AMELIORATION OF RHINOVIRUS COLDS BY VITAMIN C (ASCORBIC ACID) SUPPLEMENTATION
L. C. Jennings*, E. C. Dick, K. A. Mink and S. L. Inhorn.
Cantabrus Health Laboratories, Chestnut, New England, and University of Wisconsin, Madison, Wisconsin, U.S.A.

ABSTRACT
The efficacy of Vitamin C (Vit C) supplementation in preventing or ameliorating common colds in open populations has been controversial. Therefore Vit C efficacy was evaluated in a controlled human volunteer model wherein virus is transmitted naturally. In each of three double-blind trials, rhinovirus type 16 (RV16) susceptible males (recipients) were supplemented with Vit C (2.0 - 2.5 g daily; n = 8) and interacted with eight RV16 infected volunteers (donors) for one week. Interaction primarily included playing poker and sharing sleeping quarters. Recipients' colds were then thoroughly characterised. Vit C recipients (n=24) had markedly fewer symptoms (p=0.002 to 0.022) and signs (p=0.020) than placebo recipients (n = 24). These findings correlated with Vit C recipients' substantially higher serum Vit C levels (mean ± SD = 2.10 ± 0.27 [2.07] vs 0.47 ± 0.15mg/100ml). However, there was no significant difference in incidence of total infection between Vit C (19/24) and placebo (22/24) recipients nor in virus shedding and serologic response to RV16. Thus, Vit C supplementation significantly moderated cold severity but did not prevent infection.

INTRODUCTION
The effectiveness of Vit C supplementation in ameliorating or preventing common colds is a subject of controversy. Confusion is due to the difficulty in controlling a number of variables in previous trials. We have developed a human volunteer model whereby laboratory-induced colds caused by a single rhinovirus (RV) serotype can be naturally transmitted to others at a predictable rate over a one-week period. This system allows nearly complete control over a small study population. In a series of three trials, we used this model to evaluate the effect of Vit C supplementation upon naturally transmitted RV16 colds.

MATERIALS AND METHODS
In each of three, randomized double-blind trials, 16 adult male volunteers (recipients) free of neutralizing antibody to rhinovirus type 16 (RV16) were given, under direct supervision, tablets containing either Vit C 2.0 - 2.5 g daily; (n=8) or placebo (n=8). The recipients were dosed for 3.5 weeks and then housed for 7 days with eight men (donors) with laborator-induced RV16 colds. During this week, the donors and recipients engaged in a variety of supervised interactions as well as sleeping, eating and studying in the same room. Vit C and placebo tablets were continued over the interaction period and the following two weeks.

Cold in the recipients were detected by several methods. Hourly symptom diaries, in which a number of symptoms and signs were graded from 0 (absent) to 3 (severe) were kept by each recipient throughout the waking hours of the interaction period and the subsequent two weeks.

A daily total symptom score (TSS) as well as a cumulative (TSS) for the entire study was then computed. In addition, during the interaction period all volunteers were closely monitored 24 hours a day (except when at class) for clinical signs (coughs, sneezes and nose-blowes) and a combined sign score (CSS) computed (lowest 3, highest 48).

Infection was detected by virus culture and titration of daily nasal washings taken during the interaction and the two-week post-interaction periods, and by RV16 seroconversion.

Vitamin C levels in serum were monitored weekly throughout each experiment, including three times during the interaction period.

RESULTS
Vit C Supplementation
Recipients were given 2.0 - 2.5 g Vit C daily. Vit C mean 2.10 ± 0.27mg/100ml, n = 24, placebo mean 0.47 ± 0.15mg/100ml, n = 24 (p<0.001 over 3 trials).

Symptom Scores
Vit C recipients had significantly lower symptom scores than those of recipients (Figure 1a & b). 95.8% (23/24) Vit C recipients were subclinical to mild (score 0-6), while, 70.8% (17/24) placebo recipients were moderate to severe (Fig 1a).

Vit C recipients also had significantly lower cumulative Total Symptom Scores; reflecting diminished symptom severity over entire course of their illness (Fig 1b).

Sign Scores
Frequency of clinical signs was consistently lower in Vit C recipients (Table 1).

Virology
Virologic measurements of illness were not significantly affected by Vit C (Table 2).

Incidence of laboratory confirmed infections was lower in Vit C (79.2%; 19/24) vs placebo recipients (91.7%; 22/24) X² = 0.67, I.d.f.; p=0.420.

Quantity and duration of virus shedding, and number of days to first virus shedding similar (data not shown).

Treatment Blinding
Treatment blinding among study recipients was maintained (Table 3).

The number of subjects correctly guessing which treatment they received was not statistically significant.

During 24 day pre-interaction dosing (16/24 vs 10/24) X² = 0.771, I.d.f.; p=0.39.

Also true for back-up recipients (7/12 vs 5/9).

CONCLUSIONS
- Vit C supplementation significantly decreased the severity of symptoms and signs of naturally transmitted RV16 colds.
- Vit C supplementation did not prevent infection with RV16.
- A comprehensive questionnaire revealed that recipients perception of their treatment was based on guessing.
- Findings support role of Vit C in modifying the typical symptoms and signs of the common cold.

Table 1

<table>
<thead>
<tr>
<th>Recipients</th>
<th>Placebo</th>
<th>Total Symptoms</th>
<th>Placebo</th>
<th>Total Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vit C</td>
<td>24</td>
<td>105</td>
<td>Placebo</td>
<td>24</td>
</tr>
<tr>
<td>Placebo</td>
<td>24</td>
<td>120</td>
<td>Placebo</td>
<td>24</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Recipients</th>
<th>Placebo</th>
<th>Total Symptoms</th>
<th>Placebo</th>
<th>Total Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vit C</td>
<td>24</td>
<td>105</td>
<td>Placebo</td>
<td>24</td>
</tr>
<tr>
<td>Placebo</td>
<td>24</td>
<td>120</td>
<td>Placebo</td>
<td>24</td>
</tr>
</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Recipients</th>
<th>Placebo</th>
<th>Total Symptoms</th>
<th>Placebo</th>
<th>Total Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vit C</td>
<td>24</td>
<td>105</td>
<td>Placebo</td>
<td>24</td>
</tr>
<tr>
<td>Placebo</td>
<td>24</td>
<td>120</td>
<td>Placebo</td>
<td>24</td>
</tr>
</tbody>
</table>