Early Evidence About Vitamin C And the Common Cold

Linus Pauling[1]

For many years there has existed the popular belief that ascorbic acid has value in providing protection against the common cold and in ameliorating the manifestations of this viral disease. This belief has not, however, been generally shared by physicians, authorities on nutrition, and official bodies.

I was puzzled by the contradiction between the popular belief and the official opinion, and I' made a study of published reports of controlled trials of ascorbic acid in relation to the common cold. On the basis of this study and of some general arguments about Orthomolecular medicine (the preservation of good health and the treatment of disease by varying the concentrations in the human body of substances that are normally present in the body and are required for health, Pauling, 1968), I reached the conclusion that ascorbic acid, taken in the proper amounts, decreases the incidence of colds and related infections, and also decreases the severity of individual colds. These arguments were presented in my book **Vitamin C and the Common Cold,** which was published in November, 1970.

In this book I presented a discussion of the studies that had been made, including several carefully controlled double-blind studies carried out by competent medical investigators. The evidence and arguments presented in this book apparently were not convincing to some physicians, experts in nutrition, and health officials. Since 1970 several reports of new investigations have been published. An account of them will be published later (Pauling, 1975). All of the studies of subjects given ascorbic acid (or a placebo) over a period of time and exposed to cold viruses in the usual way, by contact with other people, have given the result that the ascorbic-acid subjects had less illness than the placebo subjects. There is no doubt that ascorbic acid provides some protection against the common cold, as well as against other diseases.

In the course of the years I have learned about some early studies other than those discussed in my 1970 book. These studies are not so reliable as the later ones, but they provide some significant evidence, and their existence raises again the question of why the nutritional and medical authorities have continued for 30 years to contend that vitamin C has no value in combatting the common cold.

An account of some of the early papers is given in the following sections.

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Korbsch, 1938

In 1938 Dr. Roger Korbsch of St. Elisabeth Hospital, Oberhausen, Germany, published an account of his observations. He mentioned that the fact that ascorbic acid had been reported to be effective against several diseases, including gastritis and stomach ulcers, suggested that he try it in treating acute rhinitis and colds. In 1936 he found that oral doses of up to 1 g per day were of value against rhinorrhea, acute rhinitis, and secondary rhinitis and accompanying manifestations of illness, such as headache. He then found that the injection of 250 or 500 mg of ascorbic acid on the first day of a common cold almost always led to the immediate disappearance of all the signs and symptoms of the cold, with a similar injection sometimes needed on the second day. He stated that ascorbic acid is far superior to other cold medicines, such as Pyramidon (aminopyrine) and injected calcium ion, and is, moreover, without danger, in that there is no evidence that hypervitaminosis C occurs, even with large doses.

Ertel,1941

In the spring of 1941 a trial was made of vitamin C in Germany in which 357 million daily doses of vitamin C were distributed among 3.7 million pregnant women, nursing mothers, suckling infants, and school children. Ertel reported that the recipients of the vitamin C enjoyed better health, in several different respects, than the corresponding control populations. The only quantitative information given by him is that with one group of school children for which good statistical data were collected the amount of illness with respiratory infections was 20 percent less than the year before.

Glazebrook and Thomson, 1942

Glazebrook and Thomson, of the Department of Clinical Medicine and Bacteriology, University of Edinburgh, reported a study carried out with about 1,500 boys, 15 to 20 years old, in a large training school in Scotland (1942). The subjects received a normal diet rather low in ascorbic acid, the daily ration being estimated to contain only 10 to 15 mg. The principal study, carried out over a period of six months, involved 1,100 control subjects and 335 ascorbic-acid subjects. The control subjects, in seven dining groups, received the ordinary diet. The ascorbic-acid subjects, in two dining groups, received the ordinary diet, but with ascorbic acid administered in the milk and cocoa that was served. The average amount of ascorbic acid administered is somewhat uncertain. The authors state that vitamin C was added to the supplies of cocoa or milk serving the tables for the appropriate divisions. In their discussion of preliminary experiments carried out to determine the daily urinary excretion of ascorbic acid, it is stated that initially 200 mg per day was given to each boy, 100 mg being placed in the morning cocoa and 100 mg in an evening glass of milk, the mixing being done in bulk in the kitchens. Analysis of the cocoa and milk showed an average of 63 mg per cup of cocoa and 98 mg per glass of milk, suggesting that about 160 mg per day was the average intake.

Because a number of preliminary studies had been carried out, and the ascorbic acid was added in the kitchens, it is likely that this investigation can be considered to have been a blind study. The authors mention that careful records had been kept of the incidence of all infections for 18 months before the observations described in their paper were begun and that in the preceding year there had been an epidemic of tonsillitis that had affected all the divisions uniformly, so that they could not be regarded as separate units within the larger population. All of the divisions had a population more or less the same as regards the duration of stay in the establishment. Records were kept of the common cold (coryza), tonsillitis (hemolytic streptococcal disease of the nose and throat, covering tonsillitis, sore throat, otitis media, pharyngitis, and cervical adenitis),

and other infective conditions (conjunctivitis, boils, impetigo, etc., as well as pneumonia and acute rheumatism).

The total numbers of cases of colds during the six-month period of the study are given in Table 1 for the control group and the ascorbic-acid group. There is a decrease in incidence in all colds by 17 percent, with P(one-tailed) $<$0.05, and in colds serious enough to require hospitalization (sick quarters) by 23 percent, with P (one-tailed)$<$0.02.

For other infectious diseases a decreased incidence for the ascorbic-acid group was also reported (except for tonsillitis with inclusion of the mild cases). The reported decreases of 100 percent for pneumonia and acute rheumatism are significant at the level P(one-tailed)$<$0.02.

I have chosen to give P(one-tailed) rather than P(two-tailed) because no one contends that the placebo (usually citric acid) has a greater effect than ascorbic acid in preventing or ameliorating the common cold and other diseases; the difference of opinion is between those people who state that ascorbic acid is no better than a placebo and those who say that it is better.

Giazebrook and Thomson in their paper point out that the difference in incidence of pneumonia and acute rheumatism in the control group and the ascorbic-acid group is statistically significant, and also that the period of hospitalization for tonsillitis is statistically significant. They give the average stay in the hospital for control subjects (83) hospitalized with tonsillitis as 16.7 days, standard deviation 11.86, and for the vitamin-C subjects (18) as 10.05, standard deviation 6.%, and state that analysis shows that a difference as great as or greater than that obtained would be expected only once in 50 times in a homogeneous population.

Giazebrook and Thomson give information in their paper that permits the severity of individual colds or other infectious diseases and the integrated morbidity, as measured by the number of days hospitalized, to be calculated. These values are given in Tables 2 and 3. The values of P(one-tailed) in the tables have been calculated by assuming a Poisson distribution in the days of hospitalization per period of illness.

The results described in Tables 1, 2, and 3 thus indicate that ascorbic acid has the effect of decreasing the incidence and severity of tonsillitis, pneumonia, and acute rheumatism, as well as the common cold, for the principal population studies by Giazebrook and Thomson.

A smaller study was also reported by Giazebrook and Thomson, with 150 recruits who entered the institution and

Table 1

THE PRINCIPAL STUDY BY GLAZEBROOK AND THOMSON INCIDENCE OF ILLNESSES

	Control group		Ascorbic-acid group			
	Number	Incidence	Number	Incidence	P(one-tailed)	Decrease
Number in group	1100		335			
Colds	286	0.260	72	0.215	< 0.05	17%
Colds, sick quarters	253	.230	59	.176	< 0.02	23%
Tonsillitis	94	.086	29	.087	~ 0.5	-1%
Tonsillitis, sick quarters	83	.075	18	.053	< 0.08	28%
Pneumonia	17	.016	0	.000	< 0.02	100%
Acute rheumatism	16	.015	0	.000	<0.02	100%

Table 2
THE PRINCIPAL STUDY BY GLAZEBROOK AND THOMSON
SEVERITY OF ILLNESS, MEASURED BY AVERAGE NUMBER OF
DAYS HOSPITALIZED PER HOSPITALIZED CASE

	Control group	Ascorbic-acid group	Decrease
Common Cold	1.47	1.11	24 %
Tonsillitis	1.26	0.54	57 %
All infective conditions*	5.0	2.5	50%

***Common cold, tonsillitis, pneumonia, acute rheumatism, conjunctivitis, boils, impetigo, etc.**

Table 3

THE PRINCIPAL STUDY BY GLAZEBROOK AND THOMSON
INTEGRATED MORBIDITY, MEASURED BY AVERAGE NUMBER
OF DAYS HOSPITALIZED PER SUBJECT*

	Control group	Ascorbic-acid group	**Decrease**
Common cold	0.334	0.195	**41 %**
Tonsillitis	.095	.029	**69%**

***Values for all infective conditions not available because total number of hospitalized cases not reported.**

were studied during the second half of the six-month period. The results of this trial, as reported by the authors, are given in Table 4. A decrease in the incidence of colds by 12 percent was noted, with, however, little statistical significance. The incidence of tonsillitis was 79 percent less for the ascorbic-acid group than for the control group, statistically significant at P (one-tailed)<0.05.

An interesting aspect of the report by Glazebrook and Thomson is that they refer to the numbers in Table 1 for the incidence of colds and tonsillitis in the following words: "It is obvious, therefore, that vitamin C had no effect on the incidence either of the common cold or tonsillitis." It is hard to explain why this statement is made, when in fact the observed incidence of the common cold was 17 percent less for the ascorbic-acid subjects than for the controls, and the number of subjects was so large that the decrease is significant at the 98-percent level of confidence (P[one-tailed] <0.02). The authors reported the statistical significance correctly for several of their comparisons, but apparently failed to make the calculation in this case. Some results with statistical significance were obtained also in the smaller study (Table 4). Nevertheless, in their summary the authors state that "The incidence of common cold and tonsillitis were the same in the two groups." They also say that "The average duration of illness due to the common cold was the same in the two groups," although the values that they reported in their paper (Table 2) correspond to a decrease by 24 percent for the ascorbic-acid subjects relative to the controls.

Table 4

THE SMALLER STUDY BY GLAZEBROOK AND THOMSON INCIDENCE OF COLDS AND TONSILLITIS

	Control group		Ascorbic-acid group			
	Number	**Incidence**	Number	Incidence	**P(one-tailed)**	**Decrease**
Number in group	90		60			
Colds	29	0.322	17	0.283	<0.30	12%
Tonsillitis	7	.078	1	.017	<0.05	79%
Colds plus tonsillitis	36	.400	18	.300	<0.10	25%

A similar failure of the investigators to describe their own results completely and correctly is found in the report by Cowan, Diehl, and Baker, discussed next. These misrepresentations by the investigators may well have delayed the general acceptance of vitamin C as a protective agent against the common cold and other diseases by the medical profession.

Cowan, Diehl, and Baker, 1942

The best of the early studies of ascorbic acid and the common cold was reported by Cowan, Diehl, and Baker in 1942. Dr. Diehl (now deceased) was at that time Dean of Medical Sciences in the University of Minnesota. Dr. Cowan is now Chief of the Student Health Service in the University, and Dr. Baker is Professor of Neurology there. The principal work on ascorbic acid was done during the winter "cold season" of 1939 - 1940. The subjects were all students in the University of Minnesota who volunteered to participate in this study because they were particularly susceptible to colds. Persons whose difficulties seemed to be due primarily to chronic sinusitis or allergic rhinitis, as shown by examination of the nose and throat and consideration of symptoms of allergy, were excluded from the study. The subjects were assigned alternately and without selection to an experimental group and a control group. The subjects in the control group were treated exactly like those in the experimental group, except that they received a placebo instead of the ascorbic acid. The subjects were instructed to report to the Health Service whenever a cold developed, so that special report cards could be filled in by a physician. Dr. Cowan has informed me that the study was a double-blind one, with neither the subjects nor the physicians-knowing which group a subject was in. Each subject was interviewed every three months in order to check the completeness of the reports.

The study was continued for 28 weeks. Of the 233 students initially in the ascorbic-acid group, 183 received 200 mg per day throughout the period of 28 weeks, and 50 received 200 mg per day for two weeks, followed by 100 mg per day except on inception of a cold, when an additional 400 mg per day for two days was administered. This group numbered 208 subjects at the completion of the study, 25 having dropped out. If the composition of the group remained unchanged, the average intake of ascorbic acid was 180 mg per day. The students in the control group initially numbered 194, of whom 155 completed the study (Table 5).

The authors report the observed incidence of colds by giving the average and the probable error. The corresponding values of the standard deviation, as calculated from the probable error, are given below in parentheses. The average number of colds per person during the period of study was 2.2 ± 0.08 (S.D. 0.113) for the control group and 1.9 ± 0.07 (S. D. 0.099) for the ascorbic-acid group. The difference between the average number of colds in the control group and in the experimental group is given by the authors as one-third of a cold and also as 0.3 ± 0.11 (S. D. 0.156).

The authors state in their, paper that "The actual difference between the two groups during the year of the study

Table 5 THE STUDY BY COWAN, DIEHL, AND BAKER

Number in group	Placebo group 155	Ascorbic-acid group 208	**P(one-tailed)**	**Decrease**
Incidence of colds	2.2	1.9	<0.02	14%
Severity (days of illness per cold)	0.73	0.58	<0.01	21 %
Integrated morbidity (days of illness per person)	1.6	1.1	<0.01	31 %

amounts to one-third of a cold per person. Statistical analysis of the data reveals that a difference as large as this would arise only three or four times in a hundred through chance alone. One may therefore consider this as probably a significant difference, and vitamin C supplements to the diet may therefore be judged to give a slight advantage in reducing the number of colds experienced."

Because the authors rounded off the numbers giving the actual numbers of colds per person, the difference is not known exactly. Dr. Cowan has informed me that the original records and the original calculations are no longer available. There is evidence, however, that the actual difference between the average number of colds in the two groups is 0.32, with uncertainty 0.01 . If the difference had been less than 0.29 the authors would have said "one-quarter of a cold per person," rather than "one-third of a cold per person." Moreover, the value of P (two-tailed) calculated for a difference of 0.31 with standard deviation 0.156 is 0.042, and that calculated for difference 0.33 is 0.031. The statement by the authors that the difference would arise only three or four times in a hundred through chance alone accordingly restricts the difference to the range 0.31 to 0.33, with 0.32 as the likely value.

This difference represents a decrease by 14.4 percent in the incidence of colds in the ascorbic-acid group as compared with the control group.

The value of P (one-tailed) for difference 0.31 to 0.33 is 0.021 to 0.016. We can accordingly state that the observed difference is statistically significant, with P (one-tailed) less than or equal to 0.02. The null hypothesis that ascorbic acid has the same effect as the placebo is accordingly eliminated at this level.

The average number of days lost from school per person in the placebo group was reported as 1.6, and in the ascorbic acid group as 1.1, giving a decrease of 31 percent in integrated morbidity. The average number of days lost from school per cold was 0.73 for the placebo group and 0.58 for the ascorbic-acid group, a decrease in severity of individual colds by 21 percent. For both severity and integrated morbidity the null hypothesis of equal effectiveness of ascorbic acid and placebo is decisively rejected, with P (one-tailed)<0.01.

Despite the fact that they had found statistically significant differences between their two groups (Table 5), Cowan, Diehl, and Baker wrote the following sentence as the entire summary of their important paper: "This controlled study yields no indication that either large doses of vitamin C alone or large doses of vitamin A, B1, B2, C and D and nicotinic acid have any important effect on the number or severity of infections of the upper respiratory tract when administered to young adults who presumably are already on a reasonably adequate diet." This statement would be completely false if it did not contain the adjective "important." Cowan, Diehl, and Baker apparently thought that a 31-percent decrease in the amount of illness, simply as the result of taking a vitamin C tablet every day, was not important. It is hard to understand this attitude, which, however, seems still, in 1974, to be held by some prominent physicians and nutritionists.

Dahlberg, Engel, and Rydin, 1944

The study by Dahlberg, Engel, and Rydin (1944) is sometimes quoted as showing that ascorbic acid has no value in preventing the common cold or affecting its duration. For example, in the book **The Vitamins in Medicine** by Bicknell and Prescott (1953) there is the following statement: 'Dahlberg, Engel, and Rydin carried out a mass experiment on 2,500 Army conscripts, one-half receiving 200 mg of ascorbic acid, the other half acting as controls. No difference was noted in the frequency or duration of colds, fever, endurance tests, or diseases of any description in the two groups."

Dahlberg, Engel, and Rydin themselves, in the summary of their paper, state that "No difference could be found as regards frequency or duration of colds, degrees of fever, etc. Military competitions, arranged

to relieve the tedium, disclosed no difference between the two groups. Thus, the soldiers who only received the diet of the Swedish Army, and who showed a 'pathological deficit' (in ascorbic acid in the blood), did not differ in any respect from those who had been given ascorbic acid during the entire period of investigation. Consequently, there is no reason to assume vitamin C to be at all instrumental in preventing colds when supplementing the degree of vitamin deficiency existing among soldiers in the north of Sweden."

Examination of the paper by Dahlberg, Engel, and Rydin shows, however, that these statements are not true. The investigators in fact reported a decrease in the incidence of colds, a decrease in the incidence of other infectious diseases, a decrease in the number of subjects with fever, and a small improvement in functioning in the endurance tests. The statement by the authors is misleading; presumably they meant to say that no statistically significant differences were found.

The study was carried out with 2,525 infantry soldiers stationed in an isolated region in northern Sweden, during the 90 days from 3 March to 31 May, inclusive. It was a double-blind test, the composition of the tablets being kept secret from both the doctors and the soldiers. The subjects were divided into two groups, the ascorbic acid group (1,259) and the placebo group (1,266), in a random way, by odd and even identity numbers, respectively. The placebo tablets contained a suitable amount of citric acid to disguise any difference in taste. The ascorbic-acid subjects received 200 mg per day for the first 24 days and 50 mg per day for the remaining 66 days, an average of 90 mg per day. After 24 days and after 90 days a statistically significant difference was found between the average ascorbic-acid levels in the urine of the two groups, both during a fasting period and after ingestion of 200 mg or 300 mg of ascorbic acid, in a loading test. (The loading test results are referred to in the words "pathological deficit" in the summary of their paper.)

The ascorbic-acid tablets and placebo tablets were dispensed at the first meal of the day, and special steps were taken to see that they were consumed at that time and did not go to the wrong person. The soldiers were told what the investigation was for and were requested not to eat any other food or other medicines during the time of observation than what was provided in camp. About half of the subjects (in certain companies of soldiers) in each group were carefully checked, and the average intake of ascorbic acid of 90 milligrams per day is reliable for them. For the other half, in other companies, there were some periods when some proportion of the subjects did not always take the tablets regularly. The authors present the results separately, but in fact they are closely similar, and in the following discussion all ascorbic-acid subjects are grouped together, and all placebo subjects. The failure to check the regular ingestion of the tablets occurred during only a part of the 50-mg-per-day period, and it seems likely that the average ingestion of ascorbic acid, taken as 90 mg per day, is not more than 10 percent high.

The observations, presented in the original paper in five tables, are summarized in Table 6. The second row gives the number of colds for the placebo group and the ascorbic-acid group. These numbers correspond to a 7.4-percent smaller incidence of colds for the ascorbic acid group than for the placebo group. The next three rows give further information about colds; namely, the numbers of subjects with colds (one or more during the period of the study), registered as ill with colds, and with colds and fever. In these three categories, too, there are reported decreases in incidence in the ascorbic-acid group, ranging from 2.5 percent to 3.7 percent.

It is interesting that the reported amount of protective effect for all infectious diseases (last four lines in Table 6) is somewhat larger than that for the common cold alone (average of four values 8.0 percent, as compared with 4.3 percent).

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Table 6

THE STUDY BY DAHLBERG, ENGEL, AND **RYDIN** INCIDENCE OF COLDS AND OF ALL INFECTIOUS DISEASES

		group	ascorbic-acid group
	1266	1259	
Total number of subjects Total number of colds*	152	140	7.4 %
Subjects with common cold Subjects registered as ill with	130	126	2.5 %
common cold Subjects with common cold and fever Registered cases of disease	94	90	3.7 %
Diseased subjects Subjects registered as diseased	73	70	3.6%
Subjects diseased and with fever	162	145	10.0%
	141**	131	6.6 %
	103	95	7.3%
	80	73	8.2 %
Number, placebo group	Number, ascorbic-acid	Decreased incidence in	

***From Table 1, corrected for other acute infections ** Average of 142 in Table 1 and 140 in Table** 5

A field competition was held, participated in by 359 members of the placebo group and 357 members of the ascorbic acid group. The median ranking of the ascorbic-acid participants was 2.0 percent higher than that of the control participants. Some superiority of the ascorbic-acid group over the placebo group was accordingly reported in this test (presumably the endurance test mentioned by Bicknell and Prescott), even though the superiority is small and not statistically significant.

Dahlberg, Engel, and Rydin mentioned that they had recorded the number of days each patient was on the sick list and how many days, if any, he had been treated in hospital. These numbers are, however, not given in the paper, and it is accordingly not possible to use them in assessing the severity of individual colds.

The statistical significance of the results of this large-scale study, involving 2,525 subjects, is less than that of the study of Cowan, Diehl, and Baker, involving only 363 subjects, for two reasons. First, the period of time was less than half as great in the former study, and second, the incidence of colds was much less, presumably because the soldiers were in an isolated camp in northern Sweden and not exposed to many cold viruses. The total number of colds reported by Dahlberg, Engel, and Rydin is 292, whereas the total number reported by Cowan, Diehl, and Baker is about 735. Moreover, the amount of ascorbic acid per day in the Scandinavian study was less than half as much as in the Minnesota study, so that an effect only about half as great would be anticipated.

The study by Dahlberg, Engel, and Rydin indicates that ascorbic acid in the average amount 90 mg per day has some protective effect, but the null hypothesis of no protective effect is not eliminated with statistical significance. On the other hand, it is not justified to claim that this work has shown ascorbic acid to have no value in controlling the common cold.

Franz, Sands, and Heyl, 1956

A double-blind study of ascorbic acid and the common cold was carried out by Franz, Sands, and Heyl of Dartmouth Medical School during the three-month period from February to May 1956, with 89 volunteer medical students and student nurses. The subjects were divided, in **a** random way, into four groups, three of 22 subjects and one of 23 subjects. One

group received tablets containing ascorbic acid, the second ascorbic acid and a bioflavonoid (naringin), the third a placebo, and the fourth naringin only. The daily amount of ascorbic acid was 205 mg and that of the bioflavonoid was 1000 mg. Symptoms of colds were systematically recorded. The results for the bioflavonoid groups, with or without ascorbic acid, were the same as for the corresponding groups without bioflavonoid. The authors concluded that the administration of a bioflavonoid had effect neither on the incidence or the cure of colds nor on the ascorbic-acid level of the blood.

The results reported by the authors are given in Table 7.

From this table we see that the incidence of colds in the two ascorbic-acid groups is nearly the same as in the other groups (4.5 percent less). The difference is not statistically significant. Because of the small numbers of subjects and colds, a decreased incidence would have to be as great as 50 percent to be significant at the level P(one-tailed)<0.05.

The authors point out that the subjects receiving ascorbic acid showed more rapid improvement in their colds than those not receiving it and that this difference is statistically significant. In the placebo and bioflavonoid groups eight of the total of 15 colds remained uncured or unimproved in five days, whereas of the 14 colds in the two groups receiving ascorbic acid only one remained unimproved or uncured in five days. This difference is statistically significant at the level P (one-tailed) <0.01. This double-blind study shows with statistical significance that ascorbic acid has a greater effect than a placebo in decreasing the incidence of severe colds. A comparison with statistical information about the duration of colds leads to the conclusion that the integrated morbidity for the ascorbic-acid subjects was 40 percent less than for the placebo subjects.

Scheunert, 1949

In 1949 Scheunert reported the results of a study of vitamin C in over 2,600 factory workers in Leipzig, Germany. The different tablets were given to groups of workers thought to be living and working under closely similar conditions. The study was blind, but not double blind. There were 10 groups, receiving 0, 20, 50, 100, or 300 mg of ascorbic acid over a period of eight months (242 days). Four groups received 20 mg of quinine per day, one group 0.5 mg of thiamine per day and one group 0.5 mg of thiamine and 1000 IU of vitamin A per day, in addition to ascorbic acid. There is no indication that

Table 7

THE STUDY BY FRANZ, SANDS, AND HEYL

Group	Number in group	Number of colds: Total	Number of colds: Not cured or improved in 5 days
Ascorbic acid	22	8	0
Ascorbic acid plus bioflavonoid	22	6	1
	44	14	1
Placebo	23	7	4
Bioflavonoid	22	8	4
	45	15	8

Total incidence of colds 4.6 percent less for ascorbic-acid groups than for other two groups, not statistically significant; incidence of severe colds (not cured or improved in 5 days) 87.5 percent less for ascorbic-acid groups than for other groups, statistically significant at the level P(one-tailed) <0.01.

this small amount of vitamin A affected the results. The thiamine may have contributed to the greater resistance to disease, although the amount is small (0.5 mg per day, as compared with the U.S. recommended daily allowance of 1.4 mg and the now recommended therapeutic dosage of 10 to 150 mg per day). I have averaged the results from Scheunert's second table for groups receiving the same amount of ascorbic acid. Values of the average incidence per person of respiratory diseases, gastrointestinal diseases, and others (cardiovascular, circulatory, genitourinary, hepatic and biliary, and neurologic) for the combined groups are given in Table 8.

It is seen that the amount of illness of each kind decreased steadily with increased intake of ascorbic acid to 100 mg per day, with no further decrease observed at 300 mg per day. For respiratory diseases there is a decrease of *72* percent for both 100 and 300 mg per day. This decrease is greater than the decreases observed in other studies. Part of the protection may have resulted from the decreased exposure to cold viruses, in that the other workers in the group were also receiving the dosage of vitamin C and constituted a less dangerous source of infection. Scheunert estimated that the subjects received 15 to 30 mg of ascorbic acid per day in their food. We may conclude (as did Scheunert) that the decrease by about 50 percent from increasing the supplementary intake from 50 mg to 100 mg per day shows that the optimum intake is at least 125 mg per day, for most of his subjects. At this intake the concentration of ascorbic acid in the blood is close to the value at which tubular reabsorption in the kidney is saturated. Further increase in intake then leads to a rate of increase of the serum concentration that is only 1/40th of that for low intakes. The statistical uncertainty is such that Scheunert's results do not rule out a somewhat greater protective effect of 300 mg of ascorbic acid than of 100 mg per day, but there is little doubt that the first 100 mg is the most important.

Ritzel,1961

An important study that gave results with high statistical significance was reported in 1961 by Dr. G. Ritzel, who is a physician with the medical service of the School District of the City of Basel, Switzerland. The study was carried out in a ski resort with 279 boys during two periods of five to seven days. The conditions were such that the incidence of colds during these short periods was large enough (approximately 20 percent) to permit

Table 8 THE STUDY BY SCHEUNERT

roup	Number of Subjects	Amount of Vitamin C	Respiratory		Incidence of disease Castro-		**Other**	
				Decrease	intestinal	Decrease		**Decrease**
1	243a	0 mg	0.552		0.560		**0.248**	
II	772b	20 mg	.491	11 %	.345	38 %	**.189**	**24%**
III	1146c	50 mg	.321	42 %	.308	45 %	**.166**	**33%**
IV	241	100 mg	.156	72 %	.070	**88** %	**.085**	**66%**
V	259	300 mg	.154	72 %	.096	83 %	.067	**73%**

a. This group received quinine, 20 mg d-1.
b. 447 received also quinine, 20 mg d-1.
c. Of this group 240 received also quinine, 20 mg d-1, 326 received thiamine, 0.5 mg d-1, and 339 received thiamine, 0.5 mg d-1 and vitamin A, 1000 IU d-1.

results with statistical significance to be obtained. The subjects were of the same age (15 to 17) and had similar nutrition during the period of study. The investigation was double blind, with neither the participants nor the physicians having any knowledge about the distribution of the ascorbic-acid tablets (1,000 mg) and the placebo tablets. The tablets were distributed every morning and taken by the subjects under observation such that the possibility of interchange of tablets was eliminated. The subjects were examined daily as to symptoms of colds and other infections, as listed in the footnote of Table 9. The records were largely on the basis of subjective symptoms, partially supported by objective observations (measurement of body temperature, inspection of the respiratory organs, auscultation of the lungs, and so on). Persons who showed cold symptoms on the first day were excluded from the investigation.

After the completion of the investigation a completely independent group of professional people was provided with the identification numbers for the ascorbic acid tablets and placebo tablets, and this group carried out the statistical evaluation of the observations.

The principal results of the investigation are given in Table 9. The author points out that the group receiving ascorbic acid showed only 39 percent as many days of illness per person as the group receiving the placebo, and that the number of individual symptoms per person was only 35 percent as great for the ascorbic-acid group as for the placebo group, and states that the statistical evaluation of these differences by two-by-two tables gives a significant difference, 0.001 $P<0.01$. The author also points out that the average number of days per cold for the ascorbic-acid group was 1.8 (more accurately 1.82), 29 percent less than the value for the placebo group, 2.6 (2.58), and that this difference is statistically significant, with $P<0.05$ on a t-test.

In Table 2 of the paper by Ritzel the values of the number of patients showing different symptoms (the seven classes of symptoms listed in the footnote to Table 9) are given, and the number of days of illness for each symptom. It is interesting that for each of these seven classes of symptoms the number of patients showing the symptom is less for the ascorbic-acid group than for the placebo group, and that, moreover, the number of days of illness per patient showing the symptom is

Table 9 THE STUDY BY RITZEL

	Placebo group	Ascorbic-acid group	P(one-tailed)*	Decrease
Number in group	140	139		
Number of colds	31	17		
Incidence of colds	0.221	0.122	<0.02	45 %
Total days of illness	80	31		
Total individual symptoms**	119	42		
Severity of individual colds, from days of illness per cold	2.58	1.82	<0.05	29%
from individual symptoms per cold	3.84	2.47	<0.05	36%
Integrated morbidity from days of illness per person	0.571	0.223	<0.01	61 %
from individual symptoms per person	0.850	0.302	<0.01	64%

* **For rejection of null hypothesis of equal effect of ascorbic acid and placebo.**
****Pharyngitis, laryngitis, tonsillitis, sore throat; bronchitis, coughing; fever, chills; otitis media; rhinitis; herpes labialis; other symptoms (muscle ache, headache, abdominal pain, vomiting, diarrhea, general malaise).**

also less.

Let us discuss separately the effect of ascorbic acid on the incidence of the common cold and its effect on the severity of individual colds. The number of colds was 31 for the placebo group and 17 for the ascorbic-acid group. (The number of colds was not given explicitly in the paper. However, the number of days of illness for each of the two groups was given[80, 31], and the average number of days of illness per cold [2.6, 1.8]. The only integral values for the number of colds allowed by these numbers are 31 for the placebo group and 17 for the ascorbic-acid group.) The incidence of colds is accordingly 0.221 per person for the placebo group and 0.122 for the ascorbic-acid group, a decrease by 45 percent for the ascorbic-acid group. The value X^3 is found to be 4.81, with P(one-tailed) <0.02. This investigation accordingly shows with statistical significance that the null hypothesis that ascorbic acid has only the same effect as the placebo is to be rejected.

Two values may be calculated for the effect of ascorbic acid on the severity of individual colds. In Table 9 the number of days of illness per cold for the placebo group is given as 2.58 and for the ascorbic-acid group as 1.82, 29 percent smaller. Moreover, the average number of individual symptoms recorded per cold (they were recorded daily) is given as 3.84 for the placebo group and 2.87 for the ascorbic-acid group, 36 percent smaller. Each of these differences is statistically significant, the null hypothesis that the two populations are the same with respect to the number of days of illness per cold and the individual symptoms per cold being rejected at the level P(one-tailed)< 0.05.

Two values are given in Table 9 for the integrated morbidity, one as measured by the number of days of illness per person and the other as measured by the number of symptoms (recorded daily) per person. These values are 61 percent and 64 percent less, respectively, for the ascorbic-acid subjects than for the placebo subjects, with the differences significant at the level
P<0.01

This investigation seems to have been very well planned and executed. Ritzel was aware of the problem of obtaining reliable results in the study of the common cold, and he discussed the problem in some detail. His paper is provided with an English-language summary, reading as follows: "The possibility of preventing infection by administration of vitamin C was investigated in a moderately large test population during a period of increased exposure. The trial was conducted in such a way as to exclude sources of error in assessing subjective symptoms. Statistical evaluation of the results confirmed the efficacy of vitamin C in the prophylaxis and treatment of colds. Problems of therapeutic trials with pluripotential preparations which have to be judged chiefly on the basis of subjective symptoms are discussed."

It is interesting that in an often-quoted review of the evidence about ascorbic acid and the common cold, which ended with the statement that "there is no conclusive evidence that ascorbic acid has any protective effect against, or any therapeutic effect on, the course of the common cold in healthy people not depleted of ascorbic acid," the work of Ritzel was covered in two sentences, stating quite erroneously that he had reported "a reduction of 39 percent in the number of days ill from upper respiratory infections and a reduction of 35 percent in the incidence of individual symptoms in the supplemented group as compared with the placebo group;" (the correct values are 61 percent and 64 percent, respectively, Anonymous, 1967).

Conclusion

Since 1970 several careful double-blind studies of ascorbic acid in relation to the common cold have been carried out. These studies will be summarized in a second article (Pauling, 1975). They leave no doubt that ascorbic acid in amounts greater than the officially recommended dosage decreases the amount of illness with the common cold. The point of the

present paper is that the evidence for this protective effect was already moderately strong by 1942 (Glazebrook and Thomson; Cowan, Diehl, and Baker), and was very strong by 1961. Despite the strength of the evidence, which has been systematically misrepresented by the medical and nutritional authorities, the possible value of an increased intake of vitamin C in decreasing the amount of suffering and loss of time from work of the people has been ignored by almost all physicians. The official stand of the American Medical Association is still, in 1974, that extra vitamin C has no value in controlling the common cold or in any other way, and that an increased intake of vitamin E or other vitamins also has no value in controlling disease.

The case of vitamin C and the common cold has, I believe, a lesson for us. It is that we cannot rely on the medical and nutritional establishment to give us good advice about health and nutrition. What is the optimum daily intake of vitamin C? Can vitamin C decrease the age-specific incidence of diseases other than the common cold? There is, in fact, considerable evidence that it can, in part cited above and in the review of the more recent work (see also Stone, 1972). What is the optimum daily intake of vitamin E, and of other vitamins and other nutrient factors? Very little research is being done at the present time on these important problems. I believe that it is mandatory that funds become available before long to permit work of this sort to be carried out.

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