N O T I C E

THIS DOCUMENT HAS BEEN REPRODUCED FROM MICROFICHE. ALTHOUGH IT IS RECOGNIZED THAT CERTAIN PORTIONS ARE ILLEGIBLE, IT IS BEING RELEASED IN THE INTEREST OF MAKING AVAILABLE AS MUCH INFORMATION AS POSSIBLE

(NASA-TM-76023) CONTENT OF LIPIDS IN BLOOD AND TISSUES OF ANIMALS DURING HYPODYNAMIA (National Aeronautics and Space Administration) 11 p HC A02/MF A01 CSCL 06C

N80-21967

Unclas
G3/51 47662

NASA TECHNICAL MEMORANDUM

NASA TM-76023

CONTENT OF LIPIDS IN BLOOD AND TISSUES OF ANIMALS DURING HYPODYNAMIA

I. V. Federov, Yu. P. Ryl'nikov and
T. M. Lobova

Translation of "Soderzhaniye lipidov v krovi i tkanyakh zhivotnykh pri gipodinamii", Kardiologiya, Vol. 13, No. 7, 1973, pp 50-54.

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
Washington, D. C. 20546 January, 1980

UDC 612.766.07:612.123

CONTENT OF LIPIDS IN BLOOD AND TISSUES OF ANIMALS DURING HYODYNAMIA

by

I. V. Fedorov, Yu. P. Ryl'nikov, T. M. Lobova, Department of Biochemistry (head--Professor I. V. Fedorov) of the Yaroslav Medical Institute

Experiments on 97 rats and 50 rabbits were undertaken to study the influence of hypodynamia on the lipid content in the blood, liver, heart and in the aorta. Reduction of muscular activity contributed to the increase of cholesterol and β-lipoprotein levels in the blood and to accumulation of cholesterol in the liver and the heart. The total lipid content in these tissues decreased. In the aorta the total lipid content increased, while lecithin and cephalin figures went down. The character of biochemical changes in hypodynamia resembles in many ways the lipid metabolism changes in atherosclerosis.

In the opinion of a number of authors, hypodynamia promotes the emergence and progression of atherosclerosis [24,30-32,34], while physical activity reduces the probability of this disease [20, 25, 33]. /50

With a reduction in muscular activity the fat content in the organism increases both in elderly [12] and in young people [8-10]. With prolonged hypodynamia the level is increased in the total lipids, cholesterol and β-lipoproteins in the blood of people [17] and rabbits [21,22]. The changes in the lipid composition of the tissues in these conditions have not been studied. This work makes an experimental study on two species of animals of the content of lipids in the blood and tissues.

*Numbers in margin indicate pagination in original foreign text.

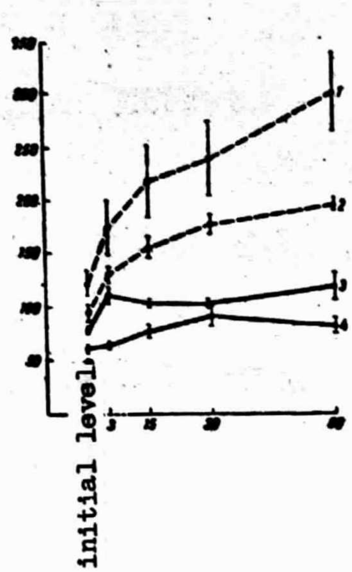
Material and Methods

The experiments were conducted on 97 rats weighing 180-220 g and 50 rabbits weighing 2.5-3 kg. The rats were placed in plaster housings [28], the rabbits were kept in close individual wooden cages with movable front and rear walls, which made it possible to alter the size of the cage during the experiment. The animals of the control groups were located in common cages in the same room. The food ration of the control and experimental rats and rabbits was the same and consisted of oats, black bread, beets, carrots; the rabbits in addition received hay. The animals had free access to food and water.

In different periods of hypodynamia in the blood and tissues (liver, heart, aorta) the following components were determined: cholesterol by the colorimetric method [3]; total lipids--in rats by the turbidimetric method of Khuerga et al. [18], and in the rabbits by the gravimetric method; phospholipids--by the Fisk-Subarrow method in the modification of A. Ye. Braunshteyn [2], and β-lipoproteins by the turbidimetric method [29].

Results and Their Discussion

The total cholesterol content in the blood serum of rats was reliably ($p<0.05$) increased from the first days of immobilization of the animals and was on a high level for 60 days (see figure). In the rabbits this index was increased in waves and in the majority of cases reliably from the tenth through 60th days of the experiment. Up to the 15th day of the experiment the increase in the level of cholesterol in the rabbits occurred mainly due to the esterified fraction, and on the 30th and 60th days--due to the free cholesterol. In rats on the third, 15th, 30th and 60th days the content of β-lipoproteins was increased respectively by 39, 74, 87 and 104%, and in the rabbits--by 58, 84, 95 and 145% as compared to the initial level (see the /51
figure). The quantity of phospholipids in the blood serum of rabbits in all periods of study was greater than in the control, but this difference was reliable only on the 3-4 and 5th days of the experiment. The coefficient phospholipids/cholesterol in the experimental animals, starting from the 10th day of hypodynamia was lower than in the control groups.



Content of Cholesterol (solid line) and β-lipoproteins (dotted line) in Blood of Rabbits (1,4) and Rats (2,3) during Hypodynamia

On x-axis--duration of hypodynamia (in days); on y-axis--content of cholesterol and β-lipoproteins (in mg%).

TABLE 1

CONTENT OF LIPIDS IN TISSUE OF LIVER OF RATS AND RABBITS IN HYPODYNAMIA

Duration of hypodynamia (in days)	Statistical index	Rats		Rabbits					
					ester fraction			alcohol fraction	
		total lipids	choles-terol	total lipids	lipids	choles-terol	lecithin cephalin	lipids	sphyngo-myelins
		% for dry weight		% per dry weight					
Control	M	5,74	2,95	29,46	9,70	1,09	1,18	19,76	14,33
	±m	0,43	0,06	0,30	0,18	0,02	0,03	0,27	0,04
	n	12	15	6	6	6	6	6	6
10 (rabbits) 15 (rats)	M	4,86	3,81	23,61	11,80	1,51	1,85	11,71	10,87
	±m	0,25	0,06	0,94	0,57	0,05	0,14	0,14	1,46
	D	>0,05	<0,01	<0,01	<0,01	<0,01	<0,01	<0 01	<0,05
	n	11	13	6	6	6	6	6	6
30	M	4,69	3,41	25,11	14,02	1,31	1,79	11,09	5,31
	±m	0,06	0,08	2,52	2,13	0,26	0,12	0,37	0,51
	D	>0,05	<0,01	>0,05	>0,05	>0,4	<0,01	<0 01	<0,01
	n	8	8	6	6	6	6	6	6
60	M	5,04	3,68	32,51	20,85	2,56	5,77	11,66	4,24
	±m	0,31	0,02	1,58	1,55	0,60	0,44	0,86	0,58
	D	>0,05	<0,01	>0,05	<0,01	<0,05	<0,01	<0 01	<0,01

The total quantity of lipids in the tissue of the liver of the animals was reduced, while the cholesterol content was increased (table 1). The content of lecithin and cephalin in the liver tissue of rabbits on the 10th 30th and 60th days was increased respectively by 57, 52 and 390%, in these same periods the sphyngomyelins were reduced respectively by 23, 63 and 71%.

The total level of lipids, especially the alcohol fraction in the tissue of the heart of the experimental rats and rabbits was moderately reduced, the cholesterol content in the heart was increased, the quantity of lecithin with cephalin and sphyngomyelin in the heart of rabbits became lower (table 2).

Study of the aorta was made only in the rabbits. The total quantity of lipids in the aorta on the 10th day of hypodynamia was significantly reduced, on the 30th day was equal to the indices of the control group and was increased by the 60th days of the experiment (table 3). The ester fractions of the lipids underwent analogous changes. The level of lipids of the alcohol fraction on the 10th and 30th days of the experiment was not altered, by the 60th it had reliably dropped (see table 3). The cholesterol content in the aorta was reduced on the 10th and 60th days of the experiment /52 and again increased on the 30th day. The quantity of lecithin with cephalin during the entire experiment was reduced almost two-fold, while the content of sphyngomyelins was increased two-three-fold.

As is known, atherosclerosis in people [16] and in experiments on animals [1, 11] is accompanied by an increase in the blood in the content of cholesterol (primarily esterified) and phospholipids. However, the increase in phospholipids occurs more slowly than the cholesterol, which results in a decrease in the lipolytic coefficient. The content of β-lipoproteins is also sharply increased.

We established that hypodynamia in rats and rabbits results in analogous /53 changes in the lipids of the blood. The relative shortage of phospholipids with a surplus of cholesterol promotes the suppression of oxidative processes [4,35,36], disruption in the function of the internal secretion glands, in

TABLE 2

CONTENT OF LIPIDS IN TISSUE OF HEART OF RATS AND RABBITS IN HYPODYNAMIA

Duration of hypodynamia (in days)	statistical index	Rats: total lipids	Rats: cholesterol	Rabbits: total lipids	Rabbits: ester fraction: lipids	Rabbits: ester fraction: cholesterol	Rabbits: alcohol fraction: lecithin cephalin	Rabbits: alcohol fraction: lipids	Rabbits: alcohol fraction: sphyngo-myelins
		% for dry weight		% for dry weight					
Control	n	12	9.	18	18	18	18	18	18
	M	4,17	1,95	37,17	25,81	0,64	5,18	11,36	5,76
	$\pm m$	0,53	0,04	0,41	0,49	0,014	0,07	0,22	0,05
10 (rabbits) 15 (rats)	n	10	10	6	6	6	6	6	6
	M	4,06	2,09	30,59	22,67	0,77	3,35	7,93	5,03
	$\pm m$	0,45	0,06	0,78	1,05	0,06	0,15	0,76	0,80
	p	$>0,1$	$>0,1$	$<0,01$	$<0,02$	$<0,05$	$<0,01$	$<0,01$	$>0,3$
30	n	8	8	6	6	6	6	6	6
	M	3,96	2,26	33,40	23,13	0,79	2,77	10,27	4,68
	$\pm m$	0,6	0,06	1,63	1,26	0,02	0,15	0,86	0,79
	p	$>0,1$	$<0,01$	$<0,05$	$>0,05$	$<0,01$	$<0,01$	$>0,2$	$>0,1$
60	n				6	6	6	6	6
	M			35,94	26,89	0,97	4,92	9,05	4,84
	$\pm m$			0,79	1,09	0,04	1,29	0,56	0,42
	p			$>0,1$	$>0,3$	$<0,01$	$>0,8$	$<0,01$	$<0,05$

the first place the thyroid gland [7, 13, 14] and change in the physical and chemical properties of cholesterol [37]. The increase in content of β-lipoproteins indicates the increase in the blood of the level of triglycerides [26] and the not very stable forms of cholesterol [15, 27, 28].

Changes in the content of lipids in the tissues during hypodynamia are similar to a great extent to those in experimental atherosclerosis. In the tissues of the liver this was manifest in the increase in concentration of cholesterol, lecithin with cephalin, and decrease in the content of sphyngomyelins. In the tissue of the heart an increase was also observed in the level of cholesterol, decrease in the content of lecithin with cephalin and sphyngomyelins. In the tissue of the aorta during hypodynamia in contrast to the experimental atherosclerosis no noticeable increase was found in the cholesterol level. However there was a significant decrease in the content of lecithin with cephalin and a sharp increase in the quantity of sphyngomyelins.

TABLE 3

CONTENT OF LIPIDS [in % for dry weight] IN TISSUE OF AORTA OF RABBITS DURING HYPODYNAMIA [M±m]

Duration of hypodynamia (in days)	Statistical index	Ester fraction: total lipids	lipids	cholesterol	Alcohol fraction: lecithin and cephalin	lipids	sphyngomyelins
Control(n=6)	M	40,21	30,67	0,66	23,91	9,54	76,34
	±m	0,47	0,67	0,02	1,04	0,19	0,48
10(n=5)	M	30,55	20,98	0,52	12,14	9,57	249,43
	±m	1,34	1,89	0,02	0,78	0,70	8,79
	D	<0,01	<0,01	<0,01	<0,01	>0,9	<0,01
30 (n=6)	M	39,27	28,62	0,78	12,67	10,65	165,11
	±m	1,73	1,06	0,06	0,64	1,10	24,88
	D	>0,6	>0,1	>0,05	<0,01	>0,3	<0,01
60(n=6)	M	45,05	38,30	0,48	14,15	6,76	144,56
	±m	1,90	2,45	0,03	2,86	0,86	5,26
	D	<0,05	<0,02	<0,01	<0,01	<0,01	<0,01

Note. Here and in table 2 D is computed in relation to the indices in the control.

With restricted muscular activity for all tissues an inclination towards decrease in the level of total lipids was characteristic. The exception was the tissue of the aorta where the quantity of total lipids by the 60th day of hypodynamia was increased due to the lipids of the ester fraction.

In atherosclerosis the content of total lipids in the tissues, including in the aorta, as a rule is increased.

A certain deficit of total lipiis in the tissues during hypodynamia is governed by intensification of their use as energy material as a consequence of the shortage of carbohydrates and decrease in the oxidation [5,6 19]. The acetyl coenzyme A that is accumulated during the breakdown of fats is used for the synthesis of cholesterol.

Thus, with a decrease in the motor activity disruptions occur in the lipid metabolism, almost coinciding with analogous changes in atherosclerosis.

In the blood, liver and heart of rabbits and rats during prolonged hypodynamia the content of cholesterol and phospholipids (in blood) is increased. Here in the tissues the quantity of phospholipids is reduced: in the liver--due to the fraction of sphyngomyelins, in the aorta--due to lecithin with cephalin, in the heart--due to both fractions. The total quantity of lipids is reduced in the liver, heart and increased in the aorta.

References

1. Anichkov, N. A. Trudy O-va russkikh vrachey v SPb ["Proceedings of Society of Russian Physicians in St. Petersburg"], St. Petersburg, 1913. p. 90.

2. Asatiani, V. S., in Biokhimicheskiy analiz ["Biochemical Analysis"], Tbilisi, 1949, Pt. 1, p. 212.

3. Balakhovskiy, S. D.; and Balakhovskiy, I. S. Metody khimicheskogo analiza krovi ["Methods of Chemical Blood Analysis"], Moscow, 1953.

4. Bavina, M. V.; and Alekseyeva, A. S. Byull. eksper. biol., No. 3 (1956) p. 42.

5. Barbashova, Z. I.; Zhukov, Ye. K.; et al., in Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii ["Adaptation to Muscular Activity and Hypokinesia"], Novosibirsk, 1970, p. 26.

6. Blinder, L. V.; Oganov, V. S.; et al., Ibid, p. 36.

7. Gol'dberg, G. A.; and Leonov, P. M. Ter. arkh., No. 4 (1958), p. 45.

8. Demidov, G. A.; Zhdanova, A. G.; and Slesarev, V. I. in Materialy k itogovoy nauchnoy sessii Vsesoyuzn. nauchno-issled. in-ta fizicheskoy kul'tury ["Materials for Summary Scientific Session of All-Union Sci. Res. Inst. of Physical Culture"], Moscow, 1962, p. 188.

9. Zhdanova, A. G. Arkh. anat., No. 12 (1970), p. 29.

10. Korobova, A. A.; and Vinichenko, Yu. B. Kosmicheskaya biol., No. 3 (1968), p. 10.

11. Kritsman, M. G.; and Bavina, M. V. in Ateroskleroz i koronarnaya nedostatochnost' ["Atherosclerosis and Coronary Insufficiency"], Moscow, 1956, p. 126.

12. Kryachko, I. A.; and Askerov, A. A. in Problemy sportivnoy meditsiny ["Problems of Sports Medicine"], Moscow, 1965, p. 136.

13. Maksudov, B. S.; and Lushnikov, L. A. Trudy 14-go Vsesoyuzn. s"yezda terapevtov ["Proceedings of 14th All-Union Congress of Therapists"], Moscow, 1958, p. 71.

14. Mamaladze, G. G. Trudy In-ta eksperimental'noy kardiologii AN Gruzinsk SSR ["Proceedings of Institute of Experimental Cardiology of Georgian SSR Academy of Sciences"], Vol. 8 (1963), p. 71.

15. Medvedev, V. P. Ter. arkh., No. 9 (1963), p. 14.

16. Myasnikov, A. L. Ibid, 1924, no. 5-6, p. 411.

17. Parin, V. V.; Krupina, T. N.; et al. Kosmicheskaya biol., No. 5 (1970) p. 59.

18. Pokrovskiy, A. . Biokhimicheskiye metody issledovaniya v klinike ["Biochemical Methods of Research in the Clinic"], Moscow, 1969.

19. Popkov, V. L.; Mailyan, E. S.; et al. Fiziol. zh. SSSR, No. 12, p. 1808.

20. Saava, M. E. Soderzhaniye lipidov v syvorotke krovi u nekotorykh grupp naseleniya Extonskoy SSR ["Content of Lipids in Blood Serum in Certain Groups of the Population of the Estonian SSR"], Tartu, Author's abstract of candidate dissertation. 1971.

21. Tyavokin, V. V. Kardiologiya, No. 5 (1969), p. 141.

22. Tyavokin, V. V. Byull. eksper. biol., No. 5 (1970), p. 34.

23. Fedorov, I. V.; Grishanina, L. A. Kosmicheskaya biol., No. 3 (1967), p. 43.

24. Acheson, R. M. Yale J. Biol. Med, Vol.35 (1962), p. 143.

25. Breslow, L.; Bull, P. J. Chron. Dis., Vol. 13 (1960), p. 421.

26. Eder, H. A. Am. J. Med. Vol. 23 (1957), p. 269.

27. Goffman, J. W. Physiol. Rev. Vol. 34 (1954), p. 589.

28. Goffman, J. W.; Young, W.; Tondy, R. Circulation, Vol. 34 (1966), p. 679.

29. Ledvina, M. Labor. delo, No. 3 (1960), p. 13.

30. Kahn, H. A. Am. J. Publ. Hlth. Vol. 53 (1963), p. 1058.'

31. Malhotra, S. L. Brit. Heart J. Vol. 29 (1967), p. 895.

32. Morris, J. N.; and Crasford, M. D. Brit. Med. J., Vol. 2 (1958), p. 1485.

33. Paul, O.; Lepper, M. H.; et al., Circulation, Vol. 28 (1963), p. 20.

34. Pell, S. et al., JAMA, Vol. 175 (1961), p. 463.

35. Tanaka, Ryo, Stricland, K. P. Arch. Biochem. Vol.111 (1965), p. 583.

36. Uyeda Kosaku, Racker, E. J. Biol. Chem., Vol. 240 (1965), p. 4689,

37. Wilkens, J. A.; and Krut, L. H. J. Atheroscler. Res. Vol. 3 (1963), p. 15.