NASA PROJECT NO. NRG 10-012-001

THE SEMI-ANNUAL REPORT

May 1 - October 31, 1966

THE MALAISE OF SPACE-MAN AND ITS POSSIBLE RELATION TO SEROTONIN

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THE PRESENT SEMI-ANNUAL REPORT CONSISTS OF TWO PARTS

PART ONE: The preliminary data essential for the experiments with animals placed in a simulated high altitude air chamber. This data relates to the blood serotonin concentration in normal animals of various genera which will be used in our experiments with high altitude air, the deviations in blood serotonin concentrations under various abnormal conditions, such as cancer and hypercholesteremia, as well as some data of blood concentration in normal men and cardiac patients.

PART TWO: The effect of simulated high altitude air on blood serotonin and serum ascorbone concentrations.

Remark: The tests on serum ascorbone concentration are included in this study because it was found that there seems to be some intrinsic relationship between serotonin and ascorbone levels, an indication that the ascorbic acid metabolism seems to be altered in cases of elevated blood serotonin concentration.

INTRODUCTORY

SEROTONIN

During the last decade, a great deal of attention has been given in this country and abroad to the biologic activity of serotonin, a metabolite, otherwise known as 5-hydroxytryptamine (5-HT). The activity of this metabolite covers a large field of physiological phenomena, including glandular function, specifically adreno-cortical hormones, inflammation, and vascular and cellular permeability.

In their classic study, Majno and Palade, using the electron microscope, demonstrated that serotonin played an important role in the increase of vascular permeability. In fact, serotonin was found more potent in this respect than histamine, on a mole-to-mole basis. The investigators, discussing the pathogenesis of the endothelial leaks, stressed the fact that the electron microscopic findings suggested that the endothelial cells became partially disconnected along the intercellular junction, with numerous endothelial openings, through which the molecules of protein and lipid were able to pass. Majno et al. pointed out that the leaking vessels always belonged to the venous side of the circulation. The heaviest deposits were found in venules 10 to 20 micra in diameter. Frimmer investigated the effect of subcutaneous injection of 5-HT on capillary permeability. He found that the permeability rate for large

colloidal molecules was considerably increased. Jenkins et al. observed an increase in the cellular membrane permeability after 5-HT application. Cater described marked changes in the blood pressure, with parallel changes in O_2 tension, in patients affected with malignant tumors and receiving 5-HT. This phenomenon indicated, according to Cater, that there was very little local masomotor control over tumor blood flow. Sullenberger et al. observed that in intravascular thrombosis there was a significant elevation of blood 5-HT, and an increased excretion of 5-hydroxy-indoleacetic acid in urine. Labendzinski and Bielski disclosed that there seemed to be a significant influence of 5-HT on the blood clotting system. Spaziani reported that administration of 5-HT creatinine sulfate to female rats produced a considerable increase in uterine water content. According to Markiewicz, 5-HT injected subcutaneously to dogs produced an adrenergic and cholinergic effect on blood fat content. Waugh and Beschel and Waugh and Pearl reported that 5-HT, injected intraperitoneally in small doses, induced in rats renal ischemia, with the lesions of a transient nature, but larger doses of the metabolite (up to 150 mg./kg.wt.) resulted in acute nephrosis and renal cortical necrosis, and occasionally also focal necrosis of the liver. Ziemlanski found that small doses of 5-HT increased and larger doses markedly inhibited secretion of gastric juice in dogs. Adams

discovered that large doses of 5-HT administered during pregnancy, might produce abortion, while smaller doses might cause anomalies in babies.

Remark: The vascular permeability and body dehydration caused by serotonin deserves particular attention.

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ASCORBONE

In our preliminary experiments we estimated the serum ascorbic concentration. Here we came to an unexpected phenomenon. The animals or men who have an elevated blood serotonin concentration contained a large amount of dehydroascorbic acid, otherwise known as ascorbone. Accordingly, in our more recent tests, we estimated both TAA (total ascorbic acid) and ascorbone.

A basic fact about ascorbic acid metabolism in the human or animal body was, for a number of years, misunderstood. For it was believed that Vitamin C exists in plasma in the reduced form of ascorbic acid. More recently, it was proved not to be so. Stewart et al. demonstrated that in certain conditions, a significant part of ascorbic acid in plasma was in the form of dehydroascorbic acid otherwise known as ascorbone. Patterson established the relationship between ascorbone and experimental diabetes. Lloyd and Sinclair suggested that dehydroascorbic acid should be called ascorbone. Patterson and Mastin have shown that ascorbone is highly toxic when given intravenously, causing hypertension in rats in doses as low as 5 mg./kg.wt., and that it might cause atrophic changes in the fur, liver and death in large doses. According to Raiha, ascorbone is ten times as fat soluble as ascorbic acid. Sokoloff et al. reported that in coronary and related diseases the concentration of

ascorbone is about three fold higher than in healthy persons of the same age group. McGraw and Desmarais, Slusher and Roberts, McGraw, Stewart et al., Harris et al., Khalil and others stressed the fact that the metabolism of ascorbic acid is influenced by cortical hormones, and it has an adversary effect on the functions of the small blood vessels, particularly of the capillaries.

Our experiments on rats, injected with 5-hydroxytryptamine creatinine sulfate have demonstrated that such a treatment resulted in the appearance of ascorbone in large quantities.

The data of this experimentation is reported in Tables 1-4.

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EXPERIMENTAL

PART I

PRELIMINARY INVESTIGATION ON SEROTONIN

NASA PROJECT: NRG 10-012-001

Tests and Data Preliminary to the Project

BLOOD SEROTONIN AND URINE 5-HIAA IN ANIMALS WITH NORMAL AND ABNORMAL PHYSIOLOGICAL CONDITIONS

1. Normal mice
2. Normal rats
3. Normal guinea pigs
4. Normal rabbits
5. Normal chicks

6-7. Cancerous rats

8. Normal humans
9. Cardiac humans
10. Humans suffering from vertigo

11. Hypercholesteremic rabbits
12. Hypercholesteremic rats
13. Hypercholesteremic rabbits given ascorbic acid
14. Hypercholesteremic rats given ascorbic acid
15. Cardiac patients receiving heavy doses of ascorbic acid

No. 17

March 1 - 5, 1966

MICE

Young, healthy male mice

Weight, gm.	Blood serotonin concentration, γ/ml
15.5	.13
16.0	.12
14.3	.18
15.4	.15
12.4	.12
13.8	.17
17.0	.11
16.2	.10
15.8	.19
16.0	.20
15.8	.19
14.3	.22

Average weight gm.	Average concentration of serotonin in the blood, γ/ml
15.2	.158

Older, healthy male mice

20.4	.23
22.4	.18
25.3	.15
23.0	.14
23.3	.19
24.8	.23
26.5	.21
27.4	.14
26.2	.13
24.0	.26
27.5	.20
26.4	.15

Average weight gm.	Average concentration of serotonin in the blood, γ/ml
24.7	.18

No. 21-3

April 6 - 13, 1966

CHICKS

Baby chicks, healthy

Body weight, gm.	Blood serotonin concentration, γ/ml
110	2.10
123	2.53
108	2.43
98	2.85
105	2.07
125	2.78
140	2.81
152	2.39
142	2.03
144	1.94

Average body weight gm.	Average concentration of serotonin in blood, γ/ml
125	2.39

Adult chicks, healthy

1850	2.65
2259	2.25
2145	3.12
2340	3.35
2450	2.94

Average body weight gm.	Average concentration of serotonin in blood, γ/ml
2209	2.86

No. 19-2

March 5 - 15, 1966

RATS

Young rats, healthy, males

Weight, gm.	Blood serotonin concentration, γ/ml
62.0	.20
75.5	.18
66.0	.25
71.2	.26
66.8	.18
62.5	.22
58.5	.28
65.5	.30
51.6	.18
64.3	.19

Average weight gm.	Average concentration of serotonin in the blood, γ/ml
64.4	.22

Older rats, healthy, males

185	.24
205	.19
199	.26
210	.28
225	.15
168	.12
176	.14
180	.18
191	.22
202	.17

Average weight gm.	Average concentration of serotonin in the blood, γ/ml
194	.19

No. 18-2

April 5 - 9, 1966

GUINEA PIGS

Young guinea pigs, males

Body weight, gm.	Blood serotonin concentration, γ/ml
342	.22
298	.26
322	.31
290	.29
345	.25
336	.34
365	.41
382	.28
302	.24
288	.23

Average body wt.	Average concentration of serotonin in the blood, γ/ml
327	.28

No. 21-1

March 18 - 23, 1966

RABBITS

Young rabbits, healthy, males

Weight, gm.	Blood serotonin concentration, γ/ml.
1252	1.21
1265	1.29
1180	1.08
1256	1.02
1345	1.12
1520	1.25
1230	1.01
1146	1.24
1205	1.25
1245	1.03

Average weight gm.	Average concentration of serotonin in blood, γ/ml.
1264	1.15

Older rabbits, healthy males

2540	1.46
2632	1.35
2525	1.25
2090	1.58
2288	1.96
2543	2.23
2446	1.85
2218	2.15
2197	2.02
2750	1.90

Average weight gm.	Average concentration of serotonin in blood, γ/ml.
2423	1.775

No. 18-3-4

April 2- 18, 1966

FLEXNER RAT CARCINOMA

Blood Serotonin before and after transplantation of the tumor, γ/ml

Rat No.	Before Transp.	Days after Transplantation 5th	12th
1	.28	.37	.42
2	.32	.48	.52
3	.18	.24	.42
4	.25	.32	.40
5	.14	.46	.48
6	.23	.33	.45
7	.17	.25	.35
8	.21	.30	.45
9	.26	.46	.48
10	.36	.66	.68
Avg.	.24	.387	.465

No. 19-3

March 6 - 20, 1966

FLEXNER RAT CARCINOMA

Blood Serotonin before and after transplantation of the tumor. γ/ml.

Rat No.	Before Transp.	Days after transplantation 4	6	8	Tumor wt. gm. 12 days after
1	.25	.21	.24	.54	26.4
2	.20	.24	.30	.68	30.4
3	.20	.34	.28	.46	15.4
4	.18	.20	.46	.24	14.8
5	.24	.37	.24	.48	20.4
6	.16	.22	.28	.48	23.8
7	.22	.28	.34	.98	24.2
8	.28	.26	.34	.54	18.5
9	.24	.32	.20	.56	12.3
10	.16	.34	.28	.68	11.8
Avg.	.216	.278	.296	.564	19.8

#13-173-23

November 1965 - August 1966

Blood Serotonin Humans, γ/100 ml.

KL, age 25	13.2
AL, age 35	18.5
PS, age 41	17.3
NM, age 22	14.3
LCS, age 43	21.2
OK, age 39	16.5
WS, age 49	20.2
DR, age 47	26.4
WH, age 52	19.9
LJK, age 33	17.7
MM, age 22	14.8
HE, age 55	22.3
HJ, age 35	17.6
AC, age 37	16.4
TM, age 59	20.3
NG, age 63	19.6
IS, age 66	23.4
NS, age 64	19.5
BB, age 68	22.3
TF, age 65	19.3
BG, age 64	19.5
JKK, age 57	20.3
JN, age 69	21.2
RV, age 66	19.9
GM, age 71	23.4

Comment: There is a slight trend, in otherwise healthy humans to increase serotonin concentration in their blood.

#16-A-24-15

October 1964 - September 1966

Blood Serotonin in Cardiac Patients, γ/100 ml

Cardiac patients with low LPL

AN, age 54	32.3
RS, age 62	34.2
SS, age 52	37.2
LP, age 55	29.4
JT, age 66	38.8
SD, age 56	25.4
LO, age 57	39.2
DR, age 50	29.9
IG, age 58	37.7
DF, age 68	41.2
GT, age 57	35.4
GK, age 69	39.2
BL, age 64	33.2
NH, age 55	40.5
TM, age 59	37.5
FD, age 64	23.5
SP, age 46	36.6
E.L., age 53	37.7
NR, age 56	38.8
LD, age 62	24.2
AS, age 56	33.2
PP, age 65	28.2
LP, age 49	29.3
DR, age 69	24.5

Comment: The cardiac patients show an elevated concentration of serotonin in blood, with very few exceptions.

#11-14-B-123, T.M.

August 1965 - August 1966

Blood Serotonin the Patients with Vertigo, γ/100 ml

HM, age 42, Vertigo Grade I	25.3
AS, age 52, Vertigo Grade II	24.4
GK, age 62, Vertigo Grade III	31.4
LM, age 39, Vertigo Grade III	32.3
AK, age 34, Vertigo Grade IV	38.2
HB, age 55, Vertigo Grade III	28.4
LS, age 32, Vertigo Grade IV	35.5
PL, age 38, Vertigo Grade III	33.4

There is some tendency to a higher concentration of serotonin in the blood of patients affected with vertigo.

Not conclusive: too small scale a trial.

BRIEF SUMMARY

(1) Out of many genera and species of animals, two genera show a very high concentration of blood serotonin: rabbits and chicks. Both of these animals have a very pronounced tendency to form atheromatous lesions.

(2) Healthy men show an insignificant deviation in blood serotonin concentration, although with aging some trend is observed to increase blood serotonin concentration.

(3) Cardiac patients manifest, as a rule, a higher blood concentration of serotonin, although some exceptions were observed from this general rule.

(4) A small scale investigation of the patients affected with vertigo seems to indicate that their blood serotonin concentration is somewhat higher than in normal persons.

On the basis of the data thus reported:

Blood Serotonin Concentration

Average for mice: .158 and .18 unit/ml.

Average for chickens: 2.39 and 2.86 unit/ml.

Average for rats: .22 and .19 unit/ml.

Average for guinea pigs: .28 unit/ml.

Average for rabbits: 1.15 and 1.775 unit/ml.

Average for cancerous rats: .465 unit/ml.

Average for cancerous tumor rats: .564 unit/ml.

Human blood serotonin concentration: between 13.2 and 26.4 unit/100 ml.

Cardiac patient blood serotonin concentration: between 24.5 and 41.2 unit/100 ml.

Blood serotonin concentration in patients affected with vertigo: between 24.4 and 35.5 unit/100 ml.

EFFECT OF HYPERCHOLESTEREMIA ON BLOOD SEROTONIN CONCENTRATION

An extensive investigation was conducted for seven months on the possible effect of cholesterol feeding on blood serotonin concentration in rabbits. In this series 86 rabbits served as control, 105 rabbits were fed cholesterol, 200 mg./kg.wt./day for 6-7 months and 112 rabbits were fed cholesterol, 200 mg./kg.wt./day and given 250 mg./kg.wt./day ascorbic acid for 6-7 months.

The results of this experimentation has shown that:

Average blood serotonin concentration of 86 control rabbits was: 1.498.

Average blood serotonin concentration of 105 cholesterol fed rabbits was: between 2.83 and 4.71 unit/ml. depending on the blood total cholesterol level.

Average blood serotonin concentration of 112 cholesterol fed rabbits, 200 mg/kg.wt./day, receiving ascorbic acid, 250 mg./kg.wt./day was between .98 and 1.94 unit/ml. depending on the blood total cholesterol level.

Conclusions: (A) Hypercholesteremia tends to increase the blood serotonin concentration.

(B) Ascorbic acid given simultaneously with cholesterol to rabbits tends to decrease significantly the blood serotonin concentration.

The records of all individual rabbit tests are available in our folder concerning this project.

CONTROL RABBITS

SEROTONIN

In the present study, the effect of cholesterol-feeding on blood serotonin and urine 5-HIAA concentration was investigated.

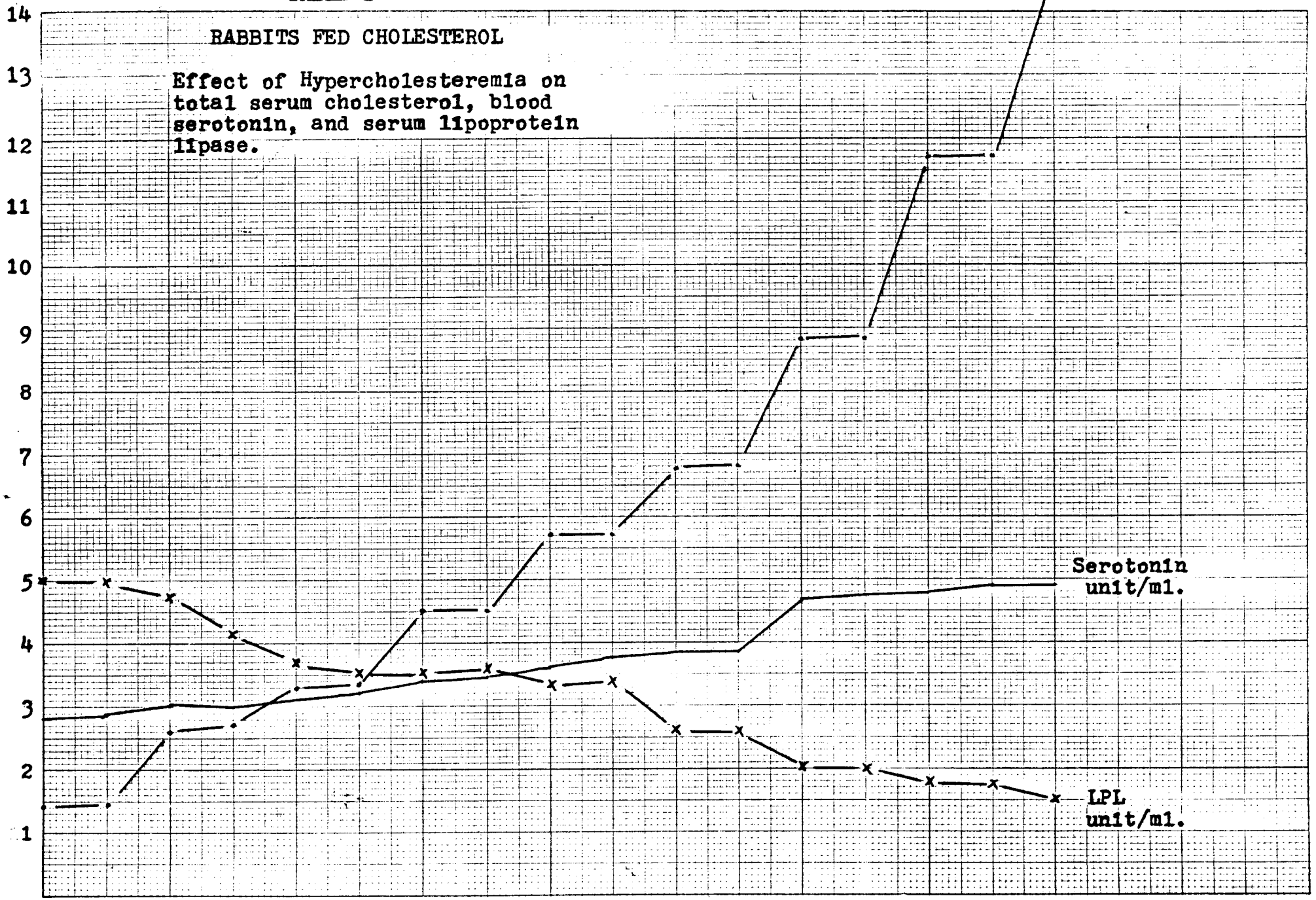
86 rabbits served as control:

Average total serum cholesterol, mg/dl:	61.6
Average blood serotonin content, unit/ml.:	1.498
Average Urine 5-HIAA concentration, unit:	.5036
Average Lipoprotein Lipase serum activity, unit:	.577
Average Body weight, gm.:	2280

EFFECT OF HYPERCHOLESTEREMIA IN RABBITS ON SEROTONIN CONCENTRATION IN THEIR BLOOD AND ON THE ACTIVITY OF LIPOPROTEIN LIPASE

All rabbits were fed cholesterol, from 150 to 200 mg/kg.wt./day for several months. Only after three-four months of feeding, a change in serotonin concentration in blood was observed.

TABLE I



EXPLANATION OF TABLE I

Rabbit Fed Cholesterol, 200 mg/kg.wt./day

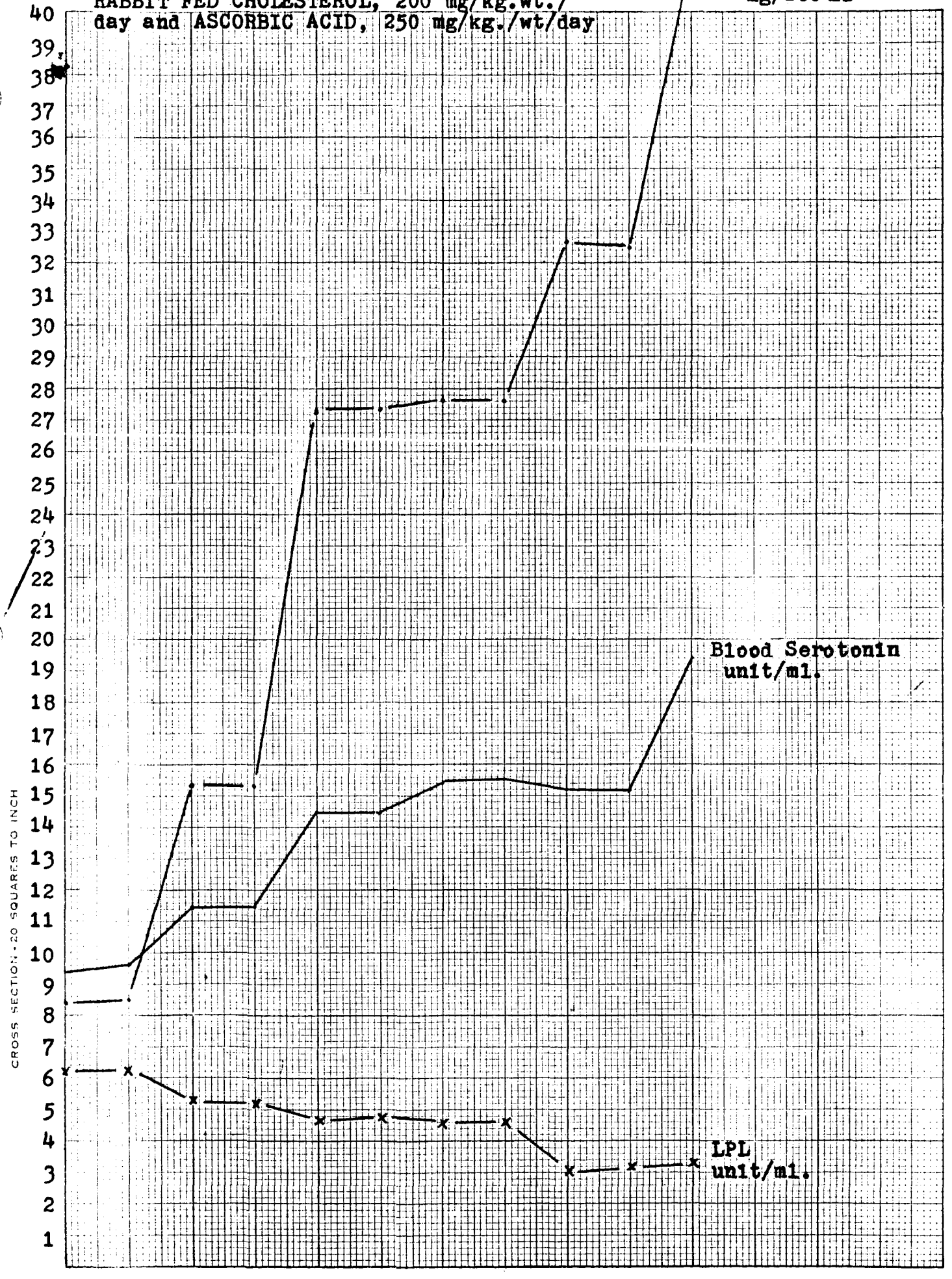
Total Chol. mg/100 ml.	No. of Rabbits	Avg. Total Cholesterol mg/100 ml.	Average Serotonin un./ml	Average LPL un./ml
88-205	18	143.0	2.83	.5018
206-299	19	259.0	3.05	.4358
300-399	16	333.0	3.08	.381
400-496	9	445.0	3.316	.327
510-607	11	560.0	3.37	.362
608-799	7	675.0	3.47	.344
800-998	13	882.0	3.86	.273
1120-1300	9	1176.0	4.617	.208
1330-1650	3	1476.0	4.71	.156

BRIEF SUMMARY

Feeding rabbits with cholesterol, 100-200 mg/kg.wt./day for 6-8 months, not only increases the blood total cholesterol from the average normal level of 5-75 mg/100 ml. up to 800-1400 mg/100 ml. but also suppresses the activity of lipoprotein lipase, from the normal level of about .600 unit/ml. to 250 units or less, and increases the blood concentration of serotonin from an average 1.2 unit/ml. to about 4.0 unit/ml.

THE INFLUENCE OF HEAVY DOSE, LONG RANGE ASCORBIC ACID THERAPY ON THE TOTAL CHOLESTEROL, LIPOPROTEIN LIPASE ACTIVITY, BLOOD SEROTONIN CONCENTRATION AND URINE 5-HIAA CONCENTRATION IN RABBITS FED CHOLESTEROL 200 MG/KG.WT./DAY FOR 2-8 MONTHS.

TABLE II
RABBIT FED CHOLESTEROL, 200 mg/kg.wt./
day and ASCORBIC ACID, 250 mg/kg./wt/day



EXPLANATION OF TABLE II

Total Chol. mg/100 ml.	No. of Rabbits	Avg. Total Cholesterol mg/100 ml.	Average Serotonin un./ml	Average LPL un/ml
48-98	7	84.6	0.98	.610
106-196	39	146.0	1.17	.553
204-250	24	227.8	1.469	.509
252-299	24	275.0	1.56	.483
320-360	17	323.0	1.52	.473
	1	652.0	1.94	.331

BRIEF SUMMARY

Ascorbic acid, given to the rabbits fed cholesterol, 200 mg/kg.wt./day, in the amount of 250 mg/kg.wt./day, decreased drastically the blood total cholesterol from 800-1200 mg/100 ml. at the end of six-eight months of feeding, to an average 300-350 mg/100 ml. It stimulated the activity of lipoprotein lipase almost to its normal blood concentration, .450-.500 unit/ml, and decreased considerably the blood concentration of serotonin, down to 1.5-1.6 unit/ml, the metabolite normal level in rabbits.

EFFECT OF 5-HYDROXYTRYPTAMINE CREATININE SULFATE (5-HT) ON SERUM ASCORBONE CONCENTRATION IN RATS

SEROTONIN AND ASCORBONE

In our previous experiments we reported that after repeated injections of serotonin, 5-HT creatinine sulfate for 5-7 days, 40 mg./kg.wt./day/rat, certain symptoms, vertigo-like, were observed. Also, an increased apathy (or fatigue) was noticed in some animals. Besides checking the serum serotonin level in animals, we determined their serum ascorbic acid. Normal rats, or rabbits, never contain in their serum the oxidized form of ascorbic acid, dehydroascorbic acid, known as ascorbone. However, in certain conditions, specifically when the serotonin level is elevated (or in grave fat metabolism disturbances), we found the presence of ascorbone in a relatively large amount, often up to 25% of the total ascorbic acid.

The following tables summarize the results of our preliminary tests which are now being repeated on a larger scale.

TABLE I

Normal rats. Serum serotonin and ascorbone concentration

Average weight 140 gm.

	Serotonin unit/ml.	Total Ascorbic Acid, mg./100 ml.	Ascorbone mg./100 ml.
1.	.13	.45	--
2.	.15	.48	--
3.	.135	.46	--
4.	.18	.42	.004
5.	.16	.38	--
6.	.15	.42	--
7.	.12	.48	--
8.	.14	.38	--
9.	.135	.48	--
10.	.16	.47	.006

In normal rats, no reduced form of ascorbic acid is detectable, except traces in two cases.

TABLE II

Serotonin treated rats. Total dose: 280 mg./kg.wt./rat
Serum serotonin and ascorbone concentration

Average weight 137 gm.

	Serotonin unit/ml.	Total Ascorbic Acid, mg./100 ml.	Ascorbone mg./100 ml.
1.	.35	.38	.11
2.	.38	.34	.12
3.	.42	.33	.09
4.	.51	.28	.13
5.	.44	.38	.10
6.	.37	.34	.09
7.	.39	.33	.08
8.	.52	.41	.11
9.	.56	.34	.08
10.	.43	.29	.07

In serotonin treated rats, a part of ascorbic acid appears in the form of its reduced form, ascorbone. In some animals 25 or more % of total ascorbic acid is in the form of ascorbone.

TABLE III

Normal rabbits. Serum serotonin and ascorbone concentration

	Serotonin unit/ml.	Ascorbone mg./100 ml.
1.	2.3	--
2.	2.5	--
3.	2.7	--
4.	2.1	--
5.	2.8	.001
6.	3.1	--
7.	2.7	--
8.	2.55	--
9.	2.9	--
10.	2.8	--

No presence of ascorbone was detected in normal rabbits, except a small trace in one case.

TABLE IV

Serotonin treated rabbits. Total dose: 280 mg./kg.wt./rabbit
Serum serotonin and ascorbone concentration

	Serotonin unit/ml.	Total Ascorbic Acid, mg./100 ml.	Ascorbone mg./100 ml.
1.	6.8	.67	.16
2.	7.2	.56	.13
3.	5.7	.66	.18
4.	6.3	.69	.17
5.	6.9	.49	.12
6.	7.2	.82	.22
7.	7.1	.77	.21
8.	7.9	.89	.23
9.	6.8	.78	.21
10.	8.1	.73	.19

In serotonin treated rabbits serum, ascorbone is present in the concentration from 20 to 25%. There are signs in animals of a mild vertigo and of considerable fatigue. Certain dehydration.

INTRODUCTORY

From our preliminary study, we arrived at the conclusion that rats seem to be the best subjects for experiments with high altitude air. A rat is very similar in its physiology and metabolic factors to man. A normal rat has a rather low blood serotonin concentration and it is quite constant, unless there are present some abnormal conditions, such as cancer or a disturbance of fat metabolism factors. Its average blood serotonin concentration is $.18 \pm .3$, and any significant increase in the blood serotonin levels is clearly determined. Furthermore, for more than three years we have been investigating in rats various factors, enzyme and fat metabolism factors, and have considerable and well-standardized methods. All this is very important when we shall start to try various anti-serotonin (antimetabolites) agents in order to prevent the increase in blood serotonin levels at high altitude. Technically rats offer an easy subject too. We are able to test per week, 24 rat blood or about 100 rats per month. In this respect rats offer a much better opportunity for exact results than rabbits with their very high natural blood serotonin. It is essential that the blood be taken immediately after the rats are removed from the chamber. At 30,000 feet altitude, they show signs of vertigo and

also of considerable dehydration. We have not yet started to collect their urine, but we are planning to do this after a sufficient number of tests have been conducted.

On the other hand, rats differ from man in the ability to produce ascorbic acid and therefore the data we are now collecting on the effect of simulated high altitude air on ascorbone is only of relative value. For this reason, we are planning also to use guinea pigs, who are unable, like man, to produce ascorbic acid.

Thus as far as our current study is concerned, we intend to use for our experiments only rats and guinea pigs.

In order to obtain a sufficient amount of blood, both rats and guinea pigs are killed, with blood taken from their heart.

EFFECT OF SIMULATED HIGH ALTITUDE AIR ON BLOOD SEROTONIN CONCENTRATION

Patient: NASA PROJECT - RAT TEST #1-4-A Age: Sex Number:

~~Effect of simulated high altitude air on blood serotonin concentration and serum~~

Address Simulated altitude 30,000 feet ascorbone concentration.

Physician Average for 6 rats, males, beginning weight 112.0 g.

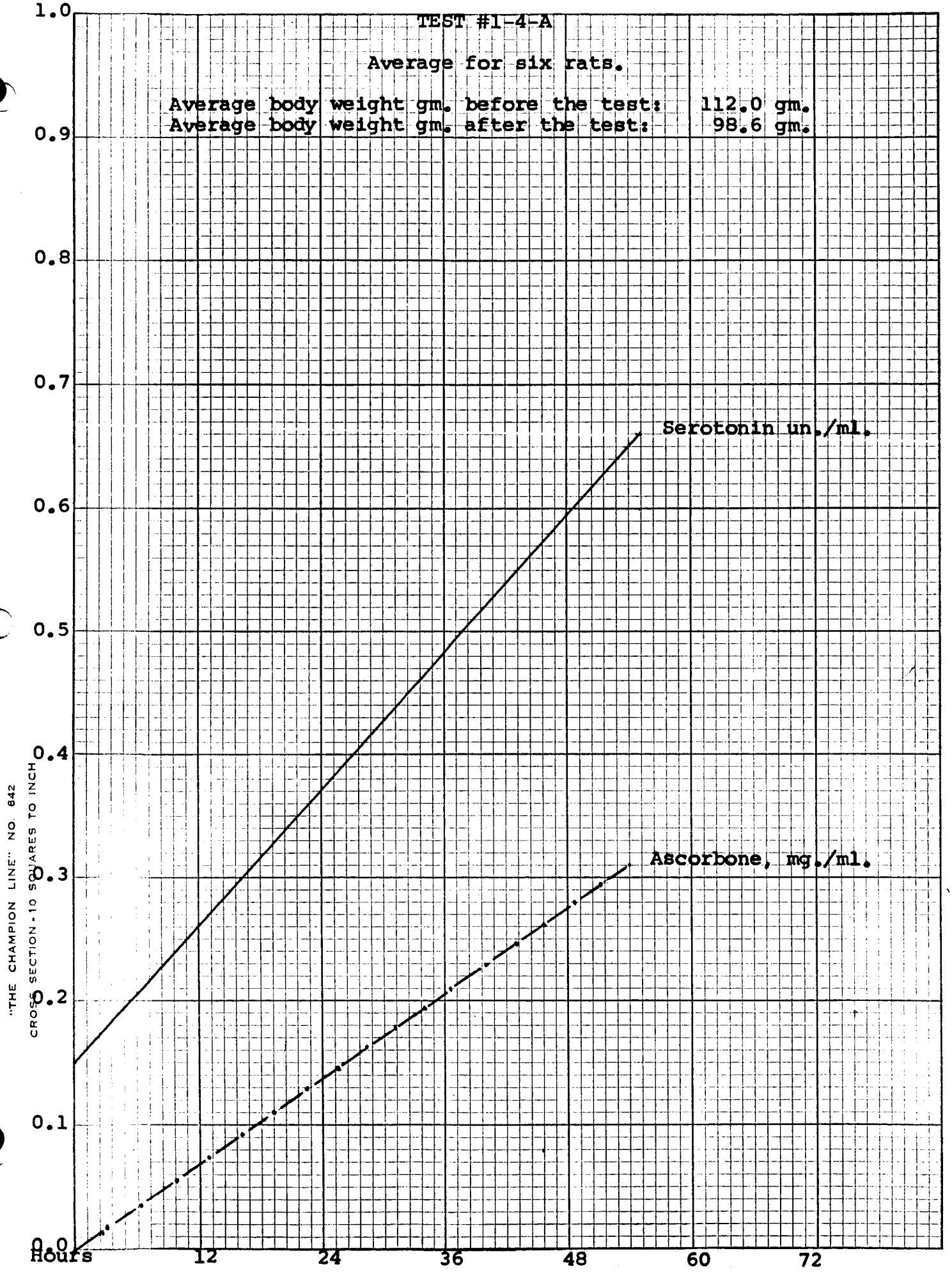
Past History

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	95
Free Cholesterol, mg/dl	43
Cholesterol ester, mg/dl	52
Cholesterol ester ratio %	54
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~dk~~ ml, blood	.60
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl, TAA serum	0.88
Ascorbic acid, mg/dl AA, serum	0.30
Ascorbone, mg/dl serum	0.58
Blood Pressure	
Body weight, gm., Final Average	98.6

Comment: In this experiment, the blood serotonin concentration was, at the altitude of 30,000 feet 400% higher than in the control rats of the same age (.15 unit/ml). Serum ascorbone concentration was increased considerably, reaching 50% of the Total AA.

EFFECT OF SIMULATED HIGH ALTITUDE AIR, 30,000 FEET ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



Patient: NASA PROJECT - RAT TEST #1-4-B Age: _____ Sex _____ Number: _____

Effect of simulated high altitude air on blood serotonin concentration and serum ascorbone concentration.

Address Simulated altitude 30,000 feet

Physician Average for 6 rats, males, beginning weight 114.0 g.

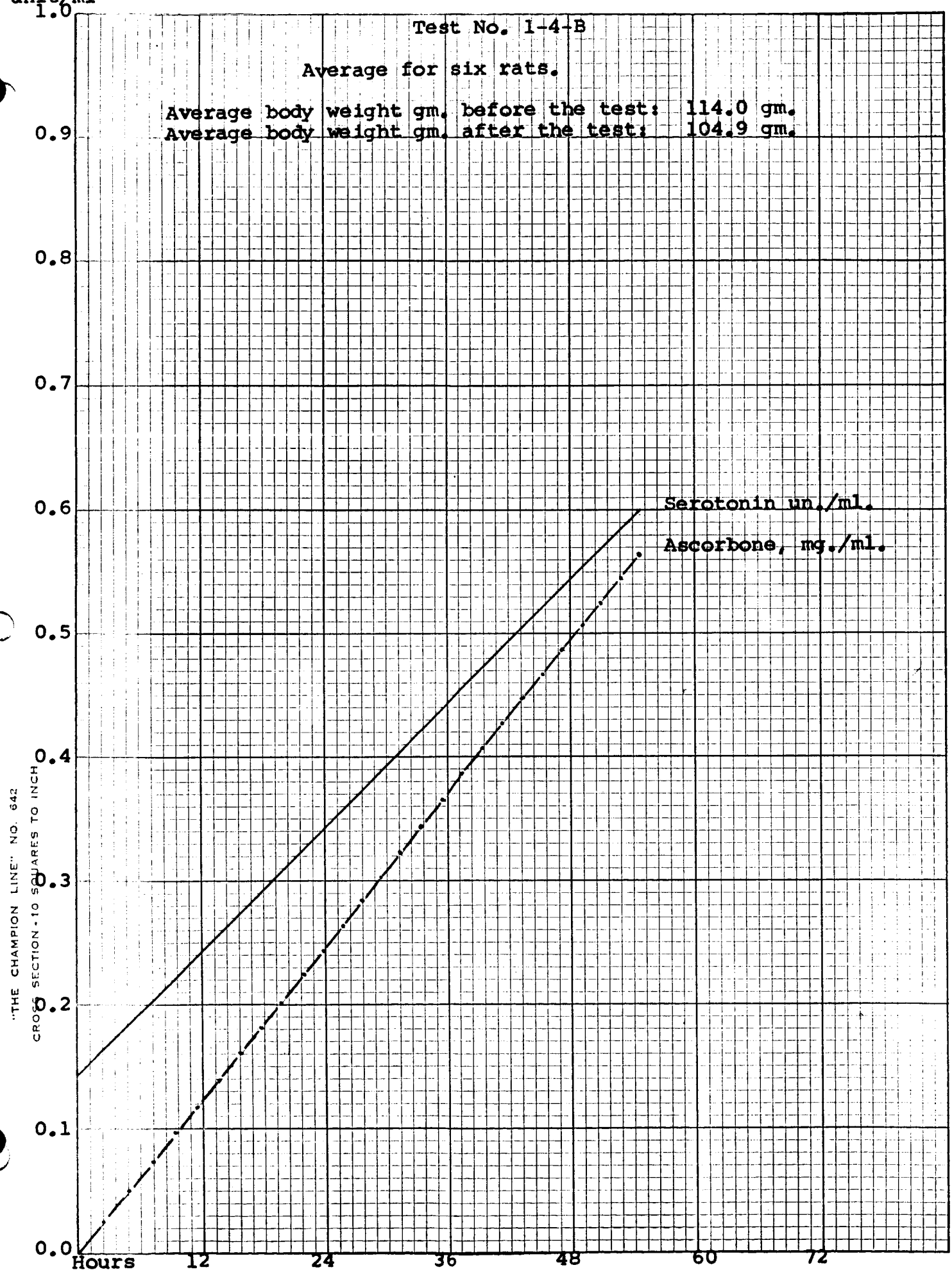
Past History _____

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	95
Free Cholesterol, mg/dl	50
Cholesterol ester, mg/dl	45
Cholesterol ester ratio %	48
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~dl~~ ml, blood	.67
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl, TAA serum	0.60
Ascorbic acid, mg/dl AA, serum	0.29
Ascorbone, mg/dl serum	0.31
Blood Pressure	
Body weight gm., Final Average	104.9

Comment: In this experiment, the blood serotonin concentration was, at the altitude of 30,000 feet 446% higher than in the control rats of the same age (.15 unit/ml.). Serum ascorbone concentration was increased considerably, reaching 50% of the Total AA.

EFFECT OF SIMULATED HIGH ALTITUDE AIR, 30,000 FEET ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



Patient: NASA PROJECT - RAT TEST #1-5-A Age: _____ Sex _____ Number: _____

Effect of simulated high altitude air on blood serotonin concentration and serum ascorbone concentration.

Address Simulated altitude 30,000 feet

Physician Average for 6 rats, males, beginning wt. 115.6 g.

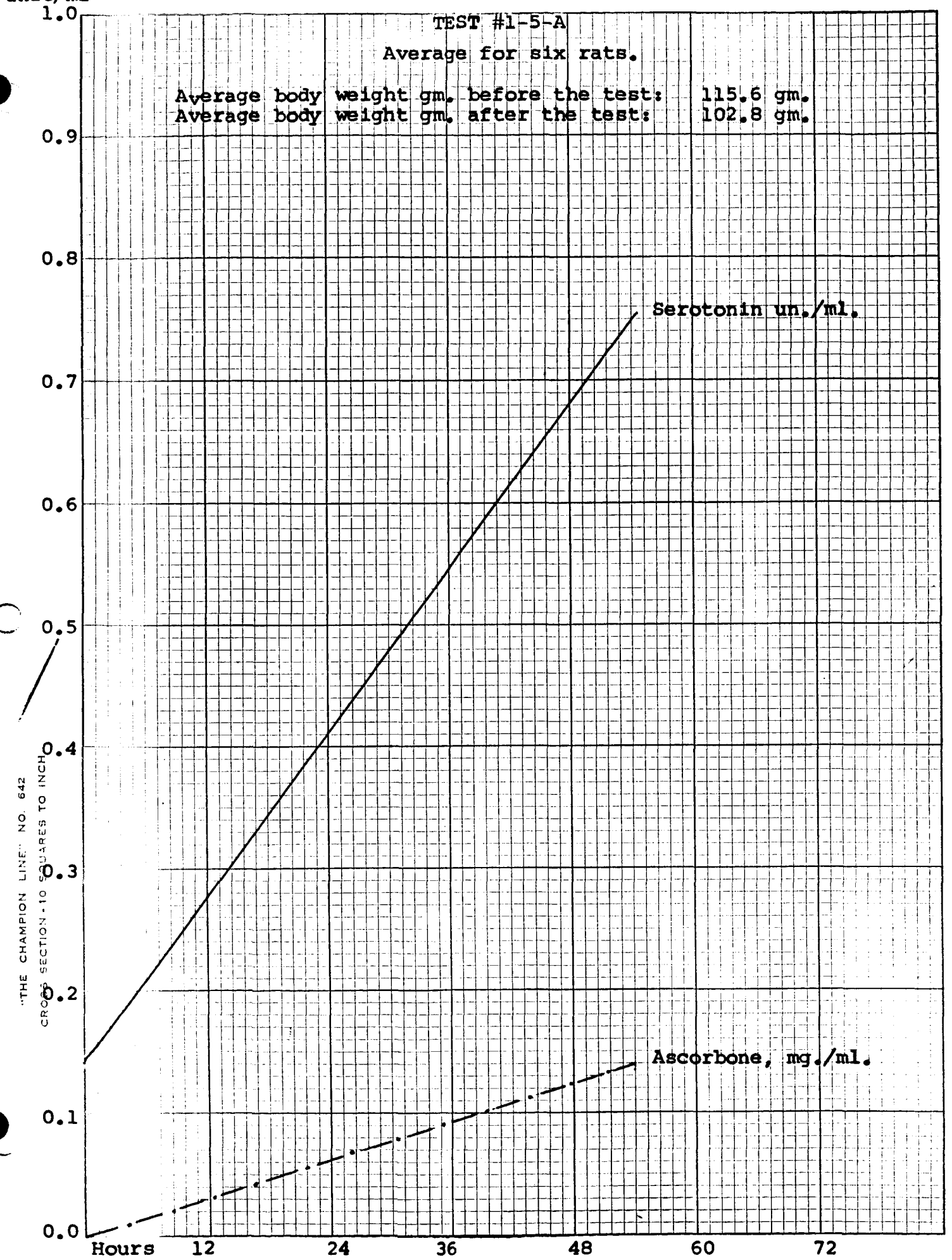
Past History _____

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	104
Free Cholesterol, mg/dl	28
Cholesterol ester, mg/dl	76
Cholesterol ester ratio %	73
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~xx~~ ml, blood	0.75
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl, TAA serum	0.84
Ascorbic acid, mg/dl AA, serum	0.70
Ascorbone, mg/dl serum	0.14
Blood Pressure	
Body weight gm., Final average	102.8

Comment: The blood serotonin concentration at 30,000 feet of simulated high altitude air was 500% higher than at normal altitude for the same age (.15 unit/ml.).

EFFECT OF SIMULATED HIGH ALTITUDE AIR, 30,000 FEET ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



Patient: NASA PROJECT - RAT TEST #1-5-B Age: _____ Sex _____ Number: _____

Effect of simulated high altitude air on blood serotonin concentration and serum ascorbone concentration.

Address Simulated altitude 30,000 feet

Physician Average for 6 rats, males, beginning wt. 124.6 gm.

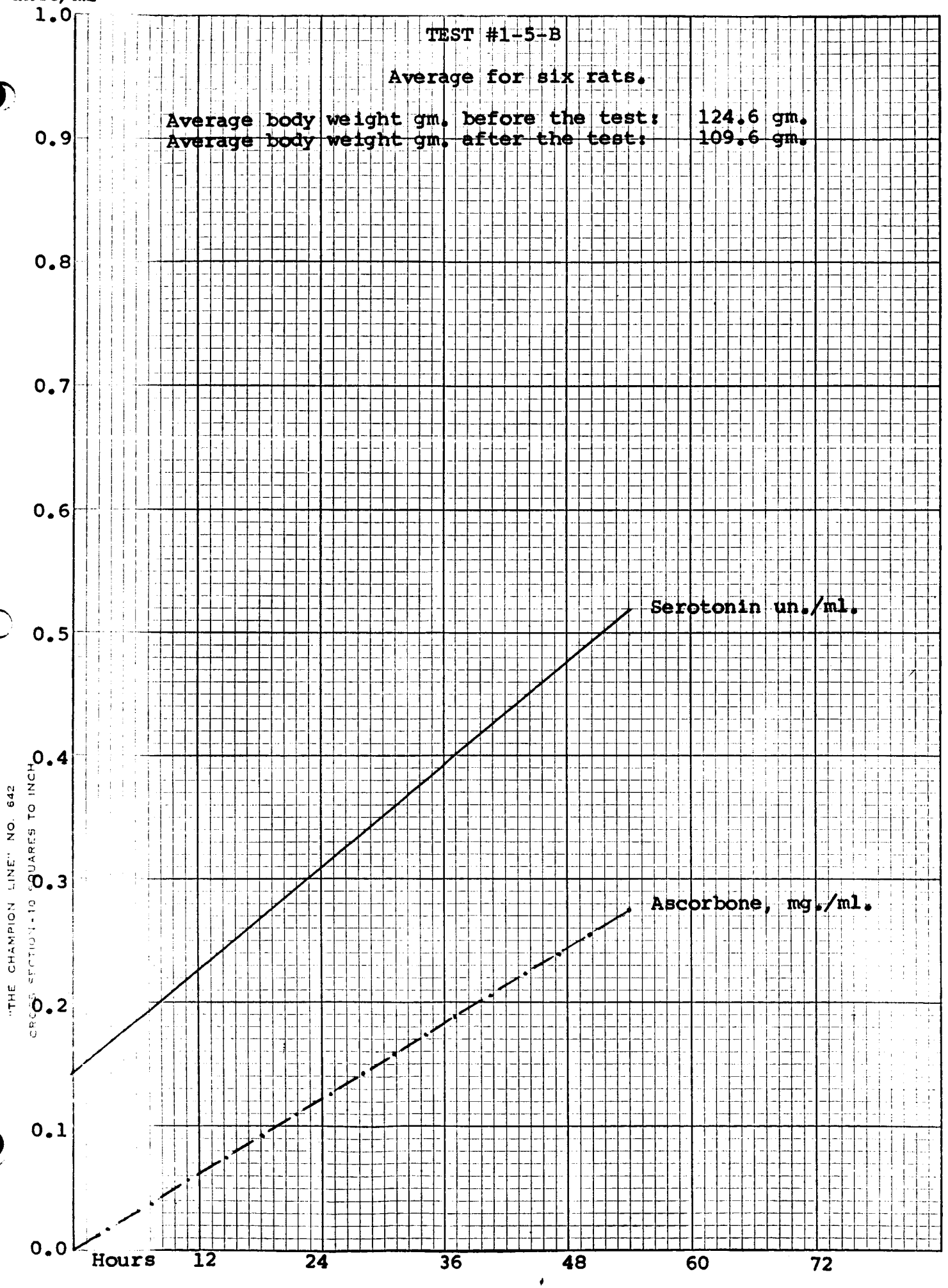
Past History _____

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	102
Free Cholesterol, mg/dl	34
Cholesterol ester, mg/dl	68
Cholesterol ester ratio %	67
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~dx~~ ml. blood	0.52
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl, TAA serum	0.88
Ascorbic acid, mg/dl AA, serum	0.60
Ascorbone, mg/dl serum	0.28
Blood Pressure	
Body weight gm., Final Average	109.6

Comment: The blood serotonin concentration at 30,000 feet of simulated high altitude air was 346% higher than at normal altitude for the same age (.15 unit/ml.).

EFFECT OF SIMULATED HIGH ALTITUDE AIR, 30,000 FEET ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



Patient: NASA PROJECT - RAT TEST #1-6-A Age: _____ Sex _____ Number: _____

Address Effect of simulated high altitude air on blood serotonin concentration and serum ascorbone concentration.

Physician Simulated altitude 30,000 feet

Average for five rats, males.

Past History Average body wt. gm. before the test: 158.0 gm.

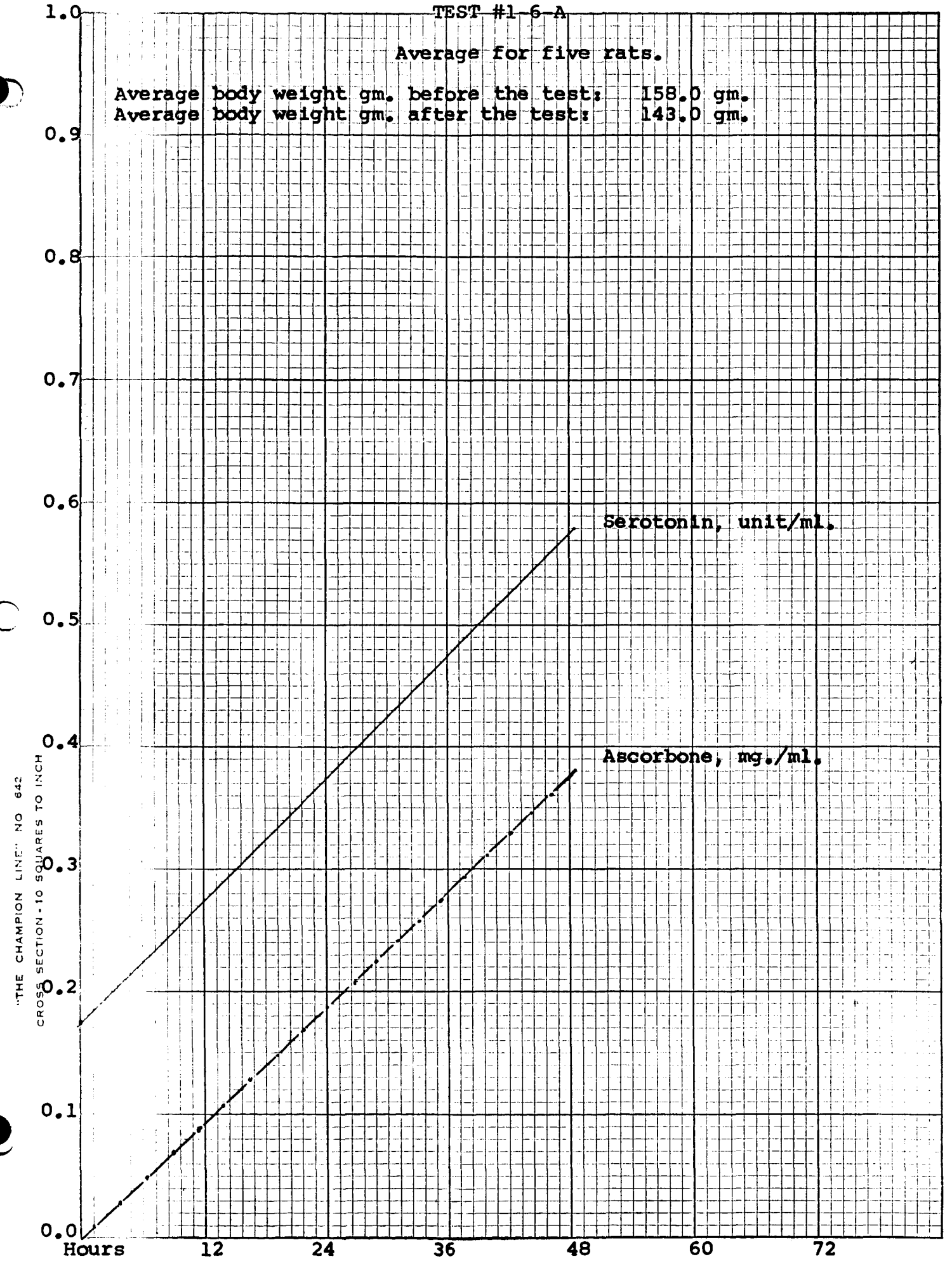
Average body wt. gm. after the test: 143.0 gm.

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	82
Free Cholesterol, mg/dl	20
Cholesterol ester, mg/dl	62
Cholesterol ester ratio %	75
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~xx~~ ml. blood	.58
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl TAA serum	1.28
Ascorbic acid, mg/dl AA, serum	0.80
Ascorbone, mg/dl serum	0.38
Blood Pressure	
Body weight	

Comment: The blood serotonin concentration at 30,000 feet of simulated high altitude air was 322% higher than at normal altitude for the same age (.18 unit/ml.).

EFFECT OF SIMULATED HIGH ALTITUDE AIR, 30,000 FEET ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



Patient: NASA PROJECT - RAT TEST #1-6-B Age: Sex Number:

Address Effect of simulated high altitude air on blood sertonin concentration and serum ascorbone concentration.

Physician Simulated altitude 30,000 feet
Average for five rats, males.

Past History Average body wt. gm. before the test: 168.0 gm.
Average body wt. gm. after the test: 149.5 gm.

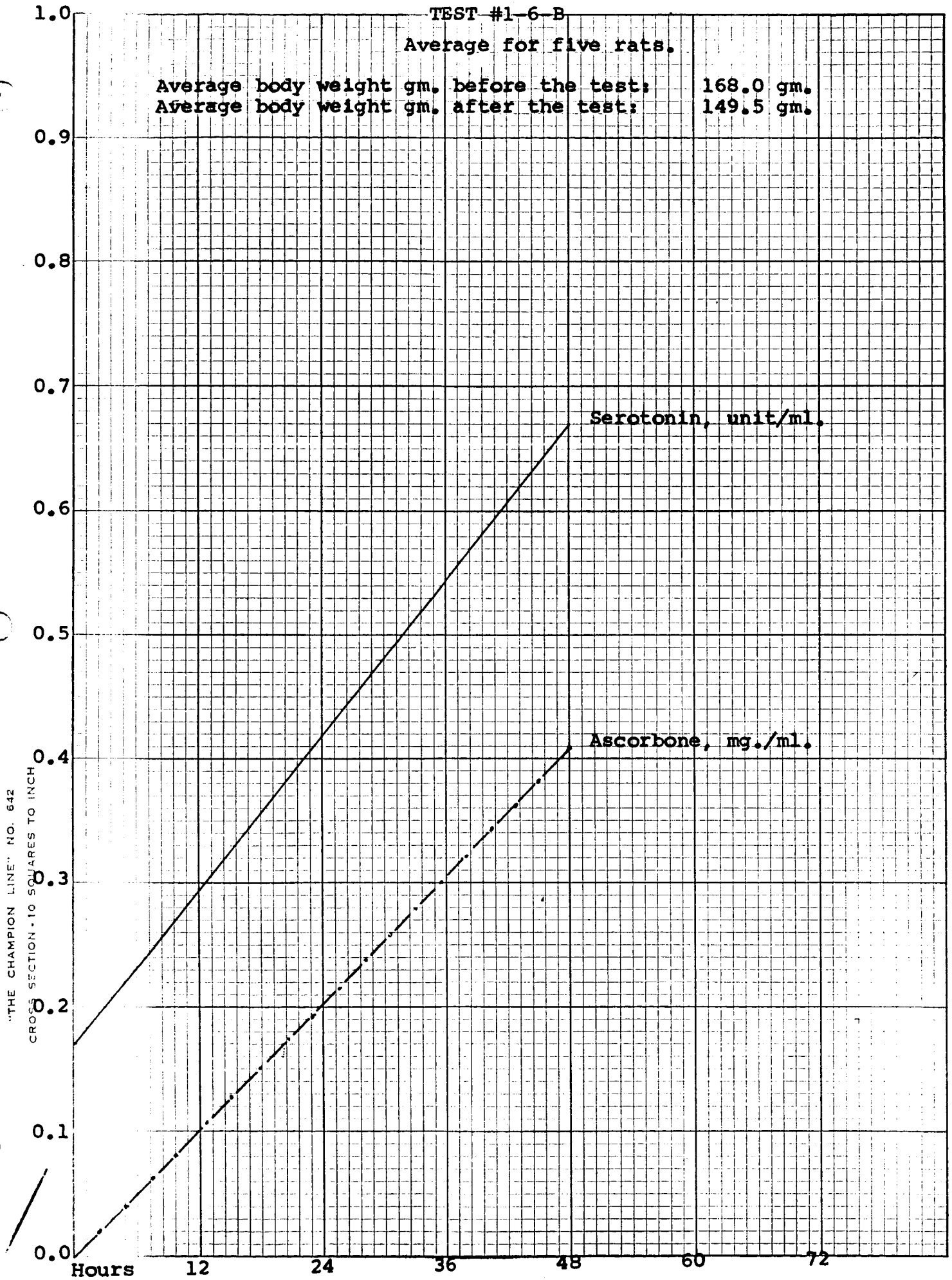
BLOOD EXAMINATION:

Total Cholesterol, mg/dl	75
Free Cholesterol, mg/dl	23
Cholesterol ester, mg/dl	52
Cholesterol ester ratio %	69
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~ml~~ ml. blood	.67
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl TAA serum	1.16
Ascorbic acid, mg/dl AA, serum	0.75
Ascorbone, mg/dl Serum	0.41
Blood Pressure	
Body weight	

Comment: The blood serotonin concentration at 30,000 feet of simulated high altitude air was 372% higher than at normal altitude for the same age (.18 unit/ml.).

mg/ml.
unit/ml.

EFFECT OF SIMULATED HIGH ALTITUDE AIR, 30,000 FEET ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



Patient: NASA PROJECT - RAT TEST #1-7-A Age: _____ Sex _____ Number: _____

Address Effect of simulated high altitude air on blood serotonin concentration and serum ascorbone concentration.
Simulated altitude 20,000 feet for 26 hours.

Physician Average for five rats, males.
Average body wt. gm. before the test: 275 gm.

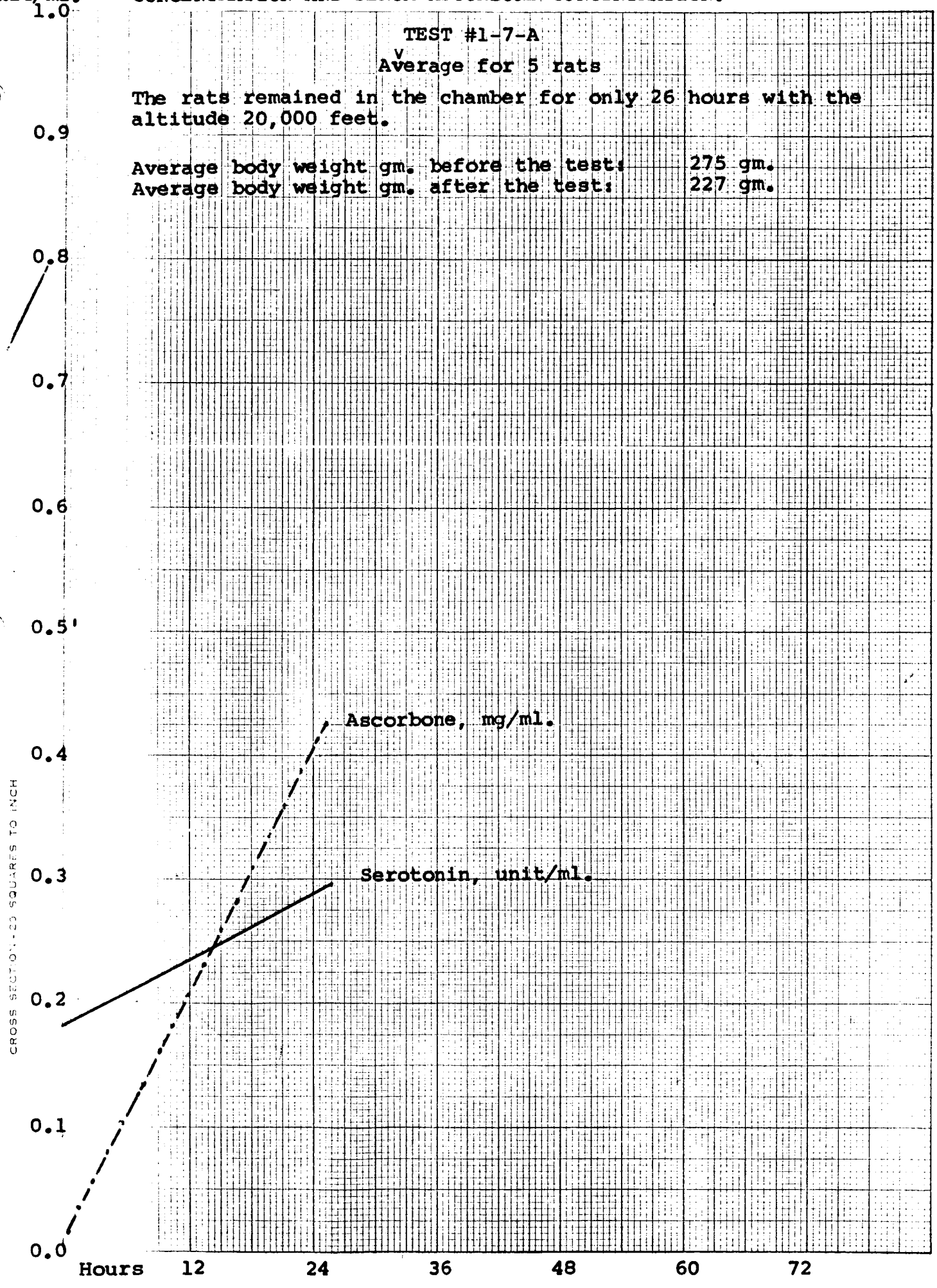
Past History Average body wt. gm. after the test: 227 gm.

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	54
Free Cholesterol, mg/dl	16
Cholesterol ester, mg/dl	38
Cholesterol ester ratio %	70
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~dl~~ ml. blood	0.30
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl TAA serum	1.20
Ascorbic acid, mg/dl AA, serum	0.80
Ascorbone, mg/dl serum	0.40
Blood Pressure	
Body weight	

Comment: In this experiment the rats remained in the chamber 26 hours, reaching the altitude of only 20,000 feet. Accordingly, there was very small increase in blood serotonin concentration and in serum ascorbone level.

EFFECT OF SIMULATED HIGH ALTITUDE AIR ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



Patient: NASA PROJECT - RAT TEST #1-7-B Age: _____ Sex _____ Number: _____

Address Effect of simulated high altitude air on blood serotonin concentration and serum ascorbone concentration.

Physician Simulated altitude 20,000 feet for 26 hours.
Average for five rats, males.

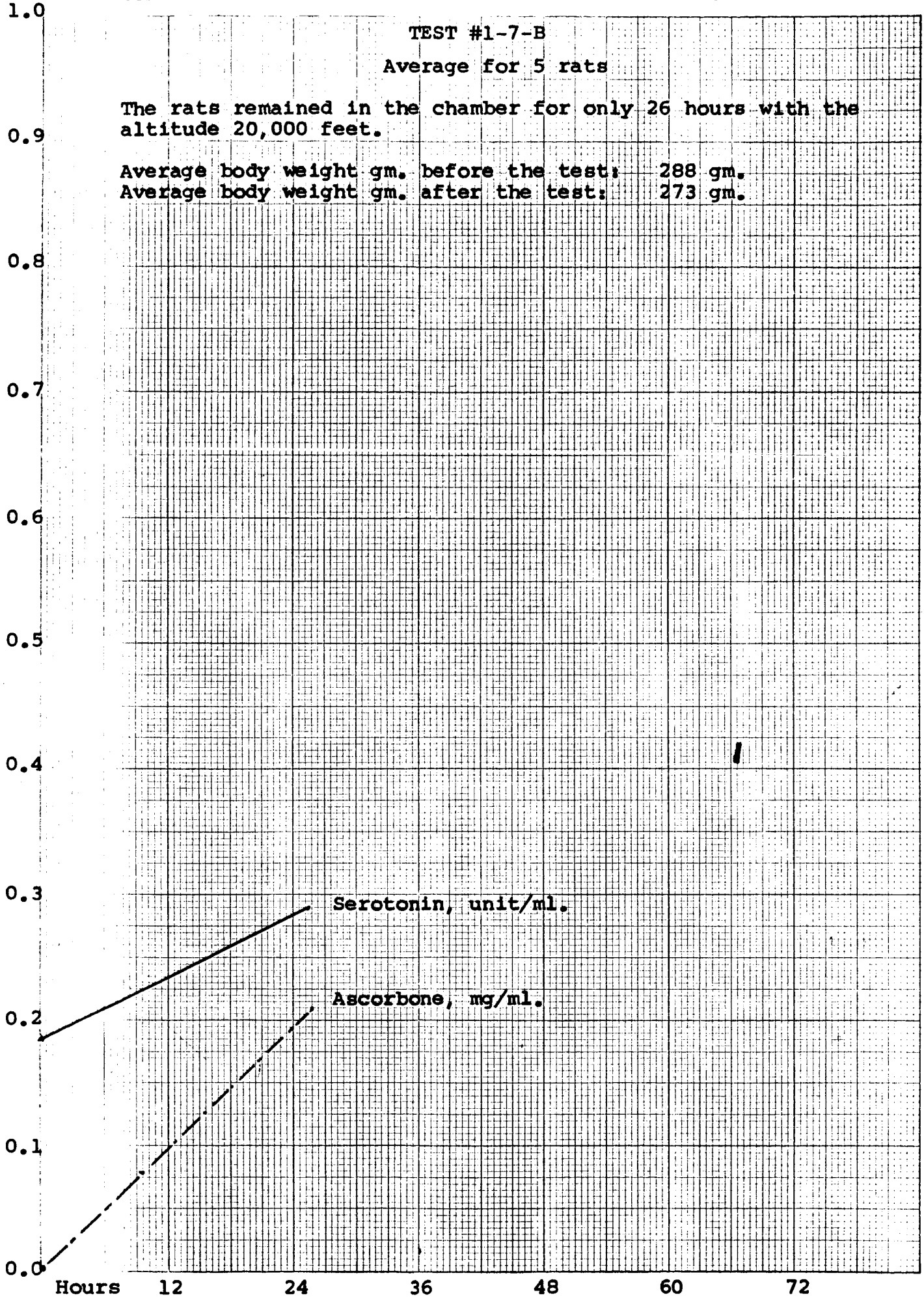
Past History Average body wt. gm. before the test: 288 gm.
Average body wt. gm. after the test: 273 gm.

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	77
Free Cholesterol, mg/dl	28
Cholesterol ester, mg/dl	49
Cholesterol ester ratio %	63
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~ml~~ ml. blood	0.27
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl TAA, serum	1.26
Ascorbic acid, mg/dl AA, serum	1.05
Ascorbone, mg/dl serum	0.21
Blood Pressure	
Body weight	

Comment: In this experiment the rats remained in the chamber 26 hours, reaching the altitude of only 20,000 feet. Accordingly, there was very small increase in blood serotonin concentration and in serum ascorbone level.

EFFECT OF SIMULATED HIGH ALTITUDE AIR ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



TEST #1-7-B

Average for 5 rats

The rats remained in the chamber for only 26 hours with the altitude 20,000 feet.

Average body weight gm. before the test: 288 gm.
Average body weight gm. after the test: 273 gm.

Patient: NASA TEST #1-9-0 Age: _____ Sex _____ Number: _____

Address GUINEA PIGS

Physician Survival test -- 33,000-34,000 Feet

Past History No blood test

BLOOD EXAMINATION:

The animals survived.

Total Cholesterol, mg/dl

Free Cholesterol, mg/dl

Cholesterol ester, mg/dl

Cholesterol ester ratio %

Clearing Factor, unit
(Lipoprotein Lipase)

Triglycerides, mg/dl

Serotonin, γ/dl

Urine 5-HIAA, unit

Blood Sugar, mg/dl

Total Ascorbic Acid mg/dl

Ascorbic acid, mg/dl

Ascorbone, mg/dl

Blood Pressure

Body weight

Test #9 NASA Project

Survival test for guinea pig.

Animal o.k. at 30,000 feet.

Patient: NASA PROJECT TEST #10-A Age: Sex Number:

Address ~~Effect of simulated high altitude air on blood serotonin concentration and serum~~ ascorbone concentration.

Physician ~~Simulated altitude 30,000 feet~~ Average for six rats, males

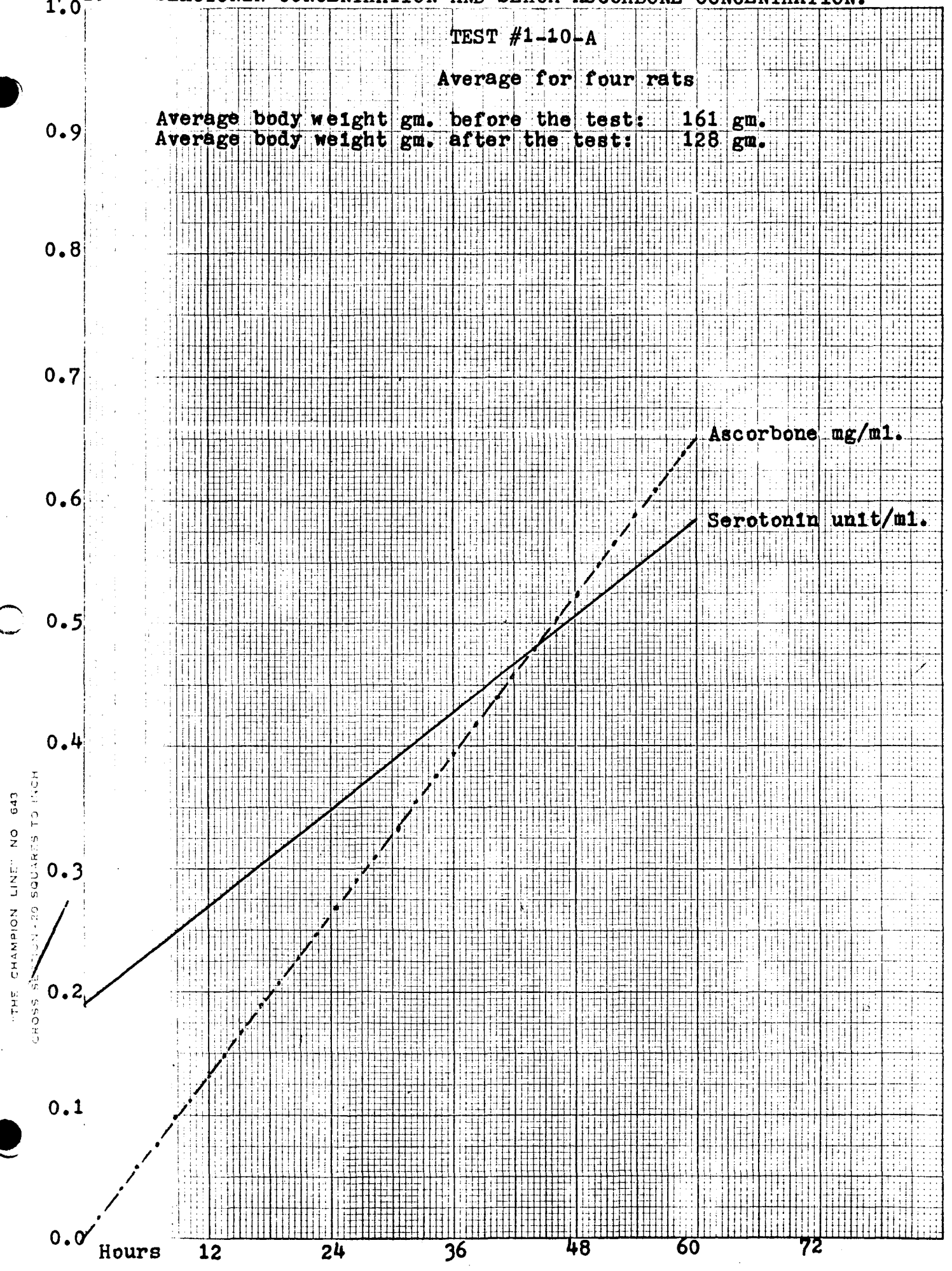
Past History ~~Average body wt. gm. before the test: 144 gm.~~ Average body wt. gm. after the test: 127.6 gm.

Two rats died during the test.

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	100
Free Cholesterol, mg/dl	25
Cholesterol ester, mg/dl	75
Cholesterol ester ratio %	75
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/ml. blood	0.58
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl TAA serum	1.75
Ascorbic acid, mg/dl AA serum	1.10
Ascorbone, mg/dl serum	0.65
Blood Pressure	
Body weight	

EFFECT OF SIMULATED HIGH ALTITUDE AIR, 30,000 FEET ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



Patient: NASA PROJECT TEST #10-B Age: Sex Number:

Address Effect of simulated high altitude air on blood serotonin concentration and serum ascorbone concentration.

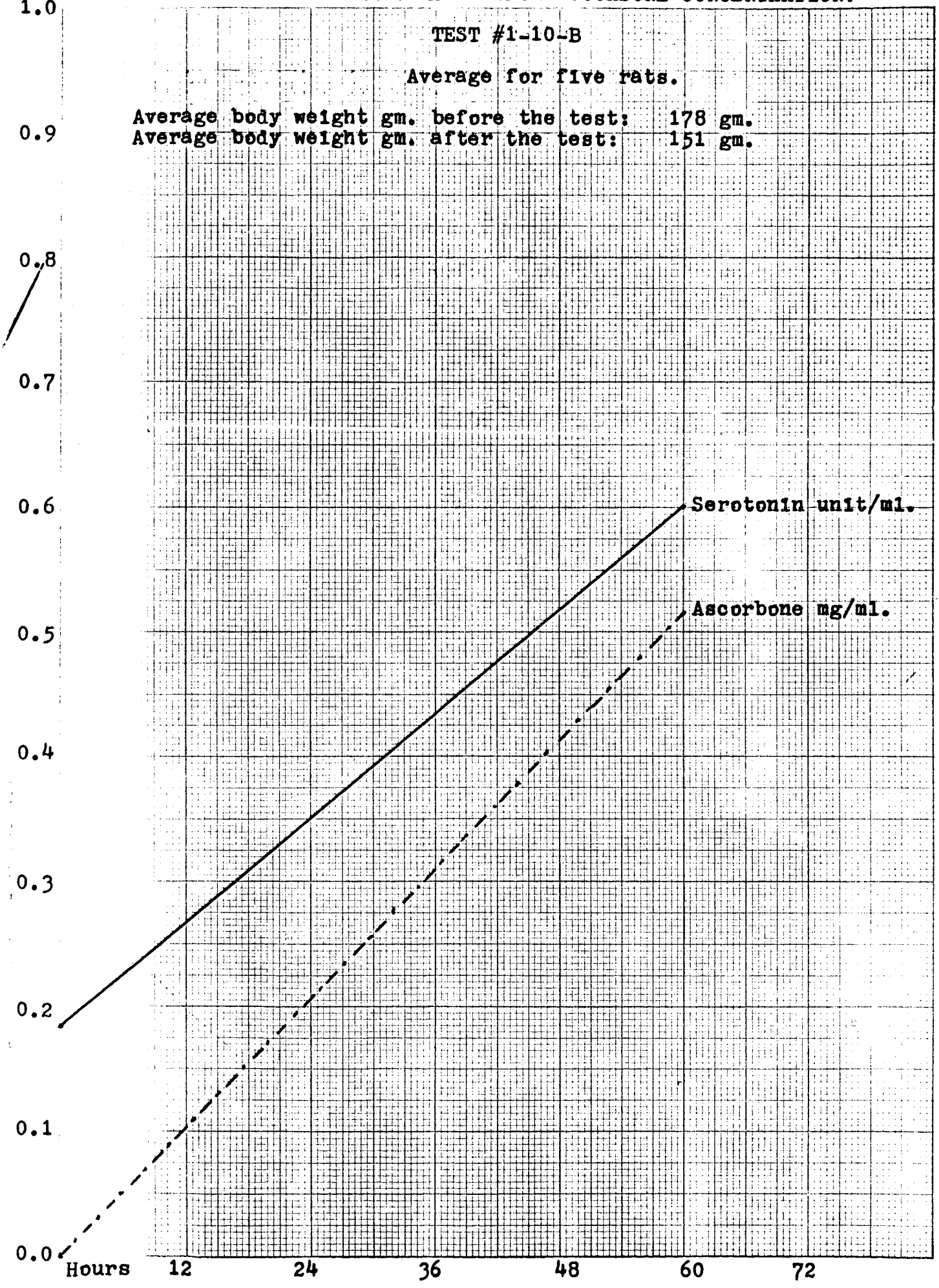
Physician Simulated altitude 30,000 feet
Average for six rats, males

Past History Average body wt. gm. before the test: 178 gm.
Average body wt. gm. after the test: 151.4 gm
One rat died

BLOOD EXAMINATION:

Total Cholesterol, mg/dl	70
Free Cholesterol, mg/dl	23
Cholesterol ester, mg/dl	47
Cholesterol ester ratio %	67
Clearing Factor, unit (Lipoprotein Lipase)	
Triglycerides, mg/dl	
Serotonin, γ/~~dl~~ ml. blood	0.60
Urine 5-HIAA, unit	
Blood Sugar, mg/dl	
Total Ascorbic Acid mg/dl TAA serum	1.32
Ascorbic acid, mg/dl AA serum	0.70
Ascorbone, mg/dl serum	0.52
Blood Pressure	
Body weight	

EFFECT OF SIMULATED HIGH ALTITUDE AIR, 30,000 FEET ON BLOOD SEROTONIN CONCENTRATION AND SERUM ASCORBONE CONCENTRATION.



SUMMARY

of

PART II

The preliminary tests with a simulated high altitude air chamber indicate that the blood serotonin concentration in rats was significantly increased at 30,000 feet. This increase was much less pronounced at the altitude of 20,000 feet.

Extensive tests with rats, as well as with guinea pigs and rabbits with simulated high altitude air, both on blood serotonin concentration and plasma ascorbone concentration will be conducted during the next months.