

## Supplemental ascorbate in the supportive treatment of cancer: Prolongation of survival times in terminal human cancer\*

(vitamin C)

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**ABSTRACT** Ascorbic acid metabolism is associated with a number of mechanisms known to be involved in host resistance to malignant disease. Cancer patients are significantly depleted of ascorbic acid, and in our opinion this demonstrable biochemical characteristic indicates a substantially increased requirement and utilization of this substance to potentiate these various host resistance factors.

The results of a clinical trial are presented in which 100 terminal cancer patients were given supplemental ascorbate as part of their routine management. Their progress is compared to that of 1000 similar patients treated identically, but who received no supplemental ascorbate. The mean survival time is more than 4.2 times as great for the ascorbate subjects (more than 210 days) as for the controls (50 days). Analysis of the survival-time curves indicates that deaths occur for about 90% of the ascorbate-treated patients at one-third the rate for the controls and that the other 10% have a much greater survival time, averaging more than 20 times that for the controls.

The results clearly indicate that this simple and safe form of medication is of definite value in the treatment of patients with advanced cancer.

There is increasing awareness that the progress of human cancer is determined to some extent by the natural resistance of the patient to his disease. Consequently there is growing recognition that improvement in the management of these patients could come from the development of practical supportive measures specifically designed to enhance host resistance to malignant invasive growth.

We have advanced arguments elsewhere indicating that one important factor in host resistance is the free availability of ascorbic acid (1-3). These arguments are based upon the demonstration that cancer patients have a much greater requirement for this substance than normal healthy individuals, on the realization that ascorbic acid metabolism can be implicated in a number of mechanisms known to be involved in host resistance, and finally, and most convincingly, on the published evidence that ascorbic acid can sometimes produce quite dramatic remissions in advanced human cancer (4, 5).

In this communication we present the results of a clinical trial in which 100 terminal cancer patients received supplemental ascorbate as their only definitive form of treatment and compare their progress with that of 1000 matched patients managed by the same clinicians in the same hospital who did not receive any ascorbate supplementation or any other definitive form of specific anti-cancer treatment.

### Protocol

The study involved a treated group of 100 patients with terminal cancer of various kinds and a control group of 1000 untreated and matched patients. The treated group consists of 100 patients who began ascorbate treatment, as described by

Cameron and Campbell (4) (usually 10 g/day, by intravenous infusion for about 10 days and orally thereafter), at the time in the progress of their disease when in the considered opinion of at least two independent clinicians the continuance of any conventional form of treatment would offer no further benefit. Fifty of the treated subjects are those described in ref. 4 and the other 50 were obtained by random selection from the alphabetical index of ascorbate-treated patients in Vale of Leven District General Hospital, where treatment of some terminal cancer patients with ascorbate has been under clinical trial since November 1971. We believe that the ascorbate-treated patients represent a random selection of all of the terminal patients in this hospital, even though no formal randomization process was used. In the random selection three patients were excluded because supplemental ascorbate had been deliberately discontinued by order of another physician, and five were excluded because matching controls could not be found for them. Patients suspected or known to have voluntarily discontinued ascorbate treatment have been retained in the group, as have those who died from some cause other than their cancer. No patient was excluded because of short survival time. Eighteen patients, marked with a plus sign in Table 1, were still alive on 10 August 1976, 16 of them clinically "well." These 100 cancer patients, given ascorbate from the presentation date in their illness when their disease process was recognized to be "untreatable" by any conventional method, comprise the treated group.

The control group was obtained by a random search of the case record index of similar patients treated by the same clinicians in Vale of Leven Hospital over the last 10 years. For each treated patient, 10 controls were found of the same sex, within 5 years of the same age, and who had suffered from cancer of the same primary organ and histological tumor type. These 1000 cancer patients comprise the control group.

The detailed case records of these 1000 were then analyzed quite independently by Dr. Frances Meuli, M.B., Ch.B. (Otago, New Zealand), who established their presentation date of "untreatability" by such conventional standards as the establishment of inoperability at laparotomy, the abandonment of any definitive form of anti-cancer treatment, or the final date of admission for "terminal care." This presentation date of untreatability corresponds to the date when ascorbate supplementation was initiated in the treated group. Comparable survival times of the 10 matched controls could then be calculated. We accept that "the presentation date of untreatability" can be influenced by many factors in individual patients, but we contend that the use of 1000 controls managed by the same clinicians in the same hospital over the last 10 years provides a sound basis for this comparative study. We record our thanks to Dr. Meuli for her unbiased and valuable contribution to this investigation.

Even though no formal process of randomization was carried

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Table 1. Comparison of time of survival of 100 cancer patients who received ascorbic acid and 1000 matched patients with no treatment<sup>a</sup>

| Case no. | Primary tumor type | Sex | Age | Survival time (days) |     |     |     |     |     |       |      |      |      |       | Test case/mean control (%) |      |
|----------|--------------------|-----|-----|----------------------|-----|-----|-----|-----|-----|-------|------|------|------|-------|----------------------------|------|
|          |                    |     |     | Ten matched controls |     |     |     |     |     |       |      |      |      |       |                            |      |
|          |                    |     |     | Individuals          |     |     |     |     |     |       |      |      |      | Mean  |                            |      |
| 1.       | Stomach            | F   | 61  | 12                   | 41  | 5   | 29  | 85  | 124 | 8     | 54   | 21   | 36   | 38.5  | 121                        | 314  |
| 2.       | Stomach            | M   | 69  | 8                    | 6   | 3   | 9   | 4   | 26  | 8     | 114  | 15   | 14   | 20.7  | 12                         | 58   |
| 3.       | Stomach            | F   | 62  | 15                   | 1   | 72  | 19  | 19  | 27  | 35    | 99   | 76   | 111  | 47.4  | 9                          | 19   |
| 4.       | Stomach            | F   | 66  | 4                    | 87  | 7   | 11  | 3   | 13  | 12    | 6    | 34   | 35   | 21.2  | 18                         | 85   |
| 5.       | Stomach            | M   | 42  | 8                    | 1   | 74  | 358 | 9   | 84  | 14    | 16   | 16   | 128  | 70.8  | 258                        | 368  |
| 6.       | Stomach            | M   | 79  | 45                   | 4   | 12  | 1   | 9   | 6   | 12    | 130  | 4    | 11   | 23.4  | 43                         | 184  |
| 7.       | Stomach            | M   | 76  | 22                   | 19  | 12  | 9   | 14  | 7   | 15    | 3    | 5    | 14   | 12.0  | 142                        | 1183 |
| 8.       | Stomach            | M   | 54  | 24                   | 26  | 21  | 61  | 27  | 48  | 7     | 26   | 2    | 221  | 46.3  | 36                         | 78   |
| 9.       | Stomach            | M   | 62  | 14                   | 23  | 13  | 89  | 4   | 11  | 4     | 4    | 36   | 27   | 22.5  | 149+                       | 622  |
| 10.      | Stomach            | F   | 69  | 6                    | 19  | 55  | 2   | 21  | 8   | 53    | 11   | 103  | 17   | 29.5  | 182+                       | 617  |
| 11.      | Stomach            | M   | 45  | 17                   | 24  | 7   | 57  | 128 | 16  | 44    | 64   | 110  | 78   | 54.5  | 82                         | 150  |
| 12.      | Stomach            | M   | 57  | 19                   | 13  | 8   | 11  | 39  | 29  | 41    | 17   | 170  | 5    | 36.9  | 64                         | 173  |
| 13.      | Bronchus           | M   | 74  | 16                   | 56  | 29  | 27  | 67  | 41  | 25    | 26   | 6    | 40   | 33.3  | 39                         | 117  |
| 14.      | Bronchus           | M   | 74  | 21                   | 2   | 27  | 30  | 18  | 1   | 31    | 1    | 21   | 16   | 16.8  | 427                        | 2542 |
| 15.      | Bronchus           | M   | 66  | 47                   | 94  | 7   | 39  | 3   | 53  | 5     | 4    | 82   | 9    | 34.3  | 17                         | 50   |
| 16.      | Bronchus           | M   | 52  | 35                   | 4   | 70  | 21  | 126 | 8   | 46    | 272  | 39   | 75   | 69.6  | 460                        | 661  |
| 17.      | Bronchus           | F   | 48  | 11                   | 33  | 30  | 5   | 6   | 1   | 45    | 24   | 81   | 57   | 29.3  | 90                         | 307  |
| 18.      | Bronchus           | F   | 64  | 7                    | 1   | 26  | 13  | 71  | 14  | 4     | 30   | 103  | 2    | 27.1  | 187                        | 690  |
| 19.      | Bronchus           | M   | 70  | 24                   | 8   | 20  | 7   | 62  | 20  | 5     | 41   | 19   | 49   | 25.5  | 58                         | 227  |
| 20.      | Bronchus           | M   | 78  | 32                   | 19  | 39  | 40  | 24  | 21  | 43    | 103  | 2    | 21   | 34.4  | 52                         | 151  |
| 21.      | Bronchus           | M   | 71  | 5                    | 53  | 7   | 30  | 2   | 5   | 20    | 39   | 31   | 16   | 20.8  | 100                        | 481  |
| 22.      | Bronchus           | M   | 70  | 3                    | 2   | 33  | 24  | 25  | 35  | 25    | 62   | 2    | 63   | 27.4  | 200+                       | 730  |
| 23.      | Bronchus           | M   | 39  | 42                   | 31  | 74  | 5   | 88  | 45  | 28    | 3    | 15   | 70   | 40.1  | 42                         | 105  |
| 24.      | Bronchus           | M   | 70  | 24                   | 1   | 30  | 2   | 5   | 42  | 46    | 41   | 7    | 57   | 25.5  | 167                        | 655  |
| 25.      | Bronchus           | M   | 70  | 8                    | 34  | 29  | 24  | 5   | 4   | 32    | 129  | 20   | 51   | 40.7  | 33                         | 81   |
| 26.      | Esophagus          | M   | 72  | 12                   | 21  | 19  | 14  | 81  | 26  | 59    | 21   | 28   | 33   | 57.4  | 50                         | 87   |
| 27.      | Esophagus          | F   | 80  | 2                    | 29  | 6   | 45  | 48  | 24  | 13    | 238  | 56   | 2    | 46.3  | 43                         | 93   |
| 28.      | Colon              | F   | 76  | 2                    | 2   | 18  | 5   | 20  | 22  | 1     | 1    | 4    | 1    | 7.6   | 57                         | 750  |
| 29.      | Colon              | F   | 58  | 56                   | 39  | 31  | 15  | 9   | 11  | 8     | 10   | 6    | 62   | 24.7  | 32                         | 130  |
| 30.      | Colon              | M   | 49  | 35                   | 122 | 107 | 28  | 30  | 13  | 78    | 65   | 46   | 56   | 58.0  | 201                        | 347  |
| 31.      | Colon              | M   | 69  | 48                   | 9   | 7   | 15  | 30  | 90  | 26    | 94   | 38   | 15   | 37.3  | 1267                       | 4343 |
| 32.      | Colon              | F   | 70  | 64                   | 102 | 13  | 82  | 8   | 51  | 33    | 144  | 17   | 11   | 52.5  | 144                        | 274  |
| 33.      | Colon              | F   | 68  | 9                    | 15  | 40  | 11  | 17  | 217 | 163   | 59   | 18   | 38   | 38.5  | 170                        | 442  |
| 34.      | Colon              | M   | 50  | 7                    | 108 | 7   | 18  | 17  | 14  | 51    | 69   | 16   | (32) | 33.8  | 428                        | 1266 |
| 35.      | Colon              | F   | 74  | 11                   | 45  | 50  | 6   | 18  | 26  | 40    | 11   | 88   | 23   | 31.8  | 157+                       | 494  |
| 36.      | Colon              | M   | 66  | 13                   | 7   | 224 | 31  | 72  | 11  | 1     | 4    | 11   | 14   | 38.8  | 58                         | 149  |
| 37.      | Colon              | F   | 76  | 23                   | 129 | 8   | 63  | 60  | 21  | 28    | 3    | 15   | 70   | 43.8  | 123+                       | 281  |
| 38.      | Colon              | F   | 56  | 24                   | 1   | 30  | 2   | 5   | 42  | 46    | 41   | 7    | 57   | 25.5  | 861                        | 3376 |
| 39.      | Rectum             | F   | 56  | 51                   | 406 | 74  | 36  | 41  | 106 | 30    | 82   | 82   | 98   | 100.6 | 62                         | 62   |
| 40.      | Rectum             | F   | 75  | 3                    | 40  | 46  | 58  | 7   | 9   | 19    | 68   | 16   | 178  | 44.4  | 223                        | 502  |
| 41.      | Rectum             | M   | 56  | 3                    | 18  | 52  | 36  | 34  | 7   | 49    | 3    | 6    | (13) | 22.2  | 18                         | 81   |
| 42.      | Rectum             | F   | 57  | 9                    | 73  | 11  | 19  | 98  | 82  | (184) | (97) | (89) | (47) | 70.9  | 223                        | 314  |
| 43.      | Rectum             | M   | 68  | 11                   | 11  | 91  | 47  | 18  | 23  | 4     | 13   | 79   | 84   | 38.1  | 140+                       | 367  |
| 44.      | Rectum             | M   | 54  | 52                   | 36  | 10  | 127 | 18  | 98  | 6     | 73   | 11   | 19   | 45.0  | 198                        | 440  |
| 45.      | Rectum             | M   | 59  | 15                   | 2   | 78  | 8   | 98  | 30  | 140   | 54   | 233  | (14) | 67.2  | 759                        | 1129 |
| 46.      | Ovary              | F   | 49  | 36                   | 5   | 117 | 29  | 31  | 22  | 101   | 140  | 94   | 73   | 64.8  | 226                        | 349  |
| 47.      | Ovary              | F   | 68  | 41                   | 39  | 18  | 37  | 67  | 3   | 91    | 40   | 6    | 13   | 35.5  | 33                         | 93   |
| 48.      | Ovary              | F   | 49  | 53                   | 15  | 38  | 122 | 68  | 33  | 841   | 18   | 21   | 40   | 124.9 | 183                        | 146  |
| 49.      | Ovary              | F   | 67  | 19                   | 36  | 22  | 2   | 10  | 32  | 48    | 132  | 21   | 97   | 41.9  | 240+                       | 573  |
| 50.      | Ovary              | F   | 56  | 49                   | 39  | 22  | 85  | 160 | 1   | 86    | 106  | 99   | 107  | 75.4  | 123+                       | 163  |
| 51.      | Breast             | F   | 56  | 1                    | 65  | 26  | 6   | 2   | 15  | 19    | 102  | 71   | 131  | 43.8  | 4                          | 9    |
| 52.      | Breast             | F   | 57  | 3                    | 28  | 15  | 4   | 14  | 16  | 14    | 48   | 61   | 15   | 21.8  | 22                         | 101  |
| 53.      | Breast             | F   | 53  | 33                   | 183 | 6   | 190 | 45  | 29  | 16    | 45   | 109  | 34   | 69.0  | 576                        | 835  |
| 54.      | Breast             | F   | 66  | 22                   | 12  | 94  | 55  | 7   | 38  | 2     | 10   | 76   | 12   | 102.8 | 342                        | 333  |
| 55.      | Breast             | F   | 68  | 107                  | 41  | 69  | 19  | 17  | 251 | 101   | 81   | 50   | 52   | 78.8  | 567                        | 720  |
| 56.      | Breast             | F   | 53  | 8                    | 2   | 2   | 42  | 31  | 17  | 96    | 231  | 42   | 20   | 49.1  | 86                         | 175  |
| 57.      | Breast             | F   | 75  | 45                   | 175 | 12  | 91  | 27  | 5   | 20    | 11   | 63   | 73   | 74.2  | 590                        | 795  |
| 58.      | Breast             | F   | 74  | 12                   | 2   | 35  | 6   | 18  | 33  | 30    | 107  | 85   | 47   | 37.5  | 8                          | 21   |
| 59.      | Breast             | F   | 49  | 3                    | 16  | 62  | 44  | 1   | 17  | 93    | 73   | 5    | 57   | 37.1  | 35                         | 94   |
| 60.      | Breast             | F   | 50  | 31                   | 29  | 28  | 40  | 265 | 14  | 31    | 24   | 104  | 229  | 82.6  | 1644+                      | 1990 |

Table 1. (Continued)

| Case no. | Primary tumor type | Sex | Age | Survival time (days) |     |      |       |                 |                 |                 |                  |                  |                 | Test case | Test case/mean control (%) |      |
|----------|--------------------|-----|-----|----------------------|-----|------|-------|-----------------|-----------------|-----------------|------------------|------------------|-----------------|-----------|----------------------------|------|
|          |                    |     |     | Ten matched controls |     |      |       |                 |                 |                 |                  |                  |                 |           |                            |      |
|          |                    |     |     | Individuals          |     |      |       |                 | Mean            |                 |                  |                  |                 |           |                            |      |
| 61.      | Breast             | F   | 53  | 105                  | 73  | 193  | 159   | 8               | 127             | 126             | 167              | 71               | 42              | 107.1     | 173+                       | 162  |
| 62.      | Bladder            | M   | 93  | 17                   | 47  | 21   | 12    | 2               | 18              | 21              | 46               | 133              | 48              | 36.5      | 241                        | 660  |
| 63.      | Bladder            | F   | 70  | 39                   | 9   | 126  | 52    | 26              | 97              | 10              | 8                | 7                | 79              | 45.3      | 253                        | 556  |
| 64.      | Bladder            | F   | 73  | 1                    | 23  | 52   | 30    | 38              | 38              | 25              | 13               | 45               | 24              | 28.9      | 110                        | 381  |
| 65.      | Bladder            | F   | 77  | 3                    | 52  | 48   | 142   | 118             | 34              | 33              | 10               | 38               | 26              | 50.4      | 34                         | 67   |
| 66.      | Bladder            | M   | 44  | 6                    | 9   | 36   | 48    | 10              | 21              | 8               | 52               | 42               | 16              | 24.8      | 34                         | 137  |
| 67.      | Bladder            | M   | 62  | 47                   | 118 | 85   | 76    | 19              | 58              | 127             | 72               | 10               | 15              | 62.7      | 669+                       | 1067 |
| 68.      | Bladder            | M   | 69  | 39                   | 5   | 66   | 26    | 25              | 267             | 85              | 12               | 13               | 27              | 56.5      | 30                         | 53   |
| 69.      | Gallbladder        | F   | 71  | 7                    | 8   | 56   | 22    | 91              | 44              | 30              | 22               | 47               | 14              | 34.1      | 22                         | 64   |
| 70.      | Gallbladder        | M   | 67  | 20                   | 159 | 4    | 212   | 73              | 60              | 94              | 31               | 16               | 91              | 76.0      | 209                        | 275  |
| 71.      | Kidney (Ca)        | F   | 71  | 6                    | 2   | 17   | 83    | 81              | 55              | 14              | 114              | 60               | 106             | 53.8      | 176                        | 327  |
| 72.      | Kidney (Ca)        | F   | 63  | 68                   | 76  | 8    | 31    | 26              | 5               | 8               | 69               | 29               | 49              | 36.9      | 89                         | 241  |
| 73.      | Kidney (Ca)        | F   | 51  | 16                   | 82  | 27   | 41    | 65              | 29              | 8               | 125              | (95)             | (117)           | 60.6      | 147                        | 243  |
| 74.      | Kidney (Ca)        | M   | 53  | 7                    | 15  | 7    | 49    | 95              | 21              | 91              | 35               | 19               | 76              | 41.5      | 58                         | 140  |
| 75.      | Kidney (Ca)        | M   | 55  | 15                   | 13  | 12   | 16    | 45              | 48              | 89              | 95               | 6                | 83              | 42.2      | 659                        | 1562 |
| 76.      | Kidney (Ca)        | M   | 73  | 25                   | 11  | 209  | 19    | 30              | 198             | 31              | 7                | 30               | 50              | 61.0      | 293                        | 480  |
| 77.      | Kidney (Ca)        | M   | 45  | 91                   | 35  | 19   | 77    | 64              | 12              | 127             | 74               | 34               | 82              | 61.5      | 3                          | 5    |
| 78.      | Kidney (Pap)       | M   | 69  | 67                   | 74  | (24) | (37)  | 87 <sup>b</sup> | 43 <sup>b</sup> | 21 <sup>b</sup> | 82 <sup>b</sup>  | 14 <sup>b</sup>  | 41 <sup>b</sup> | 49.0      | 24                         | 49   |
| 79.      | Kidney (Pap)       | M   | 74  | 57                   | 67  | 51   | (491) | (127)           | 324             | 174             | 126 <sup>b</sup> | 179 <sup>b</sup> | 97 <sup>b</sup> | 169.3     | 1554+                      | 918  |
| 80.      | Lymphoma           | M   | 40  | 144                  | 41  | 53   | 29    | 16              | 20              | 41              | 279              | 302              | 103             | 102.8     | 1016+                      | 988  |
| 81.      | Lymphoma           | M   | 65  | 28                   | 68  | 51   | 56    | 117             | 138             | 10              | 36               | 51               | 142             | 69.7      | 82                         | 118  |
| 82.      | Prostate           | M   | 47  | 24                   | 14  | 22   | 23    | 101             | 53              | 157             | 123              | 16               | 80              | 82.3      | 166+                       | 202  |
| 83.      | Uterus             | F   | 56  | 25                   | 11  | 7    | 67    | 130             | 126             | 30              | 18               | 185              | 61              | 66.0      | 68                         | 103  |
| 84.      | Chondrosarcoma     | M   | 63  | 20                   | 25  | 3    | 17    | 136             | 17              | 31              | 23               | 19               | 157             | 44.8      | 9                          | 20   |
| 85.      | "Brain"            | M   | 49  | 1                    | 85  | 56   | (187) | 57              | 24              | 13              | 29               | 1                | 95              | 54.8      | 37                         | 67   |
| 86.      | Pancreas           | M   | 77  | 11                   | 25  | 19   | 38    | 91              | 78              | 13              | 41               | 40               | 94              | 45.0      | 317                        | 704  |
| 87.      | Pancreas           | M   | 67  | 112                  | 6   | 55   | 36    | 256             | 25              | 91              | 76               | 67               | 52              | 77.6      | 21                         | 27   |
| 88.      | Pancreas           | F   | 60  | 11                   | 42  | 23   | 49    | 57              | 69              | 122             | 253              | 89               | 59              | 77.4      | 16                         | 21   |
| 89.      | Fibrosarcoma       | F   | 54  | 13                   | 1   | 171  | 10    | 30              | 64              | (101)           | (9)              | (25)             | (17)            | 44.1      | 22                         | 50   |
| 90.      | Testicle           | M   | 42  | 11                   | 10  | 56   | 46    | 39              | 102             | 17              | (19)             | (29)             | (87)            | 41.6      | 15                         | 36   |
| 91.      | Pseudomyxoma       | M   | 47  | 35                   | 16  | 1    | 19    | (37)            | (27)            | (12)            | (15)             | (87)             | (162)           | 41.1      | 132                        | 321  |
| 92.      | Carcinoid          | F   | 68  | 19                   | 12  | 45   | 8     | 31              | 12              | 18              | 15               | 82               | (38)            | 28.0      | 162+                       | 579  |
| 93.      | Leiomyosarcoma     | F   | 32  | 31                   | 74  | 66   | (28)  | (87)            | (121)           | [21]            | [44]             | [27]             | [242]           | 74.1      | 453+                       | 611  |
| 94.      | Leukemia           | F   | 59  | 6                    | 36  | 183  | 6     | 36              | 32              | 44              | 36               | 112              | 63              | 55.4      | 430+                       | 776  |
| 95.      | Stomach            | M   | 55  | 34                   | 34  | 12   | 78    | 5               | 253             | 77              | 79               | 72               | 49              | 69.3      | 27                         | 39   |
| 96.      | Ovary              | F   | 51  | 128                  | 13  | 76   | 31    | 65              | 216             | 62              | 140              | 62               | 40              | 83.3      | 82                         | 98   |
| 97.      | Bronchus           | M   | 69  | 92                   | 30  | 90   | 160   | 43              | 147             | 32              | 20               | 135              | 125             | 87.4      | 31                         | 35   |
| 98.      | Bronchus           | F   | 67  | 93                   | 20  | 29   | 90    | 97              | 68              | 185             | 8                | 37               | 26              | 65.3      | 138                        | 211  |
| 99.      | Colon              | M   | 77  | 8                    | 69  | 80   | 14    | 30              | 9               | 57              | 68               | 14               | 21              | 37.0      | 15                         | 40   |
| 100.     | Colon              | M   | 38  | 3                    | 41  | 78   | 17    | 58              | 40              | 66              | 98               | 42               | (80)            | 52.3      | 152+                       | 291  |

<sup>a</sup> The sign + following the survival time of the patients treated with ascorbic acid means that the patient was alive on August 10, 1976. Parentheses ( ) indicate that the matched patient had the same sex, same kind of tumor, and same dissemination, but had an age difference greater than 5 years. Brackets [ ] indicate opposite sex, same tumor, same dissemination, age difference greater than 5 years. For kidney, Ca indicates carcinoma, Pap, papilloma.

<sup>b</sup> Diffuse urinary tract papillomatosis. The test cases (78 and 79) had lesions in both kidney and bladder. The nine control cases indicated had tumors of identical histology, but their disease was confined to bladder mucosa.

out in the selection of our two groups, we believe that they come close to representing random subpopulations of the population of terminal cancer patients in Vale of Leven Hospital. There is some internal evidence in the data in Table 1 to support this conclusion.

A somewhat detailed description of the circumstances under which the study was made may be called for. Of the 375 beds in Vale of Leven Hospital, 100 are in the surgical unit, 50 in the medical unit, and 25 in the gynecological unit. The 100 beds in the surgical unit are in the administrative charge of Ewan Cameron, and 50 of them are in his complete clinical charge, the other 50 being in the charge of the second Consultant Sur-

geon of the Hospital. The two Consultant Surgeons are assisted by a changing group of four Surgical Registrars, who are qualified surgeons on assignment for terms of 6 or 12 months from one or another of the Glasgow teaching hospitals. They are assisted by residents and interns. Although some cancer patients are initially treated in the medical or gynecological unit, there is a tendency for cases of advanced cancer of all kinds except leukemia and some rare childhood cancers, which are dealt with in a pediatric hospital in Glasgow, to gravitate into the surgical unit, in total probably 90% of all cases of cancer in the Loch Lomondside area.

All of the patients are treated initially in a perfectly con-

Table 2. Ratios of average survival times for ascorbate patients and matched controls, with statistical significance

| A             | B<br>(Days) | C<br>(Days) | D    | E<br>(Days) | F<br>(%) | G<br>(%) | H     | I        |
|---------------|-------------|-------------|------|-------------|----------|----------|-------|----------|
| Bronchus (15) | 136         | 38.5        | 3.53 | 47          | 47       | 8.7      | 24.5  | <<0.0001 |
| Colon (13)    | 282         | 37.0        | 7.61 | 59          | 54       | 20       | 7.63  | <0.003   |
| Stomach (13)  | 98.9        | 37.9        | 2.61 | 43          | 46       | 17       | 6.41  | <0.006   |
| Breast (11)   | 367         | 64.0        | 5.75 | 91          | 55       | 22       | 5.74  | <0.026   |
| Kidney (9)    | 333         | 64.0        | 5.21 | 88          | 67       | 22       | 8.35  | <0.002   |
| Bladder (7)   | 196         | 43.6        | 4.49 | 57          | 57       | 20       | 4.90  | <0.028   |
| Rectum (7)    | 226         | 55.5        | 4.10 | 71          | 86       | 33       | 7.57  | <0.003   |
| Ovary (6)     | 148         | 71.0        | 2.08 | 78          | 83       | 30       | 6.83  | <0.005   |
| Others (19)   | 172         | 56.8        | 3.03 | 67          | 53       | 27       | 5.28  | <0.027   |
| All (100)     | 209.6       | 50.4        | 4.16 | 65          | 60       | 25.7     | 55.02 | <<0.0001 |

A, Type of cancer and, in parentheses, number of ascorbate patients. There are 10 matched controls for each ascorbic acid patient. B, Average days of survival for ascorbate patients. C, Average days of survival for controls. D, The ratio B/C. E, Average days of survival for all subjects in group. F, Percentage of ascorbate patients surviving longer than E. G, Percentage of controls surviving longer than E. H, Value of  $\chi^2$  for F and G (two-by-two calculation). I, Corresponding value of  $P$  (one-tailed).

ventional way, by operation, use of radiotherapy, and administration of hormones and cytotoxic substances. For example, all of the 11 breast-cancer patients in the ascorbate-treated group, with the exception of one who first presented in a grossly advanced state, had already had mastectomy and radiotherapy and all, including the exception, had been given hormones, sometimes with considerable benefit; but all had relapsed by the time ascorbate supplementation was commenced, and it seemed clear that their tumors were escaping from hormonal control. Similarly, all of the seven bladder-cancer patients in the ascorbate-treated group, with one exception because of her frailty, had received megavoltage irradiation and several had had a partial cystectomy (one total) before ascorbate treatment was commenced when it seemed that these standard procedures had failed.

Treatment of terminal cancer patients with ascorbate was cautiously begun in November 1971, for reasons discussed in our earlier papers (1, 2), and has been continued because it seemed to have some value (4, 5). Once the practice had become locally established, the selection of a patient for treatment with ascorbate was often initiated by one of the younger surgeons (the Registrars), as they became familiar with the idea and convinced of its worth. The suggestion that ascorbate treatment be tried was made by Registrars less often during the first part of their 6 to 12 months' service than during the second part. For strong ethical reasons, every patient in the ascorbate-treated group was examined and assessed independently by at least two physicians or surgeons (often more than two) who all agreed that the situation was "totally hopeless" and "quite untreatable" before ascorbate was commenced. More than 20 different Registrars were involved in this way in allocating patients to the ascorbate-treated group. No criterion was used, except agreed "untreatability."

As described above, selection of 10 matched patients for the control group for each patient of the ascorbate-treated group was made independently by Dr. Frances Meuli. For each ascorbate-treated patient she was given a sheet listing age, sex, primary tumor type, and a brief synopsis of the clinical state and extent of dissemination at the time ascorbate was commenced, but not the survival time. She searched for cases matching these cases as closely as possible, and assigned to each, from the case history, the time when the patient was classified as "untreatable." We believe that the procedure that was followed has not introduced any serious error, and that the ascorbate-treated group and the control group are in fact sub-

populations of the population of "untreatable" patients selected in an essentially random manner.

Two hundred of the 1000 patients in the control group were completely contemporaneous with the ascorbate-treated patients. The mean survival time for these contemporaneous controls is 43.9 days, as compared with 52.4 days for the others (overlapping and historical). There has been no significant change in the treatment of patients with advanced cancer in Vale of Leven Hospital during the last 10 years, and the approximate equality of these values is not surprising.

#### The results of the study

The results of the study are given in Table 1 and summarized in Table 2, in which values for different kinds of cancer represented by six or more patients treated with ascorbate (60 or more controls) are shown. For each of the nine categories the ratio of average days of survival (ascorbate/controls) is greater than unity, the range being from 2.1 to 7.6, with ratio 4.16 for all 100 patients. The ratios are somewhat uncertain; for example, omitting the patient with longest survival in the colon group would decrease the ratio from 7.6 to 5.2. At the present time we cannot conclude that ascorbate has less value for one kind of cancer than for others. Our conclusion is that the administration of ascorbic acid in amounts of about 10 g/day to patients with advanced cancer leads to about a 4-fold increase in their life expectancy, in addition to an apparent improvement in the quality of life. This great increase in survival time results in part from the much larger numbers of the ascorbate patients than of the controls who live for long times, as is shown in Fig. 1. Sixteen percent of the patients treated with ascorbic acid survived for more than a year, 50 times the value for the controls (0.3%).

Statistical analysis shows that the null hypothesis that treatment with ascorbate has no benefit is to be rejected for each of the categories in Table 2. The results of a simple statistical test are given in the table. A reasonable dividing line, the average survival time for all the subjects, is given in column E, and the percentages exceeding this value are given in columns F and G. Column H contains the values of  $\chi^2$  obtained by a two-by-two calculation, and I gives the corresponding values of  $P$  (one-tailed). Similar values are obtained by nonparametric methods.

The fraction of survivors of the control group at time  $t$  is given to within about 2% by the exponential expression  $\exp(-t/\tau)$ . About 1.5% of the patients in this group live much

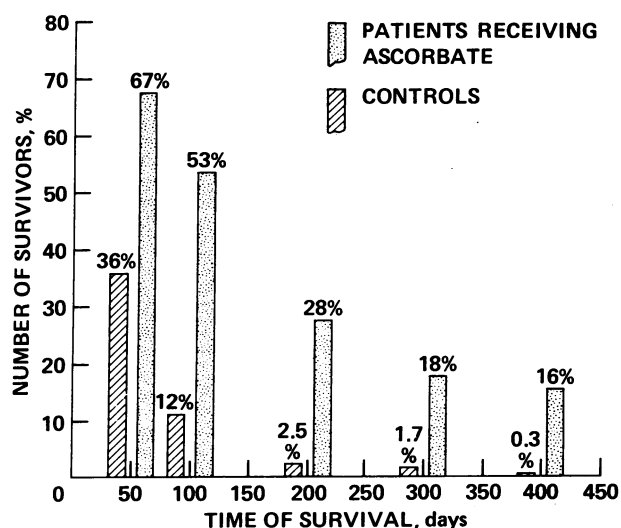


FIG. 1. The percentages of the 1000 controls (matched cancer patients) and the 100 patients treated with ascorbic acid (other treatment identical) who survived by the indicated number of days after being deemed "untreatable." The values at 200, 300, and 400 days for the patients receiving ascorbate are minimum values, corresponding to the date August 10, 1976, when 18% of these patients were still alive (none of the controls).

longer than would be indicated by this expression. A very close approximation to the observed survival curve is given by the assumption that the control group consists of two populations. One consists of 985 patients with number of survivors at time  $t$  given by the expression  $985 \exp(-t/\tau)$ , in which  $\tau$  has the value 45.5 days. This expression corresponds to a constant mortality rate for this subgroup, and its validity suggests that for them a single random process, occurring with a probability independent of time, leads to death. This probability is 2.2% per day. For 14 of the 1000 control patients the survival time is indicated to lie between 200 and 500 days. The distribution suggests that for this subgroup two random events lead to death, but the number of subjects is too small to permit this possibility to be tested thoroughly. One other patient, who survived 841 days, may constitute a third subgroup.

A similar analysis of the survival curve for the ascorbate-treated group shows that a considerably smaller fraction, 90%, constitutes the principal group, with number of survivors at time  $t$  equal to  $90 \exp(-t/\tau)$ ,  $\tau$  equal to 125 days. For the remaining 10% the average survival time is greater than 970 days. (These numbers are uncertain because the number of ascorbate-treated patients is small, only 100, and 18 of them were alive on August 10, 1976, their survival times being greater than the values used in the calculation.) A simple interpretation of these facts is that the administration of ascorbate to the patients with terminal cancer has two effects. First, it increases the effectiveness of the natural mechanisms of resistance to such an extent as to lead to an increase by a factor of 2.7 in the average survival time for most of the patients; 2.7 is the ratio of the two values of  $\tau$ , 125 and 45.5 days. Second, it has another effect on about 10% of the patients, such as to cause them to live a much longer time. This effect might be such as to "cure" them; that

is, to give them the life expectancy that they would have had if they had not developed cancer. On the other hand, it might only set them back one or more stages in the development of the cancer, in which case their life expectancy would be somewhat less than that corresponding to complete elimination of the effect of their having developed cancer. This uncertainty may be eliminated in the course of time, as the survival times of the 18 patients in the ascorbate-treated group who were still living on August 10, 1976 become known.

### Conclusion

In this study the times of survival of 100 ascorbate-treated cancer patients in Scotland (measured from the day when the patient was pronounced to have cancer untreatable by conventional methods) have been discussed in comparison with those of 1000 matched controls, 10 for each of the ascorbate-treated patients. The data indicate that deaths occur for about 90% of the ascorbate-treated patients at one third the rate for the controls, so that for this fraction there is a 3-fold increase in survival time, measured from the date when the cancer was pronounced untreatable. For the other 10% of the ascorbate-treated patients the survival time is not known with certainty, but it is indicated by the values in Table 1 to be more than 20 times the average for the untreated patients. The value 4.16 (Table 2) for the ratio of average survival times expresses the resultant of these two effects.

We conclude that there is strong evidence that treatment of patients in Scotland with terminal (untreatable) cancer with about 10 g of ascorbate (ascorbic acid, vitamin C) per day increases the survival time by the factor of about 3 for most of them and by at least 20 for a few (about 10%). It is our opinion that a similar effect would be found for untreatable cancer patients in other countries. Larger amounts than 10 g/day might have a greater effect. Moreover, we surmise that the addition of ascorbate to the treatment of patients with cancer at an earlier stage of development might well have a similar effect, changing life expectancy after the stage when ascorbate treatment is begun from, for example, 5 years to 20 years.

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