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From The Old Age Pensioners' Town Copenhagen (Head: Physician in Chief T. Geill, M. D.) and from The Bispebjerg Hospital, Department C. Copenhagen (Head: Professor K. Secher, Physician in Chief, M. D.)

The Effect of Ascorbic Acid on the Carbohydrate Metabolism.

By

OLE SYLVEST

Copenhagen.

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During the last five or six years, the question of the effect of ascorbic acid on the carbohydrate metabolism has been subjected to examination from various quarters. The procedures usually adopted were the following: It was examined whether ascorbic acid — administered either intravenously or per os — had any effect on the blood sugar in sound persons or in diabetics when fasting or after a glucose load. A few authors have also tried to give ascorbic acid together with insulin and adrenalin.

The aggregate result is difficult to sum up, as findings varied. On the whole, they may be separated into two groups:

1) Cases in which there is a fall or a smaller rise than was to be expected in the blood sugar.

2) Cases in which there is no such fall.

Stepp, Schroeder and Altenburg find that after intravenous injection of 300 mg ascorbic acid, there is a fall in the blood sugar of 20—50 mg per cent, culminating 1 hour after injection and returning to normal values 1 ½ nour aıter. On the other hand, no fall is obtained in convalescents after infectious diseases. The authors find further that the effect of insulin is enhanced when ascorbic acid is given simultaneously.

Stoicescu and Gingold show that in sound persons 240 mg ascorbic acid administered intravenously or 500 mg administered per os give a slow, but definite fall in the blood sugar. The blood sugar curve after a glucose load also becomes more flat when ascorbic acid is given simultaneously.

Azerad, Lewin and Brochemin state, however, that in fasting patients, whose blood sugar curve is followed for 2 hours, and who are given from 50 to 600 mg ascorbic acid intravenously, they have found a fall only in 1 out of 11 cases, and when the experiment is repeated, the blood sugar of the patient in question also remains constant. Similar conditions are demonstrated by Armentano, Bentsáth, Hámori and Korányi after intravenous injection of 150 mg ascorbic acid in sound persons as well as diabetics. Oshima, Terashima and Matsutani also find no changes in the blood sugar curve after 300 mg ascorbic acid administered intravenously to normal persons; in diabetics, on the other hand, a fall in the sugar of the blood and the urine is almost invariably found.

Neither has Boehncke been able to find a fall in sound persons or in diabetics after 300 mg ascorbic acid given intravenously. With glucose and galactose tolerance tests and with insulin tests, no great fall is found if ascorbic acid is given simultaneously.

Secher demonstrates that in patients with serum-ascorbic acid = 0, the blood sugar curve after glucose loading is far higher than when the serum-ascorbic acid has been raised after supply per os of ascorbic acid for some time. Hjort finds similar conditions — although not quite so definite when raising a low serum-ascorbic acid by extra supply of ascorbic acid.

Pfleger and Scholl find that increased supply of ascorbic acid does not affect the fasting blood sugar value in sound persons or in diabetics, or the glucose tolerance curve in sound persons, whereas the insulin sensibility is said to be increased thereby. Roller shows that ascorbic acid per os to diabetics gives a fall in the sugar of the urine, and that after a standard lunch, sound persons as well as diabetics do not show so great a rise in the blood sugar after oral supply of ascorbic acid.

Hamne and Söderling have described a 2 ½ years old child with diabetes and scurvy, who responded poorly to insulin treatment until the vitamin C-deficiency was done away with.

Hamne has also found that the blood sugar curve of diabetics is

time of day, in order to ensure as far as possible that the organism is in the same state. The diet was ordinary Danish hospital diet, although it would probably have been more correct to give a standard diet during the experiment period.

It may be said beforehand that great variation in the results obtained does not preclude an effect of the ascorbic acid on the blood sugar, but in a reasonable number of experiments, the variations in the experiments will equalize each other, and thus a sufficiently strong effect will hardly be suppressed, but will find expression in a uniform tendency.

In order to obtain a collective view of the experiments, Table No. 2 also states the average values for the blood sugar of the 9 patients without and after injection of ascorbic acid, and the average values for all the 23 experiments in which ascorbic acid was given intravenously and the blood sugar was watched at corresponding times.

As the figures show, there is a slight, fairly gradual fall of 5—6 mg per cent from 9 to 12 o'clock in the fasting blood sugar without injection of ascorbic acid. The same blood sugar fall is obtained in 20 minutes after injection of ascorbic acid, and in all this experiment period, a maximum fall of about 14—15 mg per cent is obtained. Each single curve often shows a far greater fall after injection of ascorbic acid, but as these maximum falls do not appear at the same time in the experiment period, they will of course not be so obvious in the mean figures.

As the mean figures only give a survey of the total findings, a more detailed analysis of how each single patient responds to a load of ascorbic acid has been attempted. The two experiments on each patient are set forth separately in a chart with blood sugar values from the ascorbic acid tolerance test as ordinate and blood sugar values from corresponding times in the control experiment as abscissa. If the load has had no effect, i. e., if the two curves were identical apart from minor biological differences in the level, the dots would cluster around the »identity line», i. e., a line with a decline of 45° through the origin. [1]

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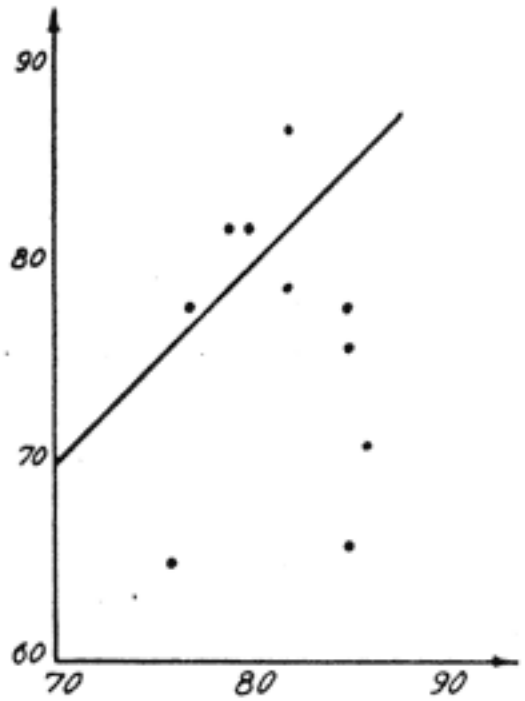
[1] It would perhaps be more correct to shift the two »identity lines» parallelly to the starting point of the two curves (i. e., for No. 7, to 87, 82); this has also been tried in all the charts, but gives at any rate only a slight difference which is of no consequence when judging of the results.



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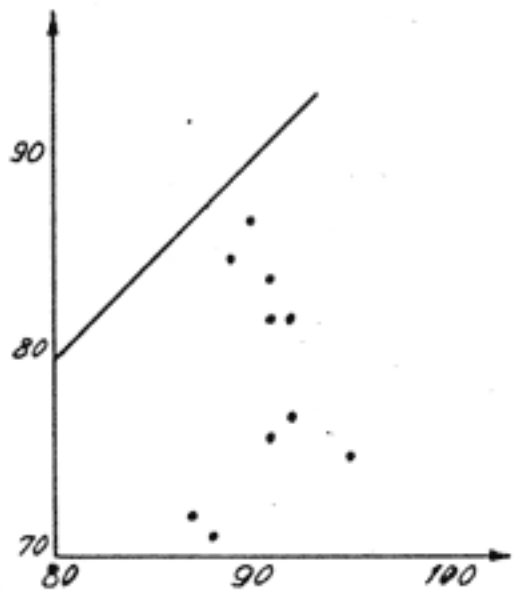

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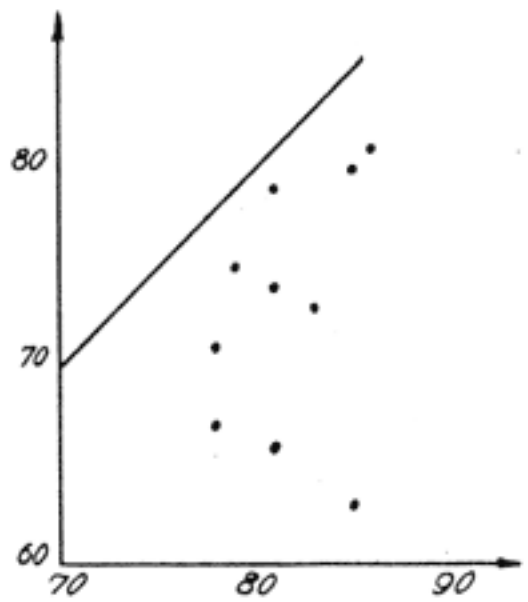

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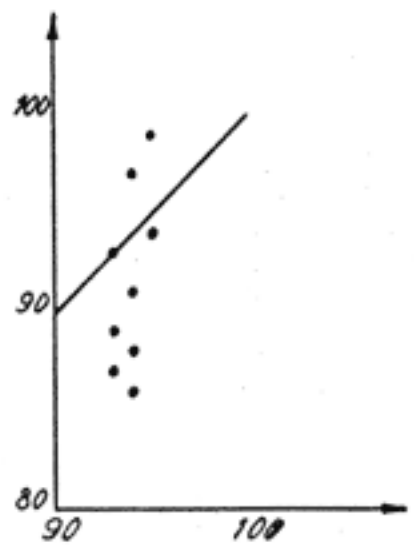

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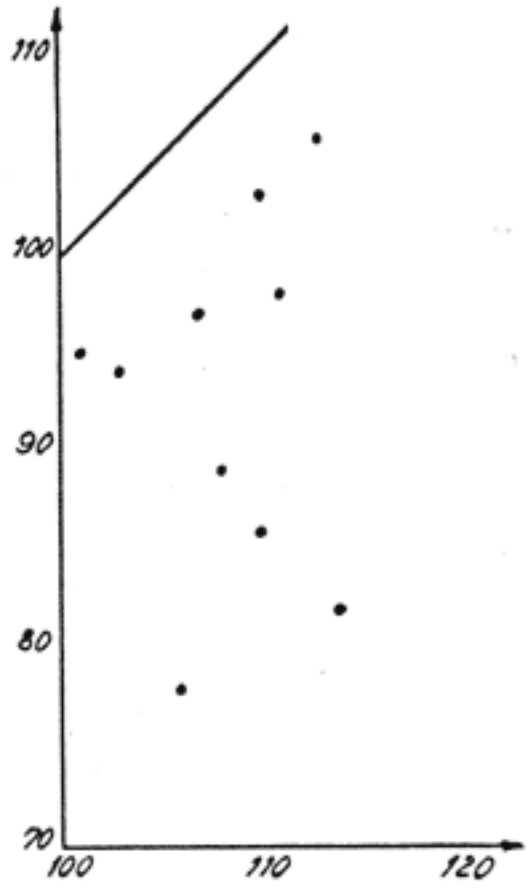

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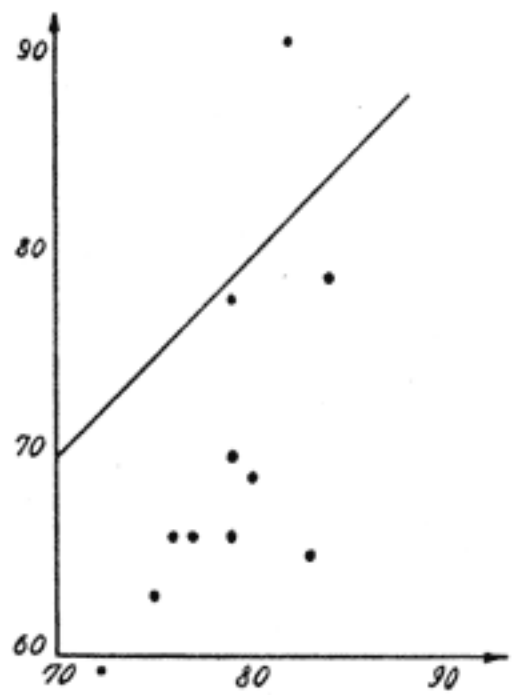

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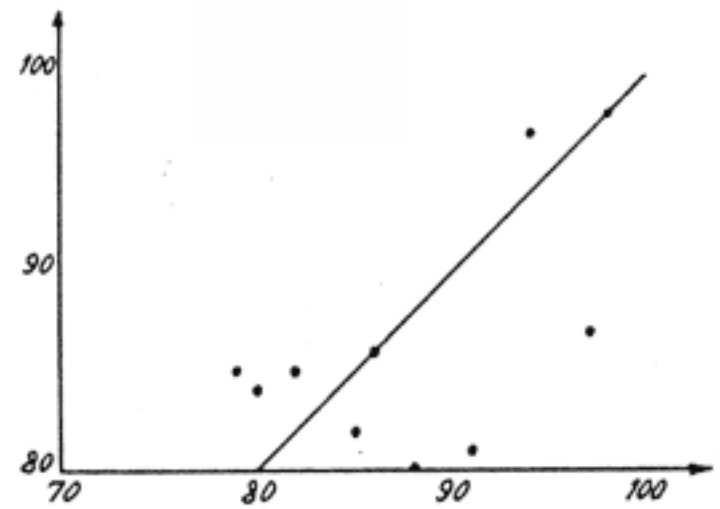

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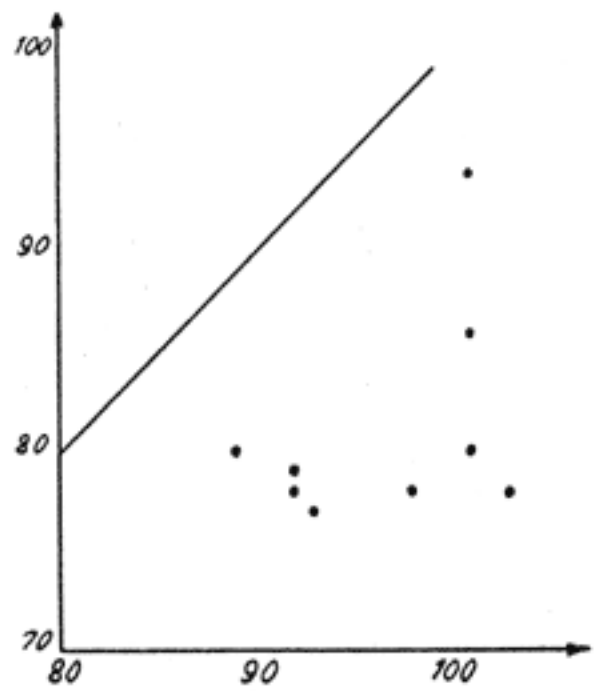

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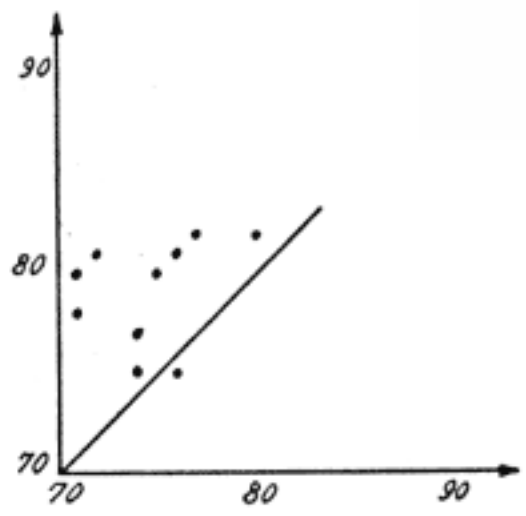

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As the charts show, in most cases the majority of the dots lies clearly below this line thereby expressing a lowering of the blood sugar level after injection of ascorbic acid. 5 of the experiments (Nos. 8, 9, 11, 12, 14) show a great lowering, 2 a smaller lowering (Nos. 7, 10), 1 is almost unchanged (No. 13) and 1 shows a great rise (No. 15). It is further seen that in the 3 experiments (Nos. 7, 8, 9), in which water was given as injection in the control experiment, a lowering of the blood sugar is also obtained after injection of ascorbic acid; consequently, it may be precluded that the fall in the blood sugar would be caused solely by the intravenous injection itself.

In order to ensure that the fall in the blood sugar is not due to the effect of ascorbic acid on the analysis of the sugar itself — an idea which would beforehand seem rather improbable — a control experiment is undertaken.

From patient No. 7, 20 cm^3 venous blood is filled into a glass containing strips of gauze prepared with lithium oxalate in view of preventing coagulation. The blood is divided into two equal portions, and to one is added a drop of an ascorbic solution of such concentration that the serum-ascorbic acid in the blood sample immediately after mixture amounts to 5.36 mg per cent — a concentration corresponding in the main to the figures obtained during the tolerance tests.

The two blood samples are placed in thermostat at 38°, and double blood sugar determination is made from each sample every 20 minutes in the usual way.

The results are given in Table No. 3. As the figures show, there is a regular fall in the blood sugar of both samples, whereby the normal glycolysis is manifest. The blood sugar is also found to fall equally low in both samples, the variations in the corresponding blood sugar samples in no case exceeding the allowable, as the error in each double determination is $\pm$ a couple of units in the last figure.

Further, the concentration of ascorbic acid in the blood sample is found to be at 9 o'clock: 5.36 mg per cent, at 10.30 : 4.72 mg per cent, at 12 : 3.92 mg per cent, a fall in a straight line which is probably owing to oxidation.

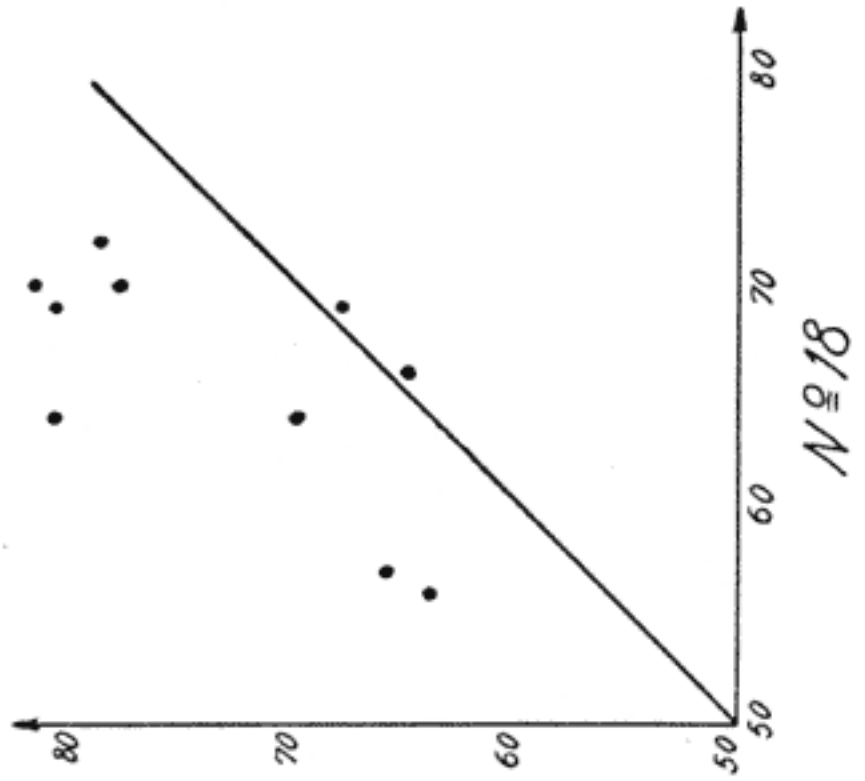
That the fall in the blood sugar is not an artificial factor caused by ascorbic acid during titration is also proved by the fact that

Table 3.

	Venous blood *without* addition of ascorbic acid	Venous blood *with* addition of ascorbic acid.
9 o'clock	79	79
9^{20} »	79	77
9^{40} »	75	74
10 »	70	74
10^{20} »	69	68
10^{40} »	67	64
11 »	64	64
11^{20} »	64	61
11^{40} »	62	59
12 »	62	60

Table 4.

No	16		17		18		19		20	
Sex	♂		♀		♀		♀		♀	
Age	32		71		79		71		72	
Diagnosis	Scurvy		Polyarthritis chr.		Polyarthritis chr.		Polyarthritis chr.		Polyarthritis chr.	
Date	$^{14}/_{10}$	$^{28}/_{10}$	$^{22}/_{10}$	$^{7}/_{11}$	$^{24}/_{10}$	$^{8}/_{11}$	$^{1}/_{11}$	$^{13}/_{11}$	$^{5}/_{11}$	$^{15}/_{11}$
Fasting serum-ascorbic acid in mg per cent.	0.00	1.64	0.00	1.72	0.00	1.64	0.00	1.52	0.00	1.92
9 o'clock ..	105	99	86	80	70	82	78	74	89	78
9^{20} » ..	104	89	74	72	69	81	66	73	82	77
9^{40} » ..	106	84	75	65	64	81	64	67	79	70
10 » ..	106	80	65	74	64	70	61	68	77	70
10^{20} »	103	81	76	76	56	64	68	65	74	71
10^{40} » ..	98	78	75	78	57	66	70	63	69	70
11 » ..	96	77	74	78	66	65	78	64	70	65
11^{20} » ..	96	78	74	77	69	68	77	67	65	61
11^{40} » ..	86	80	74	80	72	79	78	70	64	62
12 » ..	84	80	75	79	70	78	79	70	68	67


80
70
60
50
80
70
60
50

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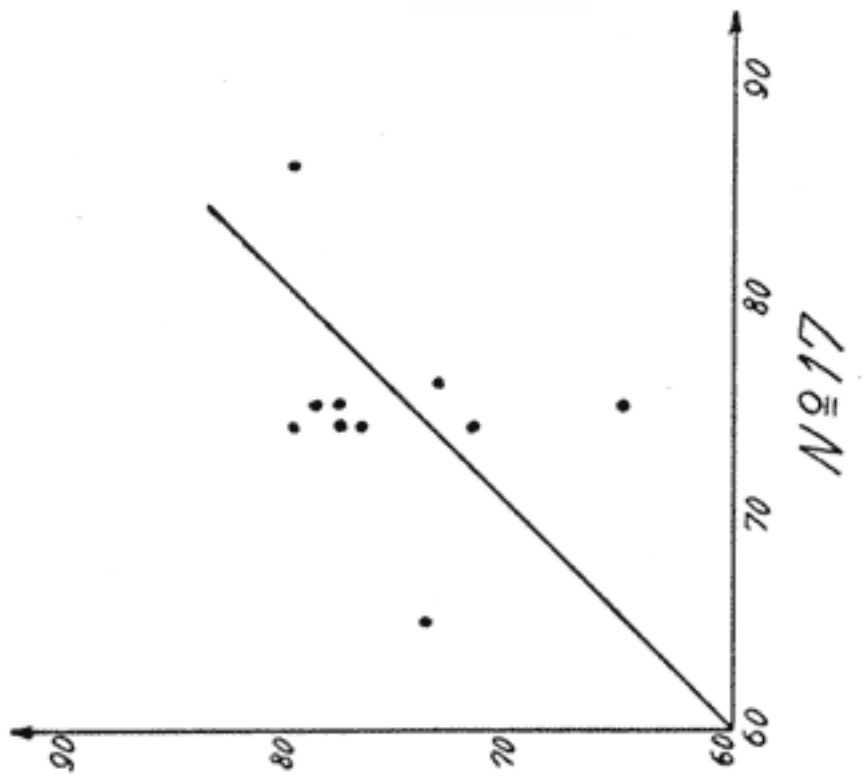
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80
70
60
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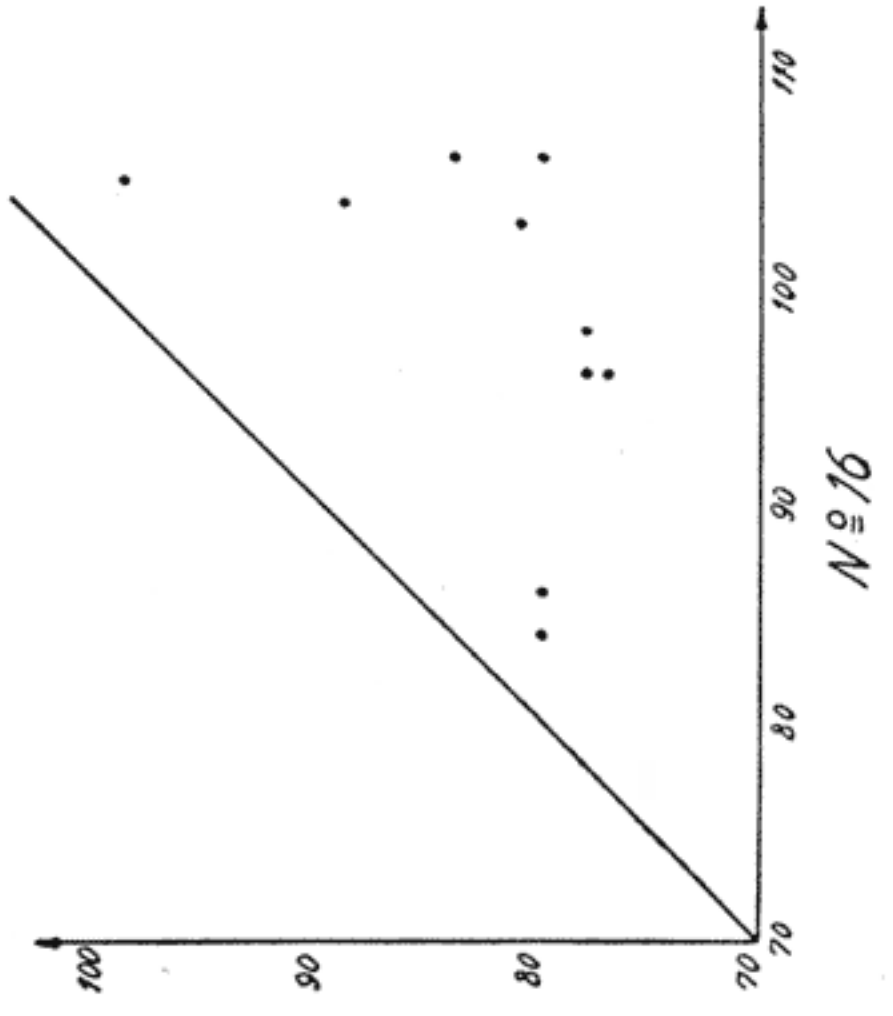
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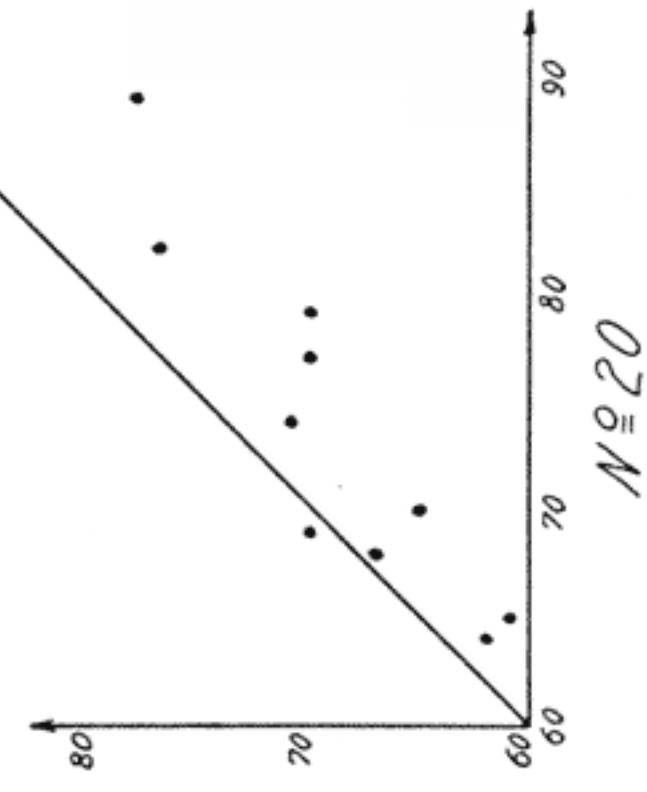
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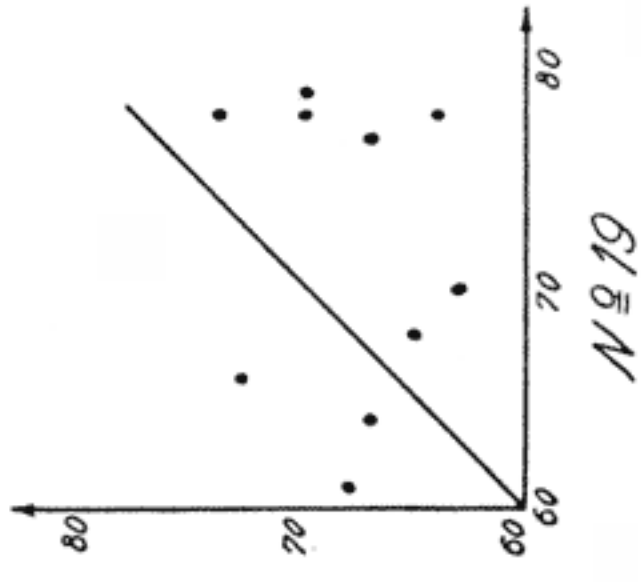
80
70
60
90
80
70
60

№ 19

during ascorbic acid tolerance tests, the greatest fall in the blood sugar never occurs simultaneously with the greatest ascorbic acid concentration.

In view of investigating whether the fall in the blood sugar during ascorbic acid load depends upon the ascorbic acid content of the blood at the commencement of the experiment, 5 patients were chosen whose serum-ascorbic acid was 0.00 mg per cent 4 of the patients (Nos. 17, 18, 19, 20) suffered from polyarthritis chr., and in such cases, the serum-ascorbic acid is usually 0 (Secher et al.), and the fifth patient (No. 16) had a pronounced scurvy.

Ascorbic acid tolerance tests have been made with these 5 patients, the ascorbic acid concentration in the blood being brought up to rather high values by addition for some time of 300 mg ascorbic acid daily per os. Thereupon a renewed loading with ascorbic acid takes place. The results have been put down in Table No. 4, and in order to compare the results, charts have been made out for each patient on the same principle as mentioned earlier, the blood sugar values of the tolerance test with serum-ascorbic acid 0 at the commencement of the experiment forming the abscissa, and the blood sugar values from the corresponding times in the experiment with high serum-ascorbic acid value at the commencement of the experiment forming the ordinate. The experiments do not seem to indicate any relation between initial ascorbic acid content and fall in blood sugar, as the results in the main equalize each other. Experiment No. 16 (the scurvy patient) is the only one of the experiments in which all the dots are clearly lodged below the »identity line», thereby expressing a deeper blood sugar fall in the tolerance test with the high initial ascorbic acid concentration; but from this isolated experiment with a patient suffering from scurvy, of course no conclusions can be drawn.

Nor does there seem to be any connection between the blood sugar fall on the one hand, and sex, age, or dosage of ascorbic acid (½ or 1 g) on the other hand; as already previously mentioned, neither is there any demonstrable dependence of the greatest blood sugar fall on the greatest serum-ascorbic acid concentration.

Conclusions.

In the material at hand, a lowering of the blood sugar has taken place in the majority of cases after intravenous injection of ascorbic acid. The experiments undertaken have not rendered it possible to demonstrate any rule for the depth of the fall in blood sugar, as there seems to be no relation between on the one and the blood sugar fall, and on the other hand the initial ascorbic acid content of the blood, the maximum serum-ascorbic acid concentration later on during the experiment period, the dosage of ascorbic acid (½ or 1 g), and sex or age.

I owe my thanks to Mr. Rasch. Ph. D., for statistical assistance.

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