Vitamin C and the common cold: a double-blind trial

T. W. Anderson, B.M., PH.D., D. B. W. Reid, M.SC., and G. H. Beaton, PH.D., *Toronto*

Summary: A large scale double-blind trial was conducted to test the claim that the intake of one gram of vitamin C per day substantially reduces the frequency and duration of "colds". It was found that in terms of the average number of colds and days of sickness per subject the vitamin group experienced less illness than the placebo group, but the differences were smaller than have been claimed and were statistically not significant. However, there was a statistically significant difference ($P < 0.05$) between the two groups in the number of subjects who remained free of illness throughout the study period. Furthermore the subjects receiving the vitamin experienced approximately 30% fewer total days of disability (confined to the house or off work) than those receiving the placebo, and this difference was statistically highly significant ($P < 0.001$). The reduction in disability appeared to be due to a lower incidence of constitutional symptoms such as chills and severe malaise, and was seen in all types of acute illness, including those which did not involve the upper respiratory tract.

Résumé: *La vitamine C et le rhume banal: étude à double inconnue*

Il s'agit d'essais à double inconnue, effectués sur une vaste échelle et dans le but d'évaluer le bien fondé de la prétention que l'ingestion quotidienne d'un gramme de vitamine C diminue considérablement la fréquence et la durée des rhumes. Il a été constaté qu'au point de vue du nombre de sujets atteints et à celui des jours de maladie par sujet, les malades recevant la vitamine C ont été moins souvent touchés que ceux recevant le placébo. Ces différences ont été cependant plus faibles qu'on ne l'avait prétendu et, au point de vue statistique, n'avaient guère de signification. Néanmoins, toujours sur le plan statistique, on notait une différence significative ($P < 0.05$) entre les deux groupes quant au nombre de sujets qui sont restés indemnes de maladie pendant toute la durée de l'étude. De plus, chez les sujets traités par la vitamine, on a noté une moins longue période d'invalidité de près de 30% (nombre total de jours de confinement à la maison ou d'absence au travail) que chez ceux qui avaient reçu le placébo. Cette différence était très significative au point de vue statistique ($P < 0.001$). Cette réduction de la période d'invalidité a semblé attribuable à une moindre fréquence des symptômes généraux, frissons et malaises sévères notamment. Cette différence a été notée dans tous les types de pathologies aiguës, y compris celles qui ne touchaient pas les voies respiratoires supérieures.

This investigation was prompted by an article by Beaton and Whalen that appeared in this journal in August 1971[1] in which the authors reviewed the much-publicized book *Vitamin C and the Common Cold* by Linus Pauling.[2] While they were critical of the limited evidence upon which Pauling based his claims, Beaton and Whalen felt that properly controlled trials of the proposed therapy were justified in view of the scientific eminence of Linus Pauling (a Nobel prize-winner in biochemistry) and the large amount of public interest in the matter.

In the subsequent issue of the Journal a letter from Linus Pauling was published in which he specified that "the regular ingestion of 1000 mg. (of vitamin C) leads to the decreased incidence of colds by about 45% . . . (and) . . . to a decrease in total illness by about 60%."[3] Pauling based these estimates on the results of a double-blind study involving 279 students at a ski-school in Switzerland,[4] and although the differences observed in this study were statistically significant, the period of observation was only one week for each individual. We therefore decided to set up a double-blind study in which this quantity (1000 mg./day) would be given to a large group of subjects for a period of three or four months.

Since most of us involved in the study design were sceptical of Pauling's claims, we aimed to enrol a large number of subjects (1000) in the hope of avoiding an indecisive negative result. Furthermore, subjects were instructed to increase their intake to 4000 mg./day at the onset of a cold, in order that a negative result would not be open to the criticism that we had not followed all of Pauling's recommendations (which include raising the dosage at the first sign of a cold).[2] We recognized that this extra dosage feature might complicate the interpretation of the results, since we were adding a therapeutic

T. W. ANDERSON, Associate Professor, Department of Epidemiology and Biometrics.
D. B. W. REID, Professor, Department of Epidemiology and Biometrics.
G. H. BEATON, Professor and Head, Department of Nutrition.
This work was supported by the Ontario Department of Health under Grant Number P.R.248.
Reprint requests to: Dr. T. W. Anderson, Dept. of Epidemiology and Biometrics, School of Hygiene, University of Toronto, 150 College Street, Toronto, Ont.

feature to an essentially prophylactic trial, but we believed that the most important thing was to establish whether or not there was any effect from large doses of vitamin C. In the event that we obtained a positive result a subsequent trial could be carried out in which the two features were studied separately. At the same time, to avoid any possibility of our negative bias affecting the results, subjects were allocated to vitamin and placebo in a strictly double-blind randomized manner and the code was not broken until after all the data had been transferred to punch cards and initial tabulations carried out.

Method and Material

Subjects: Volunteers were sought from a variety of occupations and age groups in order to obtain a reasonable cross-section of the general population. However, since we asked persons not to enrol unless they normally experienced at least one cold in the period January to March, the study group was not representative of the general population in terms of susceptibility to colds. Major sources of volunteers were the School of Hygiene (183), Ontario Hydro (120), Ryerson Polytechnical Institute (76) and the Toronto East General Hospital (72). Each volunteer was encouraged to recruit other family members and friends, and thanks to the enthusiastic cooperation of many individuals and the officials of several organizations, over 200 subjects were enrolled by December 5, 1971 and the full complement of 1000 by January 2, 1972. The study period ended on March 31, 1972, and the analysis which follows is based upon the 818 individuals who were in the study for at least two months, and for whom complete personal and sickness records were available for analysis. Almost all of the 182 subjects who dropped out of the study were subsequently contacted by telephone or letter, and it was established that most had dropped out because of loss of interest or because they found it impossible to remember to take their tablets regularly. The few who dropped out because of suspected side effects are discussed later.

Each potential volunteer received a description of the purpose and method of the study, including the fact that half of the subjects would be receiving an inert placebo preparation. In addition, each received a detailed set of instructions concerning the dosage schedule and the method of recording symptoms during an episode of illness. In the event that a subject needed to see a doctor, the doctor was to be asked to make a brief note of his physical findings and diagnosis on the patient's record-sheet. Physicians were informed of this through an announcement in the *Ontario Medical Review,* and were advised that the code could be broken for an individual patient if it was felt necessary to determine whether the patient was on the vitamin or placebo. (This contingency did not in fact arise, but if it had the patient would have been dropped from the study.)

Subjects who were in the habit of taking a daily multivitamin supplement during the winter months were asked to identify the product involved, and were accepted into the study only if the daily dose of vitamin C was 50 mg. or less.

Tablets: Each subject was given a bottle containing 500 tablets. Half of the bottles contained vitamin C in a strength of 250 mg./tablet; the rest of the bottles contained placebo tablets. Subjects were instructed to take a regular dose of four tablets each day in divided doses, increasing to 16 tablets (4 g.) each day for the first three days of any illness. Because of the increased consumption of tablets at times of illness, a number of the subjects who entered the trial in early December ran out of tablets before the end of March. This accounts in part for the variation in the total number of days that individuals spent in the study.

Particular care was taken to ensure that the vitamin and placebo tablets were indistinguishable in appearance and taste. Pure ascorbic acid has a very strong and characteristic flavour which is difficult to imitate, and we therefore used a formulation containing 200 mg. of sodium ascorbate, 75 mg. of ascorbic acid and an artificial orange flavouring. The taste of this formulation was well matched by a placebo preparation containing 30 mg. of citric acid and the same orange flavouring and fillers. The effectiveness of the matching was established by asking 30 individuals to taste both tablets, and using pure ascorbic acid as reference, to judge which tablet contained the vitamin. Sixteen persons selected the placebo tablet and 14 the vitamin tablet. The effectiveness of the matching was verified at the end of the main study by the answers to the question "Do you think you have been on the vitamin or placebo tablet?". Approximately half of the 818 subjects answered "Don't know", and the remainder were divided almost equally between those who guessed correctly and those who did not.

Each bottle of tablets was assigned a code number derived from a computer-generated list of consecutive numbers, randomized in pairs. After the bottles had been labelled the list of numbers was given for safe-keeping to a colleague who was not involved in the study. The bottles were subsequently given out in numerical order to the subjects as they registered, so that when a group of individuals registered at the same time (e.g. a class of students) approximately half received the vitamin and half the placebo. This helped to ensure that the vitamin and placebo groups were well matched for age, sex and other characteristics (Table I).

Record-sheets: A calendar type record-sheet was provided for each month. Subjects were instructed to record

Table I
The number of subjects possessing certain characteristics in each group

		Vitamin	Placebo
Total subjects		407	411
Age:	<25	218	213
	25+	189	198
Sex:	Male	180	177
	Female	227	234
Occupation:	Student	177	180
	Other	230	231
Smokers		117	132
Usually 2+ colds		211	192
Contact with young children		140	148
Frequently in crowds		309	323
4+ ounces of juice daily		284	277
Other vitamin supplement		61	57

each day whether they were sick or well, and the total number of tablets taken during that day. On the reverse side of the sheet appeared a list of sites (nose, throat, etc.) against which, on each day of illness, was to be recorded 0 (not affected), + (mildly affected) or ++ (severely affected). The same coding was to be used to record the presence of malaise or chills, and in addition subjects were asked to record whether they had stayed indoors, stayed off work, seen a doctor, taken any prescription or non-prescription drug (and its nature) and, if possible, their highest oral temperature on that day. In addition to the monthly record-sheet, each subject completed an initial questionnaire and a final evaluation sheet.

At the end of each month the record-sheets were returned and the information coded and transferred to punch cards. On those occasions when two episodes of sickness were separated by only a few symptom-free days, the following rules were applied: if the symptom-free interval was two days or less, only a single episode was recorded; if the interval was three to six days, the episodes were counted separately unless the symptom patterns were essentially the same on the two occasions; if the interval was seven days or more, the episodes were counted separately, however similar the symptoms.

Subjects who were already sick on the day they entered the study were not considered to have started until their first symptom-free day.

A number of statistical analyses were carried out on the data. Where tests of significance were performed these were standard two-tailed tests.

Results

When the table code was broken it was found that of the 818 subjects whose experience was available for analysis 411 had been on the placebo and 407 on the vitamin. The randomization appeared to have been successful in producing two reasonably well-matched groups. The average age of the vitamin group was 28.8 years (range 10 to 64), and that of the placebo group 28.9 years (range 10 to 65). The total number of days in the study was 41,904 for the vitamin subjects (mean 103.2) and 41,864 for the placebo subjects (mean 101.9). There were no statistically significant differences in the frequency of any of the other recorded characteristics of the two groups (Table I). The relative distribution of recorded characteristics in the 182 subjects who dropped out of the study was essentially the same as that seen in the main group.

The 818 subjects recorded a total of 1170 episodes of illness. In the vitamin group 105 subjects (26%) remained free of illness throughout the study, while the corresponding figure for the placebo group was 76 (18%). This difference was statistically significant at the 0.05 level of probability ($X^2 = 5.92$).

Table II

Overall sickness experience of the subjects in the vitamin and placebo groups

	Episodes of illness		Days			
			Symptoms present		Confined to house	
	V	P	V	P	V	P
Total number	561	609	2138	2474	531	769
Number per subject: Mean ± S. E.	1.38 ± 0.061	1.48 ± 0.056	5.25 ± 0.297	6.02 ± 0.284	1.30 ± 0.101	1.87 ± 0.138
t—value	1.21		1.87		3.33**	
V/P	93%		87%		70%	
†Mean number per episode: Mean ± S. E.	—		3.96 ± 0.162	4.18 ± 0.139	1.04 ± 0.074	1.32 ± 0.087
t—value	—		1.03		2.45*	
V/P	—		95%		79%	

V = vitamin group, P = placebo group
Approximate statistical probabilities: * < .05, ** < .001
†These figures are based on the average values for each subject. The corresponding mean values calculated directly from the over-all number of days and episodes were: (symptoms) 3.81 and 4.06, (house) .95 and 1.26.

Table III

The mean number of episodes of illness, days on which symptoms were present, and days confined to the house per subject in each group, classified according to site of predominant symptoms on day of onset

Site of predominant symptoms	Episodes per subject			Days per subject					
				Symptoms present			Confined to house		
	V	P	V/P (%)	V	P	V/P (%)	V	P	V/P (%)
Nose	0.79	0.84	**94**	2.92	3.07	**95**	0.64	0.78	**82**
Throat	0.36	0.43	**84**	1.67	2.02	**83**	0.47	0.73	**64**
†Other: a) Respiratory	0.10	0.10	**100**	0.39	0.45	**87**	0.13	0.21	**62**
b) Non-respiratory	0.12	0.11	**109**	0.32	0.31	**103**	0.10	0.15	**67**

†Episodes beginning mainly at sites other than nose or throat have been divided into those in which symptoms affecting either the nose, throat or chest appeared at some stage of the episode ("respiratory") and those in which there were no respiratory symptoms at any stage ("non-respiratory").

The overall sickness experience of the two groups is summarized in Table II in terms of frequency of episodes, duration of symptoms and duration of "disability" (as measured by days confined to the house). Although the mean number of episodes per subject was 7% lower in the vitamin group, this difference was not statistically significant. (In Table II the t-value is the ratio of the difference between means to its standard error; because of the very asymmetrical form of the distributions involved, the probability values are only approximate). Statistical evaluation of the average duration of the episodes was complicated by the fact that some individuals experienced more than one episode of illness and these episodes often varied considerably in length. The mean number of days per episode in each group has therefore been calculated from the average number of days per episode for each person. On this basis the mean duration (days of symptoms per episode) for the vitamin group was 5% lower than that for the placebo group, and the mean length of disability (days confined to the house) per episode was 21% lower for the vitamin compared to the placebo group. The latter difference was statistically significant ($P < 0.05$). (It should be noted that the percentage reductions in days per episode are underestimates, since an episode could not be less than one day in length.)

Owing to the combination of fewer episodes and fewer days per episode, the difference between the groups was marked in terms of days per subject, particularly days confined to the house, in which the mean figure for the vitamin group was 30% lower than that for the placebo group, a difference which was statistically significant ($P < 0.001$). There were 232 subjects in the vitamin group who did not report any days confined to the house, compared to 195 in the placebo group ($P < 0.01$.)

Other measures of severity or disability showed a similar pattern. The mean number of days off work was 0.88 per subject in the vitamin group, compared to 1.31 in the placebo group (V/P = 67%, $P < 0.01$). (The number of days off work was lower than the number of days confined to the house because some of the latter occurred on weekends and holidays.) The number of subjects who did not report any days off work was 275 in the vitamin group and 243 in the placebo group ($P < 0.05$). Similarly, while 40 of the vitamin subjects saw a doctor on a total of 60 occasions, 56 of the placebo subjects saw a doctor on a total of 97 occasions. The intake of antibiotics and other prescription drugs showed a similar distribution.

In Table III episodes of illness have been classified according to the site of the predominant symptoms on the first day of the episode. It is interesting, in view of the hypothesis being tested, that those episodes beginning with predominantly nasal symptoms showed the least difference between the two groups in the days of sickness and disability per subject. Indeed, the most striking feature of the figures shown in Table III is the similarity of the vitamin/placebo differences regardless of the type of onset. The only exception is in the episode-per-subject rate in those episodes with predominantly throat onset, in which there was a lower—but statistically not significantly different—rate in the vitamin group. Of particular interest, in spite of the small numbers involved, was the similarity of the pattern in the "Other: non-respiratory" group, made up of those episodes which at no time involved the nose, throat or chest. (About half of these appeared to be typical attacks of gastroenteritis, while others were characterized by malaise or chills without any localizing symptoms.)

A large number of cross-tabulations were prepared to see if the difference in the disability experience between the vitamin and placebo groups could be explained on the basis of mismatching of the two groups, or different disease patterns at different times during the trial. This line of enquiry was essentially negative, since although there were differences in the size of the "vitamin effect", the vitamin subjects always showed less disability, whatever their other characteristics. These cross-tabulations are summarized in Tables IV and V. For brevity, only the figures for days confined to the house per subject are given, since these show some of the largest differences between the groups, and are based on reasonably large numbers. They are also likely to be of more medical and economic importance than the actual number of episodes or the number of days on which symptoms were present.

In Table IV it can be seen that there was a greater reduction in disability experience for the subjects who reported that they usually had two or more colds, who were in contact with young children, or who were frequently in crowds. Since each of these characteristics might be associated with an increased vulnerability to infection, the subjects were reclassified according to the number of episodes they experienced, to see if the higher average duration of disability in the placebo group was due to the experience of a few particularly vulnerable individuals. This was found not to be the case, although there was evidence of a trend in the size of the reduction of average disability per episode, from 17% in persons with one episode to 27% in those with three or more (Table VI).

Table IV

The mean number of days confined to the house per subject in each group, subdivided according to certain other characteristics of the subjects

		Days confined to house per subject		
		V	P	V/P (%)
Age:	<25	1.40	2.00	70
	25+	1.20	1.74	69
Sex:	Male	1.15	1.79	64
	Female	1.43	1.94	74
Occupation:	Student	1.46	1.78	82
	Other	1.18	1.94	61
Usual colds:	<2	1.30	1.50	87
	2+	1.31	2.29	57
Contact with young children?	Yes	1.31	2.43	54
	No	1.30	1.56	83
Frequently in crowds?	Yes	1.27	1.92	66
	No	1.41	1.69	83
Daily juice (ounces)	0–3	0.98	1.87	52
	4+	1.45	1.87	78
Vitamin supplements?	Yes	1.36	2.39	57
	No	1.29	1.79	72
Smoker?	Yes	1.27	1.82	70
	No	1.32	1.90	69

Two other characteristics that showed substantial differences in the size of the "vitamin effect" were the daily intake of fruit or vegetable juice and the use of vitamin supplements (Table IV). The possible significance of these differences will be considered in the Discussion.

The data were also analyzed to see if there was any particular type of symptom that appeared less frequently in the vitamin group. A summary of the findings is given in Table VII, and it will be noted that the difference between the two groups was most marked in the generalized, constitutional symptoms—severe malaise, chills (mild or severe) and fever (oral temperature 100° F. or higher). The local symptoms (referable to nose, throat and chest) showed less striking differences. With the exception of severe malaise and fever, the reduction was mainly in the number of days per episode, rather than in the number of episodes per subject. In the case of fever the reduction was almost entirely in the frequency of episodes (with the majority of episodes containing only one day of fever), while in the case of severe malaise there was an almost equal reduction in both the mean number of episodes per subject and in the mean number of days per episode.

The apparent similarity between the effectiveness of the vitamin on the limitation of constitutional symptoms and on the reduction of days confined to the house is explained by the fact that it was the constitutional rather than the local symptoms which were most frequently associated with disability.

Other findings: It has been claimed that in addition to a specific effect on "colds", the intake of large doses of vitamin C produces an increased sense of well-being.[2] When questioned at the end of the study only 77 (19%) of the vitamin group said that they had felt an increased sense of well-being during the study, and 78 (19%) of the placebo group answered in the same way. This claim therefore seems to have little justification.

Of the 182 subjects who dropped out of the study 28 did so because of suspected side effects, distributed almost equally between the vitamin (15) and placebo groups (13). Gastrointestinal symptoms such as nausea, abdominal cramps or diarrhea were the symptoms in nine (vitamin: five, placebo: four), skin rash in five (vitamin: two, placebo: three) and genito-urinary in three (vitamin: none, placebo: three). The occurrence of less severe side effects was not monitored in any detail, but at the end of the study, in answer to the question "Did you have any unusual symptoms while you were taking the tablets?", the proportion answering yes was almost identical in the two groups (vitamin 12%, placebo 11%).

Table V

The mean number of days confined to the house per subject in each group during each month of the study, according to the subjects' starting date and total days in the study

	Number of subjects		Days confined to house per subject		
	V	P	V	P	V/P (%)
Month: December	212	213	0.29	0.61	**48**
January	403	404	0.52	0.66	**79**
February	407	408	0.42	0.59	**71**
March	391	385	0.23	0.34	**68**
Starting Date: December 5	160	160	1.34	1.91	**70**
January 2	133	123	1.43	1.78	**80**
Other	128	114	1.11	1.91	**58**
Total Days: 118 (Dec. 5—March 31)	122	111	0.95	1.72	**55**
90 (Jan. 2—March 31)	133	120	1.43	1.80	**79**
Other	152	180	1.48	2.01	**74**

Table VI

The mean number of days confined to the house (per episode) for subjects in each group, according to the total number of episodes of illness experienced during the study

Number of episodes	Number of subjects		Mean days confined to house (per episode)		
	V	P	V	P	V/P (%)
0	105	76	—	—	—
1	138	155	1.18	1.43	**83**
2	104	114	1.00	1.31	**76**
3+	60	66	0.81	1.11	**73**

Table VII

The mean number of days per subject in each group on which certain symptoms were recorded, (++ = severe, + = mild)

	Days symptom recorded		
	V	P	V/P (%)
Nose ++	1.59	1.67	**95**
+	2.28	2.53	**90**
Throat ++	0.88	1.03	**85**
+	1.97	2.18	**90**
Chest ++	0.40	0.45	**89**
+	1.08	1.20	**90**
Malaise ++	0.65	0.95	**68**
+	1.96	2.13	**92**
Chills ++	0.17	0.22	**77**
+	0.78	0.99	**79**
Temperature >100°F.	0.09	0.20	**45**

Table VIII

The mean number of episodes and days sick per subject in each group, for episodes during which there were symptoms affecting the nose or throat.

Symptoms	Episodes per subject			Days of symptoms		
	V	P	V/P (%)	V	P	V/P (%)
Predominant on day of onset: Nose	0.79	0.84	**94**	2.92	3.07	**95**
Nose or throat	1.16	1.27	**91**	4.49	5.20	**86**
Present at any time: Nose	1.08	1.19	**91**	4.40	5.05	**87**
Nose or throat	1.14	1.24	**92**	4.61	5.36	**86**

Discussion

The primary objective of this investigation was to test the claim that persons taking 1 g. of vitamin C per day would experience a substantial reduction in both the frequency and the total duration of "colds".[3]

We found it difficult to arrive at a single, generally acceptable definition of a "cold", other than that the episode of illness should at some time be marked by symptoms in either nose or throat. The average frequency and total duration of "colds" per subject were therefore calculated according to four different definitions of a "cold" (Table VIII). The difference between the vitamin and the placebo groups was essentially the same according to each of these definitions, the largest differences being a 9% reduction in frequency and a 14% reduction in days sick (using the definition of nose or throat symptoms predominating on day of onset). Neither these differences nor any of the others shown in Table VIII achieved statistical significance, but there was a statistically significant difference in the number of subjects who did not experience any nose or throat symptoms at any time (V: 131, P: 101, $P < 0.05$).

Our estimates are therefore considerably lower than the 45% reduction in frequency of "colds" and the 60% reduction in total days of illness that were observed in Ritzel's study of ski students,[4] on which Pauling based his claims.[3] However, both Ritzel's study and the present one involved limited numbers of subjects and therefore provide estimates that are subject to error. While it is difficult to determine exact limits for the percentage reductions observed by Ritzel, the approximate 95% confidence interval for the 45% reduction in frequency is 34% to 91%. The estimates from the two studies are therefore not necessarily in conflict.

Our finding that disability was substantially less in the vitamin group was entirely unexpected, and may have important theoretical and practical implications. Further studies will, of course, be required to confirm this finding and to establish its magnitude more precisely, but the high level of statistical significance associated with it encourages us to believe that it is likely to be a real effect rather than a statistical artefact. (The theoretical possibility that the placebo tablets were causing a prolongation of disability was considered but rejected. Citric acid is not known to be harmful at these dosages, and even at the maximum intake of 16 tablets per day, the amount of citric acid ingested was barely one tenth the quantity contained in an average-sized grapefruit.) We have therefore examined our data to see if they provide any clues as to the way in which these large doses of ascorbic acid might be exerting their effect.

One of the possibilities considered was that the reduction in days of disability in the vitamin group was due to some of our subjects being on diets that were, by conventional standards, deficient in vitamin C. (If this were the case the massive doses would be merely ensuring that the basic requirement of approximately 30 mg. a day was being received, and a much lower dose would have achieved the same effect.) While this possibility could not be ruled out, since we made no attempt to measure dietary intake or body stores of vitamin C, it would seem to be an unlikely explanation, since not only are foods containing vitamin C readily available in Canada, but over two-thirds of our subjects reported an intake of at least four ounces of fruit or vegetable juice each day.

Another question that was examined was whether the reduction in disability in the vitamin group was due to a lower incidence of complications. The data provided little support for this belief, since in both groups approximately 60% of the spells of disability began on the first day of the episode—too early to be ascribed to secondary complications. Furthermore, the number of episodes beginning with nose or throat symptoms in which chest symptoms first appeared on the second day or later was approximately the same in both groups (67 in the vitamin group, compared to 69 in the placebo group).

A third question that is of considerable theoretical interest is whether the large intake of ascorbic acid was exerting a specific anti-viral (or anti-bacterial) effect, or whether the mechanism involved was a non-specific one responding to any type of acute illness, or indeed to any acute stress. Our data cannot provide a clear answer to this question, but the fact that general rather than local symptoms were the most strongly influenced, and that different types of illness appeared to be more or less equally affected, would seem to favour a relatively non-specific mechanism. The high concentration of ascorbic acid normally found in the adrenal cortex (and its depletion at times of stress) may be relevant to this question.

Whatever the final answers may be to these and other questions, it would seem that further research in this area is well justified. In economic terms alone the rewards might be substantial, since the disability from acute (mainly respiratory) illness in Canada amounts to approximately 1.5 days per person each year.[5] In terms of total personal income (approximately 66 billion dollars in 1970[6]) this is equivalent to a loss of approximately 270 million dollars annually; even a small reduction in total disability would represent a very large saving to the national economy. However, before these potential economic benefits can be realized, further studies are required to establish the most appropriate dosage levels, the relative importance of the prophylactic and therapeutic features, and the safety of prolonged ingestion of large doses of ascorbic acid or its salts. Until more information is available on these questions we do not feel that any firm recommendations can be made concerning the place of large doses of ascorbic acid in the prevention and treatment of "colds" or other acute infections.

Many individuals assisted in the planning and execution of this investigation, and while it is impossible to name them all, we would particularly like to thank E. Van Sickle, R.N., for her valuable contribution, and S. Whalen, H. Moghadam, K. L. Weldon, A. Csima, J. Hatcher and M. Fears for their help in the design of the trial and the analysis of the results. We would also like to thank A. Harris and C. Retchford of Empire Laboratories for their assistance in preparing a convincing placebo tablet at very short notice, and, last but not least, we thank the large number of subjects who participated in the study.

References

1. BEATON GH, WHALEN S: Vitamin C and the common cold. *Can Med Assoc J* 105: 355, 1971
2. PAULING L: *Vitamin C and the Common Cold.* San Francisco, WH Freeman, 1970
3. Idem: Letter to the Editor. *Can Med Assoc J* 105: 448, 1971
4. RITZEL G: Ascorbic acid and infections of the respiratory tract. *Helv Med Acta* 28: 63, 1961
5. *Canadian Sickness Survey 1950-1951.* Ottawa, The Queen's Printer, 1960
6. Statistics Canada: *Preliminary Report on the Geographical Distribution of Personal Income,* 1970