

**[Vitamin c metabolism during the treatment of acute pneumonia with antibiotics].**

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[https://www.mv.helsinki.fi/home/hemila/VitC\\_pneumonia.htm](https://www.mv.helsinki.fi/home/hemila/VitC_pneumonia.htm)

<https://www.mv.helsinki.fi/home/hemila/CP.htm> (Cochrane review)

<https://www.mv.helsinki.fi/home/hemila/CP> (Cochrane review references)

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The data in this paper had been published previously in 1970 by Mochalkin.

See comparison of the data at the end of this PDF-file, and see the 1970 paper:

<https://www.mv.helsinki.fi/home/hemila/T5.pdf>

Thus, this paper does not seem to have new data compared with the 1970 paper.

PhD N.I.Mochalkin

## **C-VITAMIN METABOLISM IN THE TREATMENT OF ACUTE PNEUMONIA WITH ANTIBIOTICS**

The use of antibacterial drugs, in particular broad-spectrum antibiotics, causes development of a particular kind of polyhypovitaminosis, which is severe in some cases. In parallel with a reduction in the level of B, C and other vitamins in body tissues, enzyme activity changes and the body's immunoreactivity is inhibited, which has a negative impact on the course of a number of diseases. In order to establish a theoretical basis for therapeutic use of vitamins in combination with a given antibiotic, it is therefore necessary to investigate vitamin metabolism in the specific disease.

The aim of this study is to investigate ascorbic acid metabolism in healthy individuals and patients suffering from acute bronchopneumonia during treatment with the most common antibiotics: penicillin, streptomycin, and oxytetracycline, comparing the course of the disease with antibiotics as a monotreatment and with the same antibiotics in combination with vitamin C, i.e. ascorbic acid (AA). Very little is known about this issue and there is no guidance for an appropriate vitamin C dosage that would prevent both vitamin C deficiency and vitamin C hypervitaminosis during treatment of acute pneumonia with antibiotics.

During the study, we assessed the body's vitamin C balance by observing the ascorbic acid level in the blood plasma following the method of Farmer and Abt and the excretion of AA in urine following the method of N.S. Zheleznyakova. The concentration of AA in blood and urine was measured before the start of the study and then every five days over a period of one month (observation also continued after discharge from hospital).

An AA concentration in blood plasma of 0.8–1.2 mg % (S.M. Ryss, V.V. Yefremov, and Ingalls) and in urine of 0.7–0.9 mg/h (N.S. Zheleznyakova) were considered normal.

In total 160 people took part in the study, 20 of them healthy and 140 suffering from acute pneumonia.

The first phase examined how antibiotics effect the vitamin C balance in healthy people. The study was conducted with volunteers in October when the body has good natural saturation of vitamin C. The 20 healthy people aged 22 during the period of observation were in similar living conditions with similar levels of nutrition and physical and mental stress. The subjects were divided into 4 equal groups of 5 people.

**TABLE 1.** Effect of antibiotics on the AA level in blood plasma in generally healthy subjects ( $M \pm m$ )

Group of subjects	Antibiotic	Ascorbic acid content (in mg%)						
		Initial	Day of observation					
			5th	10th	15th	20th	25th	30th
1st	Penicillin	0.81+0.02	0.68+0.02	0.69+0.01	0.72+0.01	0.75+0.02	0.76+0.02	0.80+0.03
2nd	Streptomycin	0.80+0.03	0.68+0.05	0.74+0.3	0.77+0.02	0.78+0.03	0.79+0.03	0.80+0.03
3rd	Oxytetracycline	0.80+0.03	0.51+0.03	0.46+0.02	0.56+0.03	0.68+0.01	0.70+0.02	0.77+0.02
4th	No antibiotics (control)	0.80+0.03	0.78+0.03	0.79+0.03	0.78+0.03	0.79+0.04	0.78+0.04	0.79+0.04

**TABLE 2.** Ascorbic acid level in blood plasma and in urine of patients suffering from acute pneumonia treated by antibiotics without AA (1<sup>st</sup> group), by the same antibiotics in combination with a minimum dose (2<sup>nd</sup> group) and in combination with an optimal dose (3<sup>rd</sup> group) of AA

Group of patients	Total	AA content in blood plasma (in mg%)					
		Initial	Day of observation				
			5th	10th	15th	20th	30th
1st	70	0.73(100%)	0.42(57.53%)	0.41(56.16%)	0.57(78.08%)	0.62(84.93%)	0.68(93.15%)
2nd	39	0.73(100%)	0.58(79.45%)	0.62(84.93%)	0.65(89.04%)	0.71(97.26%)	0.76(104.11%)
3rd	31	0.71(100%)	0.70(98.59%)	0.76(107.04%)	0.79(111.27%)	0.80(112.68%)	0.82(115.49%)

Group of patients	Total	Excretion of AA in urine (in mg%)					
		Initial	Day of observation				
			5th	10th	15th	20th	30th
1-я	70	0.68 (100%)	0.52(76.47%)	0.42(61.76 %)	0.42(61.76%)	0.45(66.18%)	0.65(95.59%)
2-я	39	0.63(100%)	0.56(88.89%)	0.53(84.13 %)	0.56(88.89%)	0.59(93.65%)	0.63(100%)
3-я	31	0.67(100%)	0.69(102.98%)	0.69(102.98 %)	0.71(105.97%)	0.72(107.46%)	0.92(107.46%)

After determining the initial level of AA in blood plasma in all subjects, therapeutic doses of antibiotics were prescribed for a period of 10 days. The 1<sup>st</sup> group received penicillin daily in doses of 600,000 IU (100,000 IU every 4 hours with injections at 9 am and 9 pm and phenoxymethylpenicillin between the injections). The 2<sup>nd</sup> group received one 500,000 IU streptomycin injection per day. The 3<sup>rd</sup> group of patients received 600,000 IU of oxytetracycline orally per day (100,000 IU every 4 hours). The 4<sup>th</sup> group was a control group that did not receive any antibiotics. The results obtained are listed in Table 1.

The data shows a significant fall in AA level during antibioticotherapy and a continuing deficit of AA in blood after antibiotics were no longer taken up until the 30<sup>th</sup> day of observation. For subjects receiving an average therapeutic dose of penicillin, the AA level in blood fell by approximately ¼ compared to the initial value, as measured on the 5<sup>th</sup> and 10<sup>th</sup> day of observation. On the other hand, the initial level of AA in the 2<sup>nd</sup> group was 0.80 mg%, where the effect of streptomycin was to reduce the concentration to 0.68 mg% by the 5<sup>th</sup> day and to 0.74 mg% by the 10<sup>th</sup> day.

The most obvious C vitamin deficit occurred in patients receiving oxytetracycline. From an initial baseline value of 0.80 mg%, the AA level in this group fell to 0.50 mg% by the 5<sup>th</sup> day and to 0.46 mg% by the 10<sup>th</sup> day of observation ( $P < 0.001$ ).

Once patients had ceased to take antibiotics, the impaired metabolism of ascorbic acid started slowly to recover and by the 30<sup>th</sup> day the AA level was almost the same as the value for the control group and as the initial values. Systematic observation of the overall condition in the studied patients did not reveal any serious side effects, apart from loose stool in 2 out of 5 patients receiving oxytetracycline.

Once the patients had stopped taking antibiotics, the symptoms soon disappeared of their own accord.

These observations support our experimental studies on animals, where we demonstrated the negative effect of therapeutic doses of penicillin, streptomycin and oxytetracycline on C vitamin balance (N.I. Mochalkin).

We also investigated AA balance in patients suffering from acute pneumonia with antibioticotherapy and the course of the disease (as an indicator) when treated only by antibiotics and when treated by the antibiotics combined with a minimum and an optimal AA dose, determined experimentally.

The minimum and the optimal doses of ascorbic acid to prevent a deficit of AA during antibioticotherapy were determined experimentally on animals and tested in clinical settings. It was found, therefore, that 1 mg of ascorbic acid per 2000 IU of antibiotic is the minimum daily dose and an optimal daily dose is 1 mg of AA per 1000 IU of antibiotic.

A total of 140 patients with acute bronchopneumonia were observed. All patients were admitted to hospital within the first 2 days of disease, were kept under similar conditions, received similar treatment and nutrition and received complex therapy including antibiotics in average therapeutic doses over a period of 10 days. The same method of observation was used.

Depending on the specific primary treatment, the roughly homogeneous set of patients was divided into 3 groups. The first group (70 patients) was treated with antibiotics without additional AA: 25 patients received penicillin, 15 patients received streptomycin, 15 received penicillin and

streptomycin and 16 patients received tetracycline. The second group (39 patients) was treated with the same antibiotics combined with a minimum dose of AA: 15 patients received penicillin, 8 patients received streptomycin, 8 patients received penicillin and streptomycin and 8 patients received tetracycline. The third group (31 patients) was treated with the same antibiotics, but in combination with an optimal dose of AA: 10 patients received penicillin, 7 patients received streptomycin, 7 received penicillin and streptomycin and 7 patients received tetracycline. The data showing the AA level in blood and urine during treatment for all 3 groups is presented in Table 2.

While the AA level in blood fell by 43% by the 5<sup>th</sup> day of observation in patients in the group receiving antibiotics without AA, the level only fell by 20% in the group of patients receiving the same antibiotics, but in combination with a minimum dose of AA, and the C vitamin balance effectively remained constant (-1%) in the group where the same antibiotics were administered with the optimal dose of AA. After the patients stopped taking the antibiotics (from the 10<sup>th</sup> day), there was slow recovery from AA deficit and by the 30<sup>th</sup> day of observation only the AA level in the blood of the first group of patients had not reached the initial value.

The excretion of ascorbic acid in urine largely mirrored the AA concentration in blood.

According to B.E. Votchal, M.E. Slutsky, B.H. Hamzaliev and Casetta, the C vitamin balance in patients has a significant effect on the course and outcome of acute pneumonia.

An analysis of key clinical and laboratory indicators that characterise the course of acute pneumonia shows that the therapeutic efficacy of antibiotics increases considerably when given in combination with AA.

For example, by the 10<sup>th</sup> day of therapy body temperature recovered to normal on average in 77% of patients that had not received AA, whereas in the group of patients given antibiotics with a minimum dose of AA temperature had normalised in 94% of patients, and in 100% of patients in the group receiving antibiotics with an optimal dose of AA. By the 15<sup>th</sup> day of therapy moist rale disappeared in 68% of patients who had not received AA, in 97% of patients receiving a minimum dose of AA, and in 100% of patients receiving an optimal dose of AA; the ESR recovered in 58, 94, and 100% of patients respectively; leukocytosis disappeared in 81% of patients not receiving AA, in 97% of patients receiving a minimum dose of AA, and in 100% of patients receiving an optimal dose of AA; the X-ray pattern normalised only in 67% of patients not receiving AA, but in 84% of patients receiving a minimum dose of AA, and in 93% of patients receiving an optimal dose of AA. Finally, the average duration of treatment in hospital, where all observed patients were discharged only after all the above indicators had stabilized, was 23.7 days for patients not receiving AA, 19.1 days for patients receiving a minimum dose of AA, and 15.1 days for patients receiving an optimal dose of AA. The reduction in the duration of treatment for patients receiving AA is statistically significant.

When comparing key clinical and laboratory indicators for the course of the disease, the patients in the 2<sup>nd</sup> and 3<sup>rd</sup> groups did not show any statistically significant differences (except the length of stay in hospital); this shows that the minimum dose of AA was sufficiently effective in these cases.

The different outcomes of therapy can be explained by the status of AA metabolism in patients suffering from acute pneumonia. An analysis of our own data and the literature data does not leave any doubt that, in the case of acute pneumonia, as for other acute diseases fundamentally related to microbial infection, the intensity of redox processes rapidly increases. Consequently, the body's need for ascorbic acid as such a vital component in the redox reaction also increases. However, once AA consumption has increased, patients suffering from acute pneumonia do not receive sufficient amounts of AA with food to meet the body's increased demand. Using antibiotics in these

cases makes the situation worse for several reasons. Firstly, antibiotics cause the pathogen to die off on a large scale, accompanied by increasing intoxication, i.e. further intensification of redox reactions and therefore even greater demand for AA. Antibiotics also weaken the vital functions of the pathogen, creating favourable conditions for mobilization of immunobiological mechanisms, as a result of which the need for AA also rises. So the disease itself and antibioticotherapy create a web of mutually related causes resulting first in exhaustion of AA reserves in the body and then in the development and deepening of AA deficit. Additional intake of AA in these cases replaces the body's depleted reserves of AA. As a result, metabolic exchange intensifies and the body's immunoreactivity increases, which helps to shorten the duration of disease and improves the outcomes of acute pneumonia.

### Conclusion

1. Penicillin, streptomycin and oxytetracycline cause the ascorbic acid level in blood plasma and its excretion in urine to fall. Especially marked negative action was produced by oxytetracycline, somewhat lesser by streptomycin and still lesser by penicillin.

2. The recovery process lasts significantly longer in patients treated with antibiotics without ascorbic acid.

3. In order to prevent C vitamin deficiency developing, antibiotic treatment of acute pneumonia must be combined with simultaneous intake of ascorbic acid.

4. When choosing the dose of ascorbic acid, it is necessary to take into account the baseline level of AA and the type of antibiotic that is being administered. Penicillin should be combined with a minimum dose of ascorbic acid; streptomycin and, in particular, oxytetracycline should be administered with an optimal dose of AA.

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## C-VITAMIN METABOLISM IN THE TREATMENT OF ACUTE PNEUMONIA WITH ANTIBIOTICS

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Course therapeutic doses of penicillin, streptomycin and oxytetracycline in 20 healthy individuals and in 140 patients with acute pneumonia caused rapidly developing, progressing decrease of ascorbic acid content in the blood plasma and its decreased excretion with urine both in healthy individuals and in patients with acute pneumonia. Especially marked negative action on vitamin C balance in the organism was produced by oxytetracycline, somewhat lesser by streptomycin and still lesser by penicillin. Treatment with antibiotics in conjunction with the optimal dose of ascorbic acid promoted recovery of patients with acute pneumonia.

