Br J Nutr 1997;77:59-72

<http://www.ltdk.helsinki.fi/users/hemila/H7.pdf>

Discussion in: Br J Nutr

Bates CJ (1997) Schorah CJ (1997) 78:857-60

Hemilä H (1997) 78:861-6

<http://dx.doi.org/10.1079/BJN19970201>

<http://www.ltdk.helsinki.fi/users/hemila/H8.pdf>

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Hemilä H

Vitamin C, respiratory infections, and the immune system

Trends in Immunology 2003;24:579-80

<http://dx.doi.org/10.1016/j.it.2003.09.004>

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Hemilä H

Does vitamin C alleviate the symptoms of the common cold? a review of current evidence

Scand J Infect Dis 1994;26:1-6

<http://www.ltdk.helsinki.fi/users/hemila/H2.pdf>

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Hemilä H

Vitamin C supplementation and common cold symptoms: factors affecting the magnitude of the benefit

Medical Hypotheses 1999;52:171-8

<http://dx.doi.org/10.1054/mehy.1997.0639>

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Vitamin C and the common cold

Br J Nutr 1992;67:3-16

<http://dx.doi.org/10.1079/BJN19920004>

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Hemilä H, Douglas RM

Vitamin C and acute respiratory infections

Int J Tuberc Lung Dis 1999;3:756-61

<http://www.ingentaconnect.com/content/iuatld/ijtld/1999/00000003/00000009/art0004>

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Hemilä H, Herman ZS

Vitamin C and the common cold: a retrospective analysis of Chalmers' review

J Am Coll Nutr 1995;14:116-23

<http://www.ltdk.helsinki.fi/users/hemila/H3.pdf>

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Hemilä H

Vitamin C supplementation and common cold symptoms: problems with inaccurate reviews

Nutrition 1996;12:804-9

[http://dx.doi.org/10.1016/S0899-9007\(96\)00223-7](http://dx.doi.org/10.1016/S0899-9007(96)00223-7)

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Hemilä H

Vitamin C, the placebo effect, and the common cold: a case study of how preconceptions influence the analysis of results

J Clin Epidemiol 1996;49:1079-84

[http://dx.doi.org/10.1016/0895-4356\(96\)00189-8](http://dx.doi.org/10.1016/0895-4356(96)00189-8)

Discussion in: J Clin Epidemiol

Chalmers TC (1996) 49:1085 [http://dx.doi.org/10.1016/0895-4356\(96\)00190-4](http://dx.doi.org/10.1016/0895-4356(96)00190-4)

Hemilä H (1996) 49:1087 [http://dx.doi.org/10.1016/0895-4356\(96\)00191-6](http://dx.doi.org/10.1016/0895-4356(96)00191-6)

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Hemilä H

Vitamin C supplementation and the common cold - was Linus Pauling right or wrong?

Int J Vitam Nutr Res 1997;67:329-35

<http://www.ltdk.helsinki.fi/users/hemila/H5.pdf>

17a

Pauling L

The significance of the evidence about ascorbic acid and the common cold.

PNAS 1971

<http://www.pnas.org/cgi/reprint/68/11/2678>

<http://www.pubmedcentral.gov/articlerender.fcgi?artid=389499>

17b

Pauling L

Ascorbic acid and the common cold.

Am J Clin Nutr 1971

<http://www.ajcn.org/cgi/reprint/24/11/1294>

http://profiles.nlm.nih.gov/MM/B/B/G/V/_/mmbbgv.pdf

17c

Ritzel G

Critical Evaluation of the Prophylactic and Therapeutic Properties of Vitamin C with Respect to the Common Cold [in German, English translation below]

Helv Med Acta 1961

<http://www.ltdk.helsinki.fi/users/hemila/T3.pdf>

17d

Ritzel's (1961) trial was motivated by:

Bessel-Lorck C

Common Cold Prophylaxis in Young People in a Skiing Camp [in German, English translation below]
Medizinische 1959
<http://www.ltdk.helsinki.fi/users/hemila/T2.pdf>

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Hemilä H

Do vitamins C and E affect respiratory infections? p. 11-13 and 35-45

Thesis, University of Helsinki, 2006

<http://ethesis.helsinki.fi/julkaisut/laa/kansa/vk/hemila/>

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Hemilä H.

Small trials focusing on surrogate end points may be uninformative [letter].

[comments on: Davison and Gleeson (2006)]

Eur J Applied Physiology 2007: in press

<http://dx.doi.org/10.1007/s00421-006-0387-2>

Vitamin E

I found that in a subgroup of the middle-aged males of the large-scale ATBC Study, those who exercised at leisure, vitamin E reduced pneumonia risk by 50% (P=0.01) (papers 21 and 22), although it had no overall effect on pneumonia risk (Paper 23).

Vitamin E did not affect common cold risk in physically active people (Paper 24).

In a letter (Paper 25), I pointed out that a recent paper reviewing the effect of vitamin E on exercise-induced immunodepression based its conclusions on two small trials (size: 600-800 person-years) with sedentary older people, but ignored a forty times larger study analyzing the effect of vitamin E on physically active middle-aged people (size: 29,000 person-years Paper 24)

A recent review on vitamin E safety in a major nutrition journal ignored reports that found harm of vitamin E (Paper 26).

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Hemilä H, Kaprio J, Albanes D, Virtamo J

Physical activity and pneumonia in male smokers administered vitamin E and β -carotene

Int J Sports Medicine 2006;27:336-41

<http://www.thieme-connect.com/ejournals/abstract/sportsmed/doi/10.1055/s-2005-865670>

<http://dceg.cancer.gov/pdfs/hemila273362006.pdf>

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Hemilä H

Do vitamins C and E affect respiratory infections? p. 56-57, 66-67

Thesis, University of Helsinki, 2006

<http://ethesis.helsinki.fi/julkaisut/laa/kansa/vk/hemila/>

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Hemilä H, Virtamo J, Albanes D, Kaprio J

Vitamin E and beta-carotene supplementation and hospital-treated pneumonia in male smokers

Chest 2004;125:557-65

<http://dx.doi.org/10.1378/chest.125.2.557>

<http://dceg.cancer.gov/pdfs/hemila1255572004.pdf>

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Hemilä H, Virtamo J, Albanes D, Kaprio J

Physical activity and the common cold in men administered vitamin E and β -carotene

Med Sci Sports Exerc 2003;35:1815-20

<http://www.ms-se.com/pt/re/msse/abstract.00005768-200311000-00005.htm>

<http://www.lwwonline.com/pt/re/lwwonline/abstract.00005768-200311000-00005.htm>

<http://dceg.cancer.gov/pdfs/hemila3518152003.pdf>

25

Hemilä H

Letter to the editor [comments on: Gleeson (2006)]

Nutrition Rev 2006;64:476-7

<http://www.ingentaconnect.com/content/ils/nure/2006/00000064/00000010/art00006>

26

Hemilä H

Potential harm of vitamin E supplementation [letter]

Am J Clin Nutr 2005;82:1141-2 [comments on: Hathcock et al. (2005)]

<http://www.ajcn.org/cgi/content/full/82/5/1141-a>

ASSUMED BENEFITS AND HARMS OF EXERCISE ON THE IMMUNE SYSTEM

In 1994, David Nieman proposed that risk of infections follows a “J”-curve kind of relationship, so that, compared with the sedentary level, moderate level exercise would reduce the risk of infections, whereas high level exercise would increase the risk of infections (Paper J1). The 1994 paper has been cited over 100 times which reflects its impact.

The effect of antioxidants on respiratory infections in physically stressed people gives indirect support to the concept that too heavy exercise might be harmful

(Papers 1 to 7 and 21 and 22 above). Nevertheless, it is not obvious that cough and running nose after a marathon run are necessarily caused by a viral infection, as they can result from severe mechanical stress caused by several hours of exceptional ventilatory exertion.

Thus, the benefit of vitamin C (Papers 1 to 3) does not specifically indicate immune system involvement. On the other hand, the benefit of vitamin E (Papers 21 and 22) is more readily explained by the effects on the immune system.

Because the J-curve has been widely accepted and is frequently cited (see Papers J2 and J3 and J4 as examples of later discussions of the J-curve), I tested whether the large-scale ATBC Study with 29,133 male smokers might reveal a J-curve kind of relationship between the physical activity level and the incidence of respiratory infections.

Physical activity had no association with the incidence of common cold (Paper 24 above).

Physical activity had no association with the incidence of pneumonia either (Paper 21 above).

Because Nieman's paper (J1) was published in Med Sci Sports Exerc (MSSE), I submitted these two papers (21 and 24) to the same journal, as they explicitly tested the hypothesis proposed in MSSE.

Paper 24 was published in MSSE, whereas Paper 21 was rejected with reviewer comments that are not valid as shown in paper MSSE_2006 below.

Committee on Publication Ethics (COPE) was founded in 1997 to address breaches of research and publication ethics. It is a voluntary body providing a discussion forum and advice for scientific editors, it aims to find practical ways of dealing with the issues, and to develop good practice.

In their "Guidelines on Good Publication Practice" COPE suggests as a "Duty of editors"

(chapter 8), that:

"Studies that challenge previous work published in the journal should be given an especially sympathetic hearing."

<http://www.publicationethics.org.uk/guidelines> [>>> view guidelines as PDF]

Thus, the rejection of a manuscript (Paper 24) that challenged the J-curve speculation - which has been extensively promoted by MSSE in several papers - is inconsistent with the ethical recommendations of COPE, when the MSSE reviewers of the manuscript did not formulate any valid criticism. Neither has there been any post publication criticism against Paper 24.

Thus, it appears that the reviewers of MSSE may have been personally too closely involved with the J-curve speculation to make them unable to objectively evaluate the manuscript, and the editors of MSSE were unable to see the lack of any validity in the reviewers' comments. Thus, this is a good example of publication bias.

It would have been most ideal to publish the refutation of the J-curve model in the same journal, where the hypothesis was originally published – as COPE also considers (see above). Nevertheless, the Paper 24 is now freely available from the NCI server.

J1

Nieman DC

Exercise, upper respiratory tract infection, and the immune system

Med Sci Sports Exerc 1994;26:128-39

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8164529&query_hl=26

J2

Shephard RJ, Shek PN

Exercise, immunity, and susceptibility to infection: a J-shaped relationship?

Phys Sportsmed 1999;27(6):47-71

http://www.physsportsmed.com/issues/1999/06_99/shephard.htm

J3

http://www.presidentschallenge.org/misc/news_research/research_digests/June2001.pdf

J4

<http://www.abcc.co.uk/Articles/immune1.html>

MSSE_2006

Hemilä H

Some comments about the background of: Hemilä et al. (2006) Int J Sports Medicine 27: 336-341

http://www.ltdk.helsinki.fi/users/hemila/MSSE_2006.pdf