parameters of the state of the mitochondria of cardiomyocytes can be used to assess the presence and depth of ischemic myocardial damage, regardless of the state of their contractile apparatus.

Averaged parameters of the state of the cardiomyocyte mitochondria can thus be used as criteria of the presence and depth of myocardial damage during reperfusion when the effectiveness of cardioplegia is determined. These parameters include: the relative surface density, the visual index of the state of the mitochondria, and the relative volume fraction of the mitochondria, namely volume fraction relative to volume of control cells.

LITERATURE CITED

1. A. M. Vikhert, V. G. Tsyplenkova, and L. S. Velisheva, Sudden Death [in Russian], Vilnius (1984), pp. 86-95.
2. I. F. Egorova, Yu. V. Popov, and B. N. Bogonatov, Diagnosis and Surgical Treatment of Diseases of the Heart and Vessels [in Russian], Moscow (1985), pp. 383-385.
3. L. M. Nepomnyashchikh, Byull. Éksp. Biol. Med., No. 2, 188 (1984).
4. L. A. Semenova and Yu. G. Tsellarius, Ultrastructure of Heart Muscle Cells in Focal Metabolic Lesions [in Russian], Novosibirsk (1978).
5. I. D. Shperling, Arkh. Patol., No. 3, 34 (1984).
6. G. Baroldy, Recent Advances in Studies on Cardiac Structures and Metabolism, Vol. 6, Munich (1975), pp. 383-397.
7. H. David, K.-F. Lindenau, J. Bohm, et al., Exp. Pathol., 14, 141 (1977).
8. M. A. Goldstein and D. L. Murphy, J. Mol. Cell. Cardiol., 15, 325 (1983).
9. R. B. Jennings and K. A. Reimer, Am. J. Pathol., 102, 241 (1981).
10. L. P. McCallister, D. C. Daiello, and G. F. O. Tyers, J. Mol. Cell. Cardiol., 10, 67 (1978).
11. L. P. McCallister, S. Trapukdi, and J. R. Neely, J. Mol. Cell. Cardiol., 11, 619 (1979).
12. J. R. Neely, H. Liebermeister, E. J. Battersby, and H. E. Morgan, Am. J. Physiol., 212, 804 (1967).
13. J. S. Partin, G. Benzing, and J. C. Partin, J. Mol. Cell. Cardiol., 4, 345 (1972).
14. J. Schaper, J. Mulch, B. Winkler, and W. Schaper, J. Mol. Cell. Cardiol., 11, 521 (1979).
15. E. Weibel, G. Kistler, and W. Scherle, J. Cell. Biol., 30, 23 (1966).

PROTECTIVE ACTION OF PANTHETIN ON THE DENERVATED STOMACH

S. N. Fedchenko and A. G. Moiseenok

UDC 616.833-191-089.85-06:616.33.009.1-085.356:577.164.14

KEY WORDS: stomach; vagotomy; Panthetin.

Vagotomy has achieved widespread popularity in recent years in the surgical treatment of duodenal ulcer [1, 4, 8]. Whereas reduced production of hydrochloric acid and pepsin, observed after this operation, have served as the pathophysiological basis for its use in the treatment of duodenal ulcer, the neurodystrophic changes in the mucous membrane and disturbances of the motor function of the stomach, accompanied by a disturbance of the efflux of its contents from the organ, are regarded as among the leading factors in the pathogenesis of postvagotomy complications [2, 3, 5]. Accordingly the search for pathogenetic approaches to the pharmacotherapy of the complications developing after operations connected

Department of Biology, Voroshilovgrad Medical Institute, Ministry of Health of the Ukrainian SSR (Kiev). Laboratory of Coenzymes, Institute of Biochemistry, Academy of Sciences of the Belorussian SSR, Minsk.

(Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 104, No. 9, pp. 359-362, September, 1987. Original article submitted October 17, 1986.

0007-4888/87/0009-1302$12.50

TABLE 1. Number of Cells with Destructive Changes as a Percentage of Various Types of Epitheliocytes in the Mucosa Lining the Body of the Rat Stomach (M ± m)

Experimental conditions	Surface epitheliocytes	p	Chief glandulocytes	p	Parietal glandulocytes	p
1. Intact rats	16,6±1,8	—	3,2±0,3	—	5,9±0,9	—
2. Vagotomy	34,3±2,1	<0,001	9,8±0,5	<0,001	18,8±1,8	<0,001
3. Vagotomy + Panthetin	20,6±1,8	<0,05 <0,001	5,6±0,2	<0,05 <0,001	6,3±0,2	<0,05 <0,001

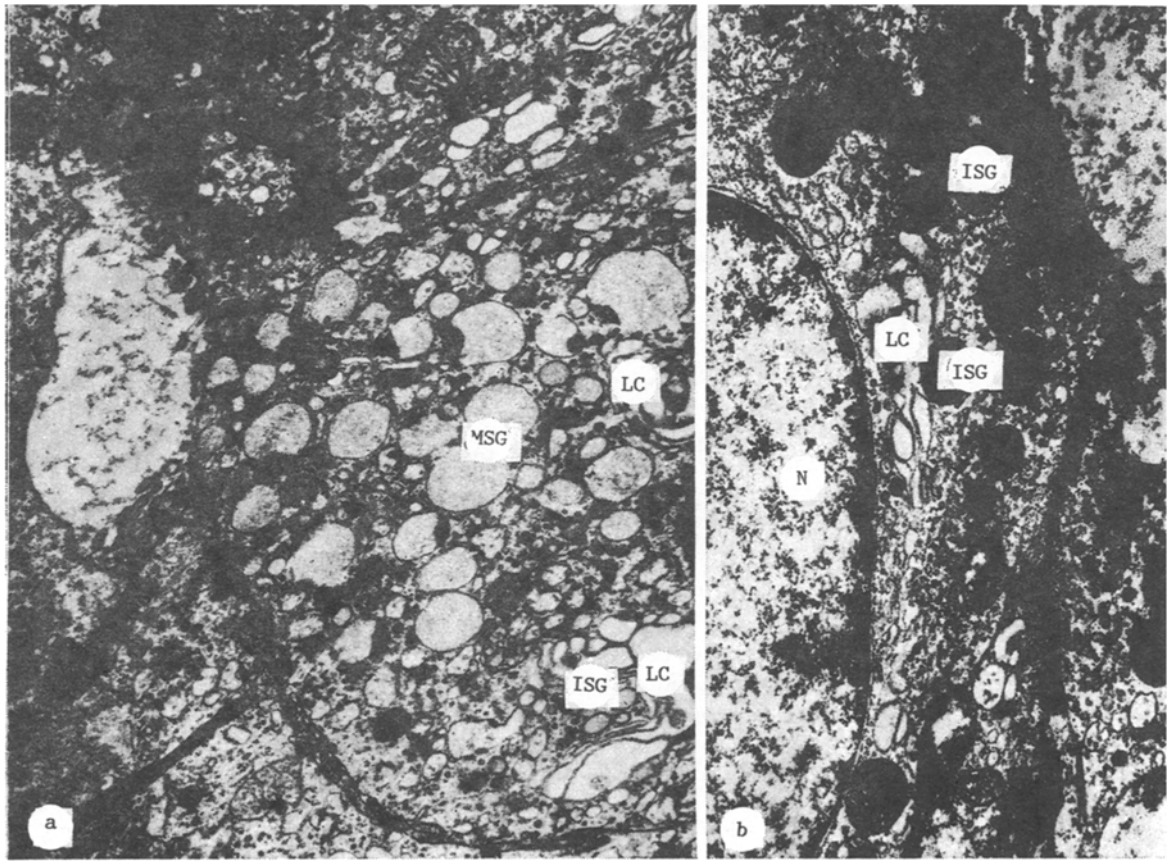

Fig. 1. Ultrastructure of GM cells: a) mucocyte in mucous membrane of vagotomized stomach: volume of lamellar complex (LC) increased, cell cytoplasm contains mature secretory granules (MSG) in the region of LC and also immature secretory granules (ISG). 12,000 × ; b) cytoplasm of superficial cells in region of LC contains many ISG. 12,000 ×.

with division of the vagus nerves or their branches is of undoubted interest for medical practice.

Our attention was concentrated on investigations conducted in the USSR in the 1960s, in order to study the effect of pantothenic acid on the acid-secretory function of the stomach and the use of this vitamin in the treatment of peptic ulcer [6, 7]. Despite the ambiguity of the results, pantothenate therapy led to a beneficial clinical effect, manifested as improvement of both the acid-secretory and the motor functions of the stomach. Observations on volunteers showed that these functions are definitely dependent on the pantothenate intake of the body.

In view of the specificity of this relationship, the writers have treated vagotomized animals with the substance Panthetin D-bis-(N-pantothenyl-β-aminoethyl)disulfide (Daiichi Seiyaku Co., Japan), which has recently undergone clinical trials in the USSR.

TABLE 2. Number of Serotonin-Producing EC Cells and Gastrin-Producing G-Cells per Square Millimeter of the Measured Area of the Rat GM (M ± m)

Experimental conditions	EC-cells	p	G-cells	p
1. Intact rats	72±5		48±6	
2. Vagotomy	30±3	<0,001	11±2	<0,001
3. Vagotomy + Panthetin	61±4	<0,05 <0,001	39±3	<0,05 <0,001

TABLE 3. Serotonin Concentrations in the Blood (in μg/ml) and GM (in μg/g tissue) of Rats (M ± m)

Experimental conditions	Blood	p	Mucous membrane of pyloric portion	p
1. Control	0,41±0,14		5,6±0.12	
2. Vagotomy	0,30±0,01	<0,05	2,6±0,23	<0,001
3. Vagotomy + Panthetin	0,50±0,02	<0,05 <0,001	4,5±0,12	<0,05 <0.001

EXPERIMENTAL METHOD

Male Wistar rats weighing 160-180 g were used. Bilateral subdiaphragmatic vagotomy was performed on 39 animals under ether anesthesia; Panthetin was injected subcutaneously into 20 vagotomized animals in a dose of 30 mg/kg 5 times with an interval of 1 day in the course of 10 days (experiment), and 19 vagotomized animals received injections of the same volume of physiological saline at the corresponding times (control). To study the problem detailed above, histochemical, biochemical, and electron-microscopic methods were used. The histological structure of the gastric mucosa (GM) was studied in paraffin sections 5-6 μ thick, stained with hematoxylin and eosin, and the epithelial formula was determined. Endocrine cells were identified by the argentaffin reaction of Masson and Hamperl, by the Grimelius method, and also electron-microscopically, by themethod described previously [9]. The number of endocrine cells in 1 mm^2 of a longitudinal section through GM was counted in specimens stained by the Masson–Hamperl and Grimelius methods. G cells were identified with the aid of antigastrin serum by the indirect Coons' method. The serotonin concentration in the blood, gastric juice, and GM was determined by the method of Snyder et al. in Kulinskii and Kostyukovskaya's modification [4]. Acid mucopolysaccharides (glycosaminoglycans) were stained with alcian blue at pH 1.0 and 2.5. Control sections were treated with testicular hyaluronidase.

EXPERIMENTAL RESULTS

The number of cells with destructive changes in animals undergoing vagotomy and receiving an injection of Panthetin was reduced by 43% among the chief glandulocytes, by 64% among the parietal cells, and by 40% among epitheliocytes of the surface epithelium and gastric pits (Table 1).

Ultrastructural analysis of the action of Panthetin on the gastric mucocytes showed that it activates release of secretory granules from all types of cells. Activation of the formation and release of mucous secretion in the mucocytes of the surface epithelium and gastric pits was accompanied by dilatation of the lumen of the gastric glands and by a decrease in the number of mature secretory granules in the cells, and an increase in the relative volume of the lamellar complex compared with the control (Fig. 1a). This increase is evidence of potentiation of the processes leading to formation of the mucous secretion. Immature secretory granules were numerous in the cytoplasm of the cells of the surface epithelium in the region of the lamellar complex (Fig. 1b). An increase in the content of sialo- and sulfomucins was observed in the cells of the surface epithelium of the animals of this group compared with intact animals.

The stomach wall is known to be protected against the action of secreted HCl by various specialized mechanisms. The most important protective function is that of the surface epithelium of GM, which is permeable with difficulty by hydrogen ions. It can be postulated that Panthetin induces a protective effect to some extent through increasing the synthesis of mucoid substances. In fact, biosynthesis of mucopolysaccharides (glycosaminoglycans) and glycoproteins takes place with the participation of N-acetylglucosamine, N-acetylgalactosamine, and derivatives of N-acetylneuraminic acid which, in turn, are formed from the acetylated product of the coenzyme form of pantothenic acid — COA. The regulatory role of intracellular changes in the free COA level has been demonstrated in the case of biosynthesis of O-acyl-N-acetylneuraminic acid by an enzyme in the submaxillary gland of domestic animals [13]. It can be tentatively suggested that Pantothetin, an effective precursor of COA, can facilitate mucoprotein synthesis by glands of the digestive system. Participation of the glycosaminoglycan and glycoprotein components of the mucus in the protection of the stomach was noted in [10].

Endocrine EC- and G-cells have been studied in the greatest detail, for interconnection of the nervous system with the enterochromaffin cells system has been demonstrated [11, 15]. Histochemical analysis showed that the number of EC-cells discovered in the mucous membrane of the antral portion of the vagotomized stomach fell from 72 ± 5 in intact rats to 30 ± 3 in vagotomized rats ($p < 0.001$), and administration of Panthetin increased the number of EC-cells to 61 ± 4 in 1 mm^2 of measured area (Table 2). The histochemical data are in agreement with the results of biochemical investigations showing that the serotonin concentration in GM of vagotomized rats receiving Panthetin rose to 4.5 ± 0.12 compared with 2.6 ± 0.23 μg/g tissue ($p < 0.01$), whereas in the blood it rose to 0.5 ± 0.02 compared with 0.3 ± 0.01 μg/ml ($p < 0.01$)); Table 2.

Vagotomy was followed by abrupt degranulation of the G-cells. The number of G-cells discovered in the antral portion of GM of vagotomized rats fell from 48 ± 6 to 11 ± 2 ($p < 0.001$).

Ultrastructural analysis of the G-cells of the vagotomized stomach after injection of Panthetin showed that most were in the phase of synthesis and storage of the secreted material, whereas the ultrastructure of GM of the vagotomized rats indicated intensive release of secretory material.

It can be concluded from these data that injections of Panthetin into vagotomized rats activate the deposition phase but depress the extrusion phase of gastrin from G-cells and of serotonin from EC-cells.

Increased release of serotonin, histamine, and gastrin from the corresponding endocrine cells of the stomach in response to vagotomy has been described in the literature [8, 11, 15]. At the same time there are indications that endogenous serotonin and gastrin play an essential role in the nutrition of GM [14, 15]. Thus the reduction of release of serotonin from EC-cells, of gastrin from G-cells and, according to the latest information, of enkephalin from G-cells [14], which we observed after injection of Panthetin, can be interpreted as a favorable factor helping to prevent destructive changes in GM. When the mechanisms of the protective effect of Panthetin on GM are evaluated, the characteristic antihistamine properties of pantothenic acid derivatives [16] and their ability to undergo transformation into the reserves of COA, which participate in acetylcholine biosynthesis [12], must be borne in mind. Involvement of COA in the regulation of the acetyl-COA-substrate level in neurotransmitter biosynthesis, and also the ability of COA and other pantothenate derivatives to regulate acetylcholine release from plexus [12] may be of the greatest importance for realization of the effects of Panthetin in vagotomized animals.

The distinct diminution of destructive lesions of GM, the intensification of biosynthesis, and also inhibition of the release of gastrin and serotonin from G- and EC-cells respectively thus suggest that administration of Panthetin is a promising method of pharmacologic correction of postoperative complications in patients with duodenal ulcer treated by surgical vagotomy.

LITERATURE CITED

1. A. A. Grinberg and L. F. Stolyarova, Klin. Khir., No. 1, 32 (1982).
2. Yu. K. Eletskii, O. V. Kulikova, and A. Yu. Tsibulevskii, Arkh. Anat. Gistd. Embriol., No. 4, 73 (1984).

3. M. I. Kuzin, P. M. Postolov, and N. M. Kuzin, Abstracts of Proceedings of the 30th All-Union Congress of Surgeons [in Russian], Minsk (1981), pp. 204-205.
4. V. I. Kulinskii and L. S. Kostyukovskaya, Lab. Delo., No. 7, 390 (1969).
5. E. M. Matrosova, A. A. Kurygin, and S. D. Groisman, Vagotomy (Sequelae and their Mechanisms) [in Russian], Leningrad (1981).
6. N. I. Mochalkin, Vrach. Delo., No. 8, 115 (1966).
7. A. P. Opikiev and A. P. Turaeva, Vrach. Delo., No. 8, 118 (1965).
8. Yu. M. Pantsirev, S. A. Chernyakevich, A. P. Éptinger, and S. P. Darenkov, Khirurgiya, No. 9, 14 (1984).
9. S. N. Fedchenko, Arkh. Anat. Gistol. Embriol., No. 3, 68 (1981).
10. A. Allen and A. Corner, Gut, 21, No. 3, 249 (1980).
11. M. A. Cook, I. T. Hamilton, and F. K. Okwuasaba, Nature, 271, No. 5647m 768 (1978).
12. A. P. Corfield, C. Ferreira do Amaral, Wember, and R. Schauer, Eur. J. Biochem., 68, No. 2, 597 (1976).
13. W. Fritsch and K. Hengels, Z. Gastroenterol., 17, No. 8, 503 (1979).
14. J. Oscarson, Scand. J. Gastroenterol., Suppl. 67, 89 (1981).
15. R. Saik, Scand. J. Gastroenterol., 16, No. 3, 337 (1981).
16. I. Szorady, E. Horvath, and E. Toth, Z. Vitaminforsch., 36, No. 2, 126 (1966).

ULTRASTRUCTURAL CHANGES IN THE ERYTHROCYTES AND PLATELETS OF PATIENTS WITH SEVERE THERMAL BURNS DURING THE BURN SHOCK PERIOD

B. V. Vtyurin, R. I. Kaem, and N. V. Chervonskaya

UDC 616.5-001.17-036.17-06:616-001.36-07:[616.155.1+616.155.25]-091.8

KEY WORDS: erythrocytes; platelets; burn shock.

An important role in the pathogenesis of burns is played by complex and little-studied changes in the blood cells, especially erythrocytes. Meanwhile information on these changes is essential for the elucidation of the pathogenesis of the first stage of burn shock, which is characterized by poikilocytosis, anisocytosis, and microcytosis, all of which can be observed under the light-optical microscope. It is in the period of burn shock that the action of erythrocyte-damaging factors such as acidosis and hyperosmolarity of the blood [7], release of catecholamines into the blood [12], and changes in the serum concentrations of lipids and lysolecithins [10] is observed. Massive infusion therapy, especially injection of preparations of the dextran type, may also undoubtedly play a definite role in the changes affecting erythrocytes [8]. The possibility cannot be ruled out that it is these same processes which lead to the development of acute anemias and various blood coagulation disturbances often observed in severe burns. In this context considerable interest is attached to changes in configuration and structure of the erythrocytes, the state of their cell membrane, with the functioning of which are linked such important factors as adhesion of the cells, transmembrane ion transfer, and so on, as well as changes in the platelets.

The aim of this investigation was to study the dynamics of changes in configuration of erythrocytes in the peripheral venous blood of patients with severe thermal burns of the skin during the period of burn shock, and also to study changes in platelet structure.

EXPERIMENTAL METHOD

Erythrocytes were taken for study from the peripheral venous blood obtained from 12 patients with severe thermal burns of the III-IV degree, affecting 35-60% of the body surface, during the period of burn shock. Two of these patients died at the end of the period

Department of Pathological Anatomy, A. V. Vishnevskii Institute of Surgery, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 104, No. 9, pp. 362-366, September, 1987. Original article submitted July 28, 1986.

 0007-4888/87/0009-1306$12.50