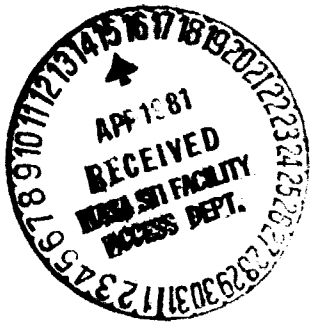
NASA TECHNICAL MEMORANDUM

NASA TM-75988

CHANGES IN MAST CELLS AND IN PERMEABILITY OF MESENTERIC MICROVESSELS UNDER THE EFFECT OF IMMOBILIZATION AND ELECTROSTIMULATION

M.P. Gorizontova and A.M. Chernukh

Translation of "Izmeneniya tuchnykh kletok i pronitsayemosti mikrososudov bryzheyki pod vliyaniyem immobilizatsii i elektrorazdrazheniya," Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya, No. 2, 1974, pp 73-76



NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON, D.C. 20546 JUNE 1980

STANDARD TITLE PAGE

1. Report No. NASA TM-75988	2. Government Accession No.	3. Recipient's Catalog No.
4. Title and Subtitle CHANGES IN MAST CELLS AND IN PERMEABILITY OF MESENTERIC MICROVESSELS UNDER THE EFFECT OF IMMOBILIZATION AND ELECTROSTIMULATION		5. Report Date June 1980 6. Performing Organization Code
7. Author(s) M.P. Gorizontova and A.M. Chernukh Laboratory of General Pathophysiology and Experimental Therapy, Institute of Normal and Pathologic Physiology, USSR Academy of Medical Sciences, Moscow		8. Performing Organization Report No. 10. Work Unit No.
9. Performing Organization Name and Address Leo Kanner Associates Redwood City, California 94063		11. Contract or Grant No. NASw-2790 13. Type of Report and Period Covered Translation
12. Sponsoring Agency Name and Address National Aeronautics and Space Administration, Washington, D.C. 20546		14. Sponsoring Agency Code

15. Supplementary Notes Translation of "Izmenenya tuchnykh kletok i pronitsayemosti mikrososudov bryzheykipod vliyaniyem immobilizatsii i elektrorazdrazheniya," Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya, No. 2, 1974, pp 73-76

16. Abstract It was shown in experiments on rats that a reduction in the amount of mast cells in the mesentery and an increase in their degranulation in case of immobilization for 24 hours and electrostimulation for 2 days (6 hours a day) was accompanied by an increase in vascular permeability of rat mesentery. It is supposed that immobilization and electrostimulation causing degranulation of mast cells prompted histamine and serotonin release from them, this increasing the permeability of the venular portion of the microvascular bed. Prophylactic use of esculamin-preparation with P-vitaminic activity decreased mast cell degranulation, which apparently prolonged the release of histamine and serotonin from them and normalized vascular permeability.

17. Key Words (Selected by Author(s))	18. Distribution Statement THIS COPYRIGHTED SOVIET WORK IS REPRODUCED AND SOLD BY NTIS UNDER LICENSE FROM VAAP, THE SOVIET COPYRIGHT AGENCY. NO FURTHER COPYING IS PERMITTED WITHOUT PERMISSION FROM VAAP.		
19. Security Classif. (of this report) Unclassified	20. Security Classif. (of this page) Unclassified	21. No. of Pages 8	22.

CHANGES IN MAST CELLS AND IN PERMEABILITY OF MESENTERIC MICROVESSELS UNDER THE EFFECT OF IMMOBILIZATION AND ELECTROSTIMULATION

M.P. Gorizontova and A.M. Chernukh
Laboratory of General Pathophysiology and Experimental Therapy, Institute of Normal and Pathologic Physiology, USSR Academy of Medical Sciences, Moscow

It is known that extensive degradation of mast cells occurs under /73* the influence of extraordinary stimuli [8]. Inasmuch as biologically active substances liberated here, particularly histamine and serotonin, may cause increased vascular permeability, we decided to study the relationship between the morphofunctional condition of mast cells and the permeability of mesenteric mast cells in rats as affected by immobilization and electrostimulation. We found no works in the literature which were devoted to this problem. In addition, we studied the possible stabilizing effect of a preparation with vitamin P activity--esculamin--on mast cell membranes under these conditions. /74* The capability of esculamin to normalize the increased permeability of biological membranes has been indicated previously [1, 2, 5].

Materials and Methods.

Experiments were conducted on 66 non-thoroughbred male rats weighing 200-280 g. The animals were subjected to immobilization (fastening to a column for 24 hours) or doses of electrical stimulation (current strength 2 milliamperes, impulse duration 3 seconds, interval between impulses 90 seconds). To accomplish this we used an apparatus set up according to a scheme proposed by V.N. Markov and I.A. Rudakov [3]. Electrical current was applied for 6 hours daily, over the course of 2 or 7 days. The animals were weighed daily, and the weight of the thymus and adrenals was also determined.

Mesenteric mast cell condition was evaluated microscopically following live fixation with Carnoy's fluid and staining with a 0.05 %

*Numbers in the margin indicate pagination in the foreign text.

solution of toluide blue. A visual field of 100 and magnification of 135 was used to view specimens from each animal.

The ink method was used to study microvascular permeability. We know that 4 variants of ink particle retention are possible for microvascular blackening [6, 7]: 1) parietal retention of them as a result of the formation of clefts or channels in the endothelium, which is evidence of disrupted permeability; 2) retention of ink where erythrocyte and thrombocyte aggregates form; 3) intravascular ink condensation associated with damaged endothelial cells; 4) phagocytosis by endothelial cells and pericytes. The last variant was lacking in our works, since the animals were sacrificed quickly. In this work we shall speak of ink markings caused by disrupted permeability, and we shall note the presence of vascular blacking where aggregates have formed. The question of aggregate formation affected by immobilization and electrostimulation, however, requires further study.

"Pelikan" ink (21 A 896) was injected intravenously into the rats in quantities of 0.1 ml for each 100 g, immediately following the cessation of stimulation. Thirty minutes after ink injection live fixation was performed and the animals were sacrified by intra-abdominal injection of 15 ml of Carnoy's fluid. Film preparations, which were cleared and filled with glycerin, were made from the mesentery. The preparations were photographed on an MBI-6 microscope at 20 X 5.7 magnification using "Mikrat-300" film. Esculamin was injected in doses of 50 mg/kg, five times over the course of 3 days, and the final time--1 hour before the beginning of the experiment.

Statistical work-up of the material was performed using Peters' method of calculating errors in the arithmetical mean, using the Moldenhaur factor [4].

Results and Discussion.

Following 24 hours immobilization, a decrease was observed in the quantity and an increase in degranulation of mast cells. Prophylactic injection of esculamin increased the quantity of mast cells and decreased

QUANTITY OF MAST CELLS IN ONE FIELD OF VIEW (X135) AND PERCENT OF DEGRANULATED MAST CELLS IN 100 FIELDS OF VIEW IN THE MESENTERY OF RATS FOLLOWING EXTREME STIMULI AND INJECTION OF ESCULAMIN ($M \pm m$; IN EACH GROUP $n = 6$) /74

Type and time of influence	Number of indices	Number of mast cells (X135)	Percent of degranulated mast cells
Control	(1)	25,2±1,6	0,09±0,06
Immobilization for 24 hours without injection of esculamin	(2)	14,4±3,1*	0,47±0,1*
following injection of esculamin	(3)	24,4±1,4	0,13±0,05
Electrostimulation 6 hr/day 2 days without injection of esculamin 7 days	(4)	20,4±0,6*	1,03±0,2*
following injection of esculamin 2 days	(5)	25,4±2,1	0,12±0,03
	(6)	23,2±1,7	0,14±0,05

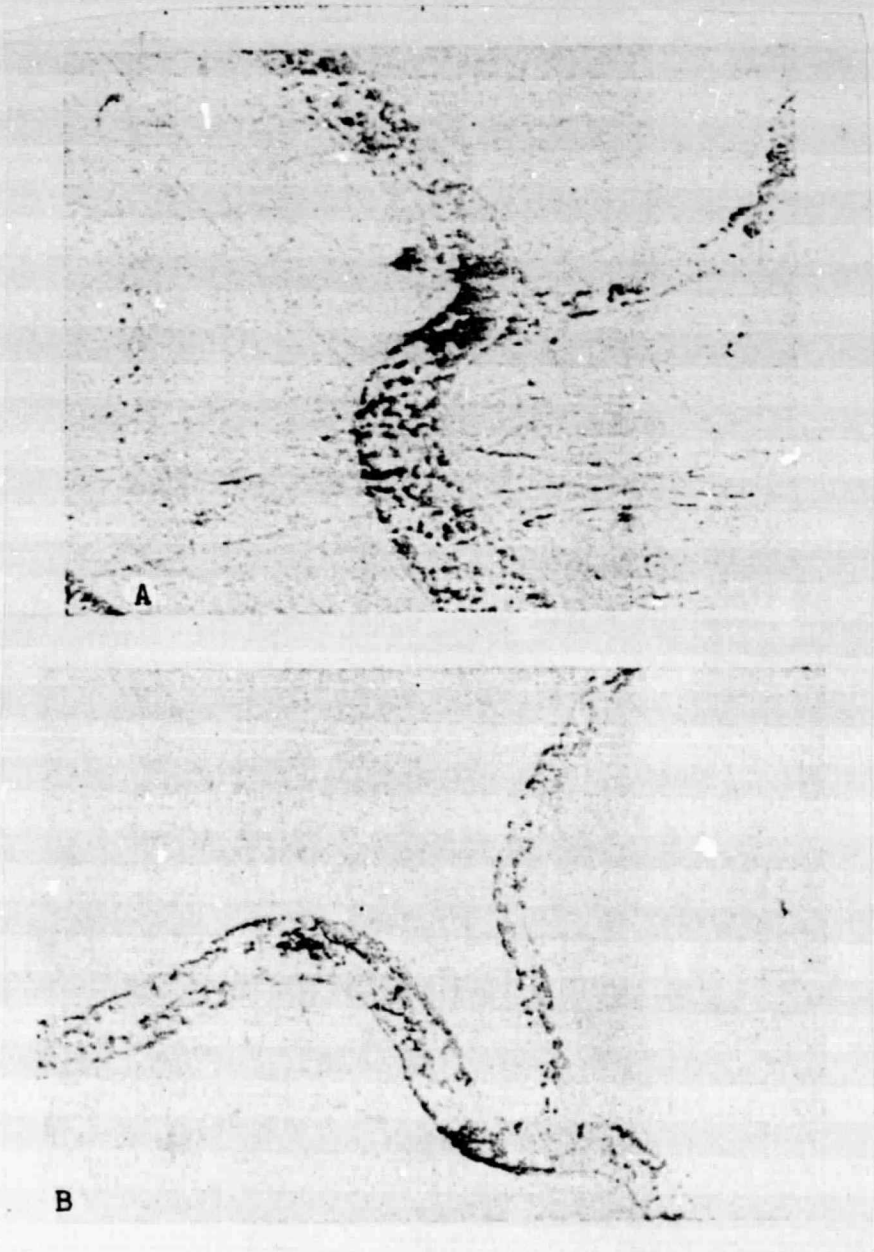
Note. In parentheses--number of the index. Reliable discrepencies at $P \leq 0.05$ are noted with an asterisk in the comparison with the corresponding control for all indices. In the column "Number of mast cells", for comparison of index 3 (immobilization for 24 hours following injection of esculamin) and index 2 (immobilization for 24 hours without injection of esculamin) $P = 0.04$; in the column "Percent of degranulated mast cells" in the comparison of indices 3 and 2, $P = 0.03$, in the comparison of index 6 (electrostimulation for 6 hours a day following injection of esculamin over the course of 2 days) and index 4 (electrostimulation for 6 hours a day without injection of esculamine over the course of 2 days) $P = 0.01$.

their degranulation in such a way that these indices did not essentially differ from the controls (see Table).

In the experiments studying vascular permeability, the presence of ink particles was noted in the venous portion of the microvascular bed in all rats. Ink deposition occurred most frequently in venules with diameters of 10-30 μm, but deposition decreased as the caliber of the /75 vessels decreased to 4 μm or increased to 75 μm (see Figure, A). Prophylactic use of esculamin prevented ink deposition in the vessels.

A decrease in the quantity of mesenteric mast cells and an increase in their degranulation was noted in rats which had been subjected to electrostimulation for 2 days (see Table). Study of permeability in this period indicated the presence of particles in the venous portion of vessels with diameters from 7 to 30 μm. Ink deposition in venules

with diameters of from 10-20 μm was most evident (see Figure, B). This period corresponded to the alarm stage (weight of the rats decreased an average of 10%, thymus weights--by 34%, and adrenal weights increased 35-40%).



Ink deposition in mesenteric venule walls of rats.

A--following 24 hours of immobilization (venule diameter 17-30 μm). B--following electrostimulation for 2 days (venule diameter 15-25 μm). X114.

With prophylactic injection of esculamin, the number of mast cells approached that noted in the controls, and their degranulation was prevented and permeability to ink increased.

Electrostimulation of rats for 7 days did not cause qualitative /7(and quantitative changes in mesenteric mast cells or an increase in permeability to ink, in comparison with the controls. This period in the experimental conditions we set up corresponded to the resistance stage, since, despite the continuing electrostimulation, the weights of the rats increased (by 8-9%).

Hence, the decrease in the quantity of mast cells in the mesentery and increase in their degranulation during immobilization and 2-day electrostimulation was associated with an increase in vascular permeability to ink particles. Prophylactic use of esculamin prior to the application of the indicated stimuli led to a decrease in mast cell degranulation in the mesentery and normalization of vascular permeability to ink.

It may be considered that immobilization and electrostimulation, causing degranulation of mast cells in the mesentery, facilitate this through the liberation of biologically active substances (histamine, serotonin), which leads to an increase in vascular permeability to ink particles. Esculamin, strengthening mast cell membranes, hinders the liberation of histamine and serotonin, which is one of the mechanisms of normalizing vascular permeability.

REFERENCES

1. Alekseyev, O. B., Ul'trastrukturnyye osnovy izmeneniya pronitsayemosti mikrotsirkulyatornogo lozha v usloviyakh oblucheniya i pri vozdeystvii eskulaminom [The Ultrastructural Bases for Alterations in Microcirculatory Bed Permeability during Irradiation and under the Influence of Esculamin], Dissertation, Moscow, 1968.

2. Gorizontova, M. P., A. M. Chernukh, in: Struktura i funktsiya gisto-gematicheskikh bar'erov [The Structure and Function of Histo-hematin Barriers], Moscow, 1971, p. 154.

3. Markov, V. N., I. A. Rudakov, Pat. fiziol., 2, 76 (1963).

4. Montsevichyute-Ergene, E. V., Pat. fiziol., 4, 71 (1964).

5. Rudakova, I. S., Vliyaniye eskuletina i ego proizvodnykh na pronitsayemost' i prochnost' sosudov pri rentgenobluchenii zhivotnykh [The Effects of Esculetin and its Derivatives on the Permeability and Stability of Vessels during the Irradiation of Animals], Dissertation, Moscow, 1963.

6. Branemark, P. J., R. Ekholm, J. Lindhe, Med. exp.(Basel), 18, 139 (1968).

7. Cotran, R. S., E. R. Suter, G. Majno, Vasc. Dis., 4, 107 (1967).

8. Selye, H., The Mast Cells, Washington, 1965.