

## Ascorbic Acid in Chronic Psychiatric Patients — A Controlled Trial

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Anxiety and excitement have been shown by Maas (1961) to increase the rate of breakdown of ascorbic acid, and in schizophrenics this process may be exaggerated by an abnormality of adrenaline metabolism (Briggs, 1962). Schizophrenics receiving "adequate" dietary amounts of vitamin C, as judged by the requirements of the normal population, are commonly found to have low blood ascorbate levels. Evidence of low blood ascorbate levels in most psychiatric patients has been gathered by Horwitt (1942), Leitner and Church (1956) and others. It has been debated whether such laboratory findings are associated with a state of "subscurvy", where the individual has the complaints of excessive tiredness, depression, irritability and vague ill-health. Many authorities claim that there is no clinical evidence to justify the distinction of a state of "hypovitaminosis C". They claim that one either absorbs sufficient ascorbic acid to maintain health, or so little that the classical condition of scurvy supervenes.

The present trial was initiated in an attempt to clarify these conflicting views, and in order to satisfy the author's own feeling that subscurvy is both a clinical entity common in chronic psychiatric patients and one the psychological concomitants of which contribute to personality disturbance.

### DESIGN OF EXPERIMENT

Forty chronic male patients agreed to take part in the investigation, although it had been decided that only 20 would have the active preparation. Their mean age was 52.6 years (range 29-69) and their mean length of hospitalization was 17.7 years (range 3-45). Four of the patients were suffering with manic-

depressive psychosis, two with G.P.I., and 34 with schizophrenia. 16 of the patients (Group B) co-operated in the collection of 24-hour specimens of urine. The remainder of the patients constituted Group A.

The pharmacist prepared two solutions, identical as near as possible, except that one contained ascorbic acid and the other was inert. The solutions were put into medicine bottles with randomly given three-figure numbers, the pharmacist keeping a key to the active and inactive solutions. On the ward the bottles were allotted in random fashion to the patients, though it had been ensured that both groups would receive equal numbers of active and inert preparations. The patients received one dose of the preparation daily for three weeks, those in the active group having 1 G. of ascorbic acid per day.

Before and after the trial all the patients were examined for scorbutic stigmata, their Hb percentage checked, blood ascorbate levels and urinary excretion of ascorbic acid estimated. In order to assess any psychological changes, firstly, the depression scale of the M.M.P.I., which would be self-rating (depending on the patient's subjective interpretation of how he felt) was administered. Secondly, the Wittenborn Psychiatric Rating Scales were used as measures of overtly observable behaviour in the patient, as seen by both doctor and ward nurse. Both the M.M.P.I. and the W.P.R.S. were used before and after the trial.

With regard to the M.M.P.I., reliability coefficients of 0.80 (Holzberg and Alessi, 1949) have been obtained with psychiatric patients. Generally speaking, a high "Depression" score indicates poor morale of the emotional type, with a feeling of uselessness and an inability to

assume a normal optimism with regard to the future. McIntosh (1959) claims that mental depression is an early sign in scurvy and may be so marked as to present as a true depressive illness.

Six of the Wittenborn subscales were used—relating to manic state, depressed state, schizophrenic excitement, paranoid state, paranoid and hebephrenic schizophrenia. The reliability coefficients ("r") of these subscales are high and were based on different samples of 100 patients each (Wittenborn, 1951); they are shown in Table 2. These psychiatric rating scales are a procedure for recording the observed behaviour of mental patients and for describing them according to their current symptoms. The scales provide for the assignment of numerical values to indicate the presence and degree of pathological symptoms in a patient. In order that their repeated use may reveal changes in the patient, the scales are restricted to currently discernible behaviour. The statistic used for rating was a mean of the raw scores given by doctor and nurse for each patient.

Whilst taking the ascorbic acid or placebo, 24-hour specimens of urine were collected from the patients of Group B and their output of ascorbic acid measured.

RESULTS

(1) Physical Examination and Hb Percentage

None of the patients were markedly anaemic and there were no significant changes in Hb percentage.

Twelve patients (eight in the active and four in the placebo group) had signs attributable to vitamin C deficiency before the trial. These signs (which included follicular hyperkeratosis, minute haemorrhages around hair follicles, haemorrhagic gingivitis and dyspepsia) cleared in five patients after saturation with ascorbic acid. The control group showed no change in this respect.

(2) Psychological Testing

The results with the patient's self-rating scale (M.M.P.I.) showed an improvement in the depression scale significant at the 1 per cent.

level of probability (see Table I), in the active group.

Since the active and placebo groups, treated separately, were relatively small samples (N = 20), a technique of paired comparisons, whereby each patient is matched with himself, was used. A critical ratio was obtained by dividing the mean difference in scores by the standard error of the difference (S.E. Diff.).

TABLE I  
M.M.P.I. Results. Depression Scale.  
(These results are shown more graphically in Fig. 1)

Group	Mean Standard Score		Mean Diff.	S.E. (m. diff.)	P
	Before	After			
Active	72.8	64.8	8.0	2.81	2.85 < 0.01
Placebo	71.3	72.75	-1.45	2.5	0.58 Not Sig.

(This result was calculated after omitting the scores of one patient, who filled out the M.M.P.I. incorrectly.)

The Wittenborn results are shown in Table II and the changes in the rating scores are shown more graphically in Fig. 1. One of the most interesting features in this diagram is that the direction of change in the active group (shown by cross hatching in Fig. 1) is always towards improvement and always more than in the placebo group. There were three subscales, manic state, depressed and paranoid states,

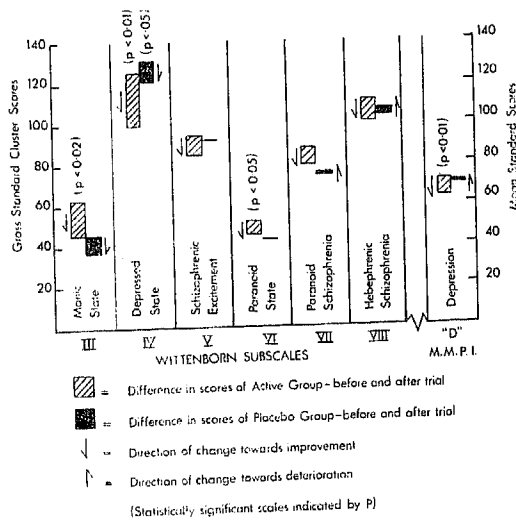


FIG. 1

TABLE II

*Wittenborn Results*

Symptom Complex	Group	Cluster Score		Mean Diff.	S.E. (m.d.)	t	P	Subscale "r"s
		Before	After					
Manic state .. .. .	Active	66	50	0.8	0.34	2.63	<0.02	0.92
	Placebo	49	42	0.35	0.22			
Depressed state .. .. .	Active	117	89	1.4	0.302	4.64	<0.01	0.67
	Placebo	124	116	0.4	0.183	2.19	<0.05	
Schizophrenic excitement .. .. .	Active	96	85	0.55	0.81			0.90
	Placebo	95	95	0	0.75			
Paranoid state ... .. .	Active	53	46	0.45	0.211	2.13	<0.05	0.76
	Placebo	45	45	0	0.183			
Paranoid schizophrenia .. .. .	Active	87	82	0.25	0.25			0.76
	Placebo	77	78	-0.05	0.235			
Hebephrenic schizophrenia .. .. .	Active	112	102	0.5	0.303			0.81
	Placebo	104	108	-0.2	0.213			

where this degree of improvement was statistically as well as clinically significant. This will be commented on in the discussion.

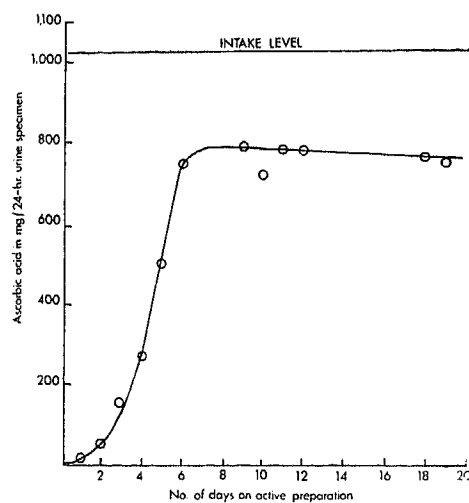
(3) *Subjective Results*

Subjective feelings of improvement in general well-being were reported by eight patients, five of these being in the active group. The nurse felt that five patients had obviously improved, while the ward doctor formed the impression, on general grounds, that four of those reported by the nurse had improved. All five patients proved to be in the active group. These subjective impressions were not submitted to statistical analysis.

(4) *Ascorbic Acid Excretion*

After the first 24-hour specimens of urine were collected, the patients were given the first dose of the test solution allotted to them.

The ascorbic acid excretion results are shown in Tables III and IV and Fig. 2. The mean urinary excretion of ascorbic acid by the patients of Group B in the placebo group was 15.2 mg.



10 REPRESENTS AVERAGE RESULT FOR 4 PATIENTS ON EACH DAY. INDIVIDUAL EXCRETION RATES SHOWN IN TABLE 41

FIG. 2

in 24 hours—at the very lowest limit of normal. The saturation curve for the active group patients is shown graphically in Fig. 2, where it can be seen that the mean time necessary for

TABLE III

*24-hour Urinary Excretion of Ascorbic Acid in Members of Group B receiving Placebo Solution  
(Expressed as mg.)*

Patient	Day of Collection												Mean
	1	2	3	4	5	6	9	10	11	12	18	19	
a	8.8		9.2		14.6		13.8		14.6		12.2		12.2
b	9.4		8.9		16.2		16.2		40.7		22.8		19.0
c	20.1		33.6		28.8		17.8		16.9		20.6		23.0
d	13.2		14.8		10.7		11.2		15.8		18.9		14.1
e		9.4		11.6		22.4		18.8		14.5		8.2	14.1
f		17.8		11.2		8.6		8.9		11.2		12.7	11.7
g		12.2		11.8		10.4		13.3		8.0		20.1	12.6
h		14.1		16.2		10.3		12.7		18		18.7	15.0
	Overall mean :												15.2

TABLE IV

*24-hour Urinary Excretion of Ascorbic Acid in Members of Group B receiving Active Solution  
(Expressed as mg.)*

Patient	Day of Collection											
	1	2	3	4	5	6	9	10	11	12	18	19
i	11.2		107		430		732		760		710	
j	17.8		197		517		800		764		803	
k	20.7		168		448		796		791		772	
l	30.2		152		602		830		824		786	
m		32.3		210		674		656		711		722
n		45.8		336		742		716		774		703
o		78.2		267		808		748		805		798
p		43.6		272		772		753		842		800
Mean =	19.9	49.8	156	271	496	739	789	719	785	783	763	753

saturation was 6 days. The consistently low readings on the 10th day were probably explained by some delay in the estimation of the urinary ascorbic acid concentration. The slight drop in excretion of the vitamin from the 8th to the 19th day of the trial was probably due to deterioration, under the influence of light, etc., of the vitamin C in the active preparation, though the bottles were protected as far as possible.

The mean urinary excretion of ascorbic acid by the patients in the placebo group was at the lowest limits of normal excretion rates. (Harris and Ray, 1935, found the minimum daily excretion in healthy subjects, having a little fruit each day, was 20 mg.) The average delay before saturation with the vitamin was six days (see Fig. 2). Harris and Ray (1935) claimed that patients with scurvy or on the borderline of scurvy, required 7 to 10 days for saturation. Normal subjects can be saturated with the vitamin within 24-48 hours, by giving them 1 G. of the vitamin per day.

#### DISCUSSION

The human organism depends on external sources for its supply of vitamin C, a daily intake of about 30-100 mg. being adequate for normal subjects (M.R.C. Report, 1948; McIntosh, 1959). Stress, anxiety and excitement accelerate the depletion of ascorbic acid, and the results of this trial indicate that these chronic psychiatric patients were suffering from sub-scurvy. Especially significant was the improvement in the depressed state of the patients. The depression scale on the M.M.P.I., seemed to reflect a general factor, as was described, and also the scales on the Wittenborn, where a significant improvement was found in the active group, were those where general personality functioning would be reflected, rather than the acuteness of any more specific psychiatric syndrome. Both active and placebo groups improved significantly with respect to their "depressed state", but the difference between the two groups was in itself statistically significant at the 1 per cent. level of probability.

The suggestion from the results is that saturation with vitamin C has brought about an

improvement in overall personality functioning. Conversely, the psychological and physical improvement shown by these long-stay psychiatric patients after saturation with ascorbic acid indicates that their diet has been unsatisfactorily low in vitamin C content. This had led to a deficiency state—sub-scurvy—having quite definite psychiatric symptoms, the most important of which are marked depression and irritability.

It would seem likely that the now fairly general upgrading of hospital catering is not enough—psychiatric patients have greater demands for ascorbic acid than normal subjects, (Briggs, 1962). States of depression and anxiety associated with psychiatric disorders are probably accentuated by an inadequate intake of ascorbic acid. The administration of synthetic ascorbic acid to psychiatric patients would seem to be indicated.

#### SUMMARY

- (1) A controlled, blind trial of ascorbic acid saturation, involving 40 male, chronic psychiatric patients, is described.
- (2) Standardized (objective and subjective) psychological techniques were used to assess changes dependent upon ascorbic acid intake.
- (3) A clinical state of sub-scurvy was found in these patients.
- (4) Psychiatric patients are shown to have an unusually high demand for ascorbic acid.
- (5) Statistically significant improvement in the depressive, manic and paranoid symptom-complexes, together with an improvement in overall personality functioning, was obtained following saturation with ascorbic acid.
- (6) It is suggested that chronic psychiatric patients would benefit from the administration of ascorbic acid.

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