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Nutrition and immune function: Problems with a 1992 report and replications

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In 2001, R. K. Chandra, a professor at Memorial University of Newfoundland, reported that a daily nutritional supplement, which he has patented, greatly improved the cognitive performance of elderly persons.[1] The improvements seemed extraordinarily large and some of the standard errors were impossible.[2] This led us to examine a *Lancet* article based on the same study, which reported large improvements in immune function and a halving of days of infection.[3]

Here too we found problems. First, Table 3 of the article gives the average values of eight immunological measures for the supplement (S) and placebo (P) groups. For each measure, it gives two *p* values: (a) For S_{12} - S_0. S_{12} and S_0 are the values at 12 and 0 months, respectively. (b) For (S_{12} - S_0) - (P_{12} - P_0). If the two changes (from S_0 to S_{12} and from P_0 to P_{12}) are in the same direction, the second *p* value must be greater than the first. But in all six cases where they were in the same direction and *p* values were reported, the second *p* value was smaller than the first. Second, the standard deviations of the number of days of infection of the two groups are 5 and 7 according to the text, but histograms indicate values of about 17 for each. One of us wrote to Chandra about this, asking to re-analyze the results, but received no reply.

Other details raised more doubts. "Senior citizens identified from the St. John's City census were contacted," the article states. Would publicly available census data give ages and addresses of individuals? Likewise, it seems unlikely that "all individuals approached enrolled in the study" (which included blood sampling and a year of biweekly visits; nothing is said about payment) or that all 96 subjects "were middle class."

Two replication attempts have used the same supplement for the same duration.[4-5] Both were reported in the same 2002 issue of *Nutrition Research*, which Chandra edits. Both articles were received at the journal the same day and accepted that day or the next. The similarity of

findings is remarkable. The reduction in the mean number of days of infection due to the supplement was 52% in the *Lancet* study; in the two replications, it was 53% and 52%.

Both articles have statistical errors of the same kind. One of the articles, by Chandra, says that over a year, subjects in the supplement group (n = 22) had 11.1 ± 0.8 days ("Mean ± SD") of infection-related illness; subjects in the placebo group (n = 19) had 23.7 ± 2.3 days. The *p* value of this difference is given as "<0.02". Using a *t* test, and assuming that SD denotes standard deviation, the actual *p* value is less than 10^{-15}. The other two comparisons in the same table have the same problem. And even if SD denoted standard error of the mean, the *p* values would still be wrong.

The other article is by Amrit L. Jain. Over one year, it reports, subjects in the supplement group (n = 18) had 14 ± 2 days ("Mean ± SD") of respiratory infection; subjects in the placebo group (n = 18) had 29 ± 4 days. The *p* value is given as "< 0.03". Assuming that SD denotes standard deviation, the actual *p* value, from a *t* test, is less than 10^{-15}. If SD denoted standard error of the mean, the actual *p* value would be .001. One of us wrote to Jain about this but received no reply.

Other things increase our doubts about Jain's article. His institutional affiliation is given as "the Medical Clinic and Nursing Home, Jaipur, India". However, a Medline search (August 11, 2002) found no entries with this affiliation. Using web-accessible directories, we were able to locate a dozen medical clinics and nursing homes in Jaipur, but not this one. Jain's mailing address is a rented mailbox in Canada. Jain's article gives no email address or phone number for him, and the journal's editorial office could not supply either one, even after asking Chandra. (Of the 19 other articles in that issue of *Nutrition Research*, all provide one or the other.) We have been unable to find any other publications by Jain.

We conclude that both the original *Lancet* article and the two replications are untrustworthy.

References

1. Chandra RK. Effect of vitamin and trace-element supplementation on cognitive function in elderly subjects. Nutrition 2001;17:709-12.

2. Roberts S, Sternberg S. Do nutritional supplements improve cognitive function in the elderly? Nutrition, in press.

3. Chandra RK. Effect of vitamin and trace-element supplementation on immune responses and infection in elderly subjects. Lancet 1992:340:1124-7.

4. Chandra RK. Influence of multinutrient supplement on immune responses and infection-related illness in 50-65 year old individuals. Nutr Res 2002;22:5-11.

5. Jain AL. Influence of vitamins and trace-elements on the incidence of respiratory infection in the elderly. Nutr Res 2002;22:85-7.