Unusual Route of Protein Discharge from the Cell

A. N. Klimov and V. A. Nagornev

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 122, No. 9, pp. 268-270, September, 1996
Original article submitted February 28, 1996

A protein-secreting plasma cell is revealed in atherosclerotic intima of the rabbit aorta by electron microscopy. Protein is secreted together with rough endoplasmic reticulum by budding of preformed processes. Mast cells also release α-granules by the budding of cell processes. It is suggested that the ability of intimal cells to export synthesized substances by this route is realized during atherogenesis.

Key Words: *experimental atherosclerosis; plasma cell; protein synthesis*

It is known that proteins destined for secretion are passed from the rough endoplasmic reticulum (RER) to the Golgi apparatus, where they are modified, sorted, encapsulated in secretory vesicles, and discharged from the cell.

While studying the role of lymphocytes in the development of atherosclerotic lesions in the subendothelial aortic intima of cholesterol-fed rabbits, we identified an active plasma cell (Fig. 1, *a*, *b*). Transmission electron microscopy showed that this cell forms structures looking like processes with a thin "neck" which, apparently, are ready to gemmate. In addition to the processes, structures that can be regarded as gemmated processes containing cellular cytoplasm can be seen (Fig. 1, *b*). It should be noted that cell cytoplasm and that contained by forming and gemmating processes is almost completely filled with the RER bearing ribosomes on its membranes (Fig. 1, *b*). This indicates an active synthesis of proteins, probably, immunoglobulins. Gemmated processes from which small electron dense particles were released by lysis are also seen (Fig. 1, *b*, *c*).

The presence of B cells synthesizing IgG supports the hypothesis that arterial atherosclerotic lesions contain immunoglobulin-producing cells (Fig. 1, *d*). Our observations suggest that the identified cell is a plasma cell synthesizing immunoglobulins, which are released by gemmation of cell processes. It is unclear whether these immunoglobulins are released by the classic pathway (via the Golgi apparatus and vesicles).

It should be noted that lymphocytes are involved in atherogenesis. T cells predominate in the arterial intima [2], which also contains B cells [6]. The contents of IgG [3,5] and autoimmune lipoprotein-antibody complexes [4] are markedly increased in the intima of atherosclerotic arteries.

Thus, the presence of plasma cells in the aortic intima of hypercholesterolemic rabbits is not an unexpected phenomenon. The appearance of these cells is likely to be associated with the necessity of antibody production *in situ* to bind modified (predominantly, peroxidized) lipoproteins with autoantigen activity. Transport of synthesized antibodies from the cell by gemmation of processes filled with RER is an intriguing issue.

It can be suggested that plasma cells migrating from peripheral blood into the arterial wall acquire this ability due to the presence of cytokine- and growth factor-synthesizing cells in atherosclerotic intima [1]. The release of protein in gemmated processes may be associated with the necessity of rapid neutralization of an antigen. A similar process was observed in mast cells. In an atheromatous plaque, histamine-like compounds from these cells are released by gemmation of processes filled with cytoplasm containing α-granules (Fig. 1, *e*). The problems of immunoglobulin synthesis and its re-

Department of Biochemistry, N. N. Anichkov Laboratory of Atherosclerosis, Institute of Experimental Medicine, Russian Academy of Medical Sciences, St. Petersburg

0007-4888/96/0009-0885$15.00

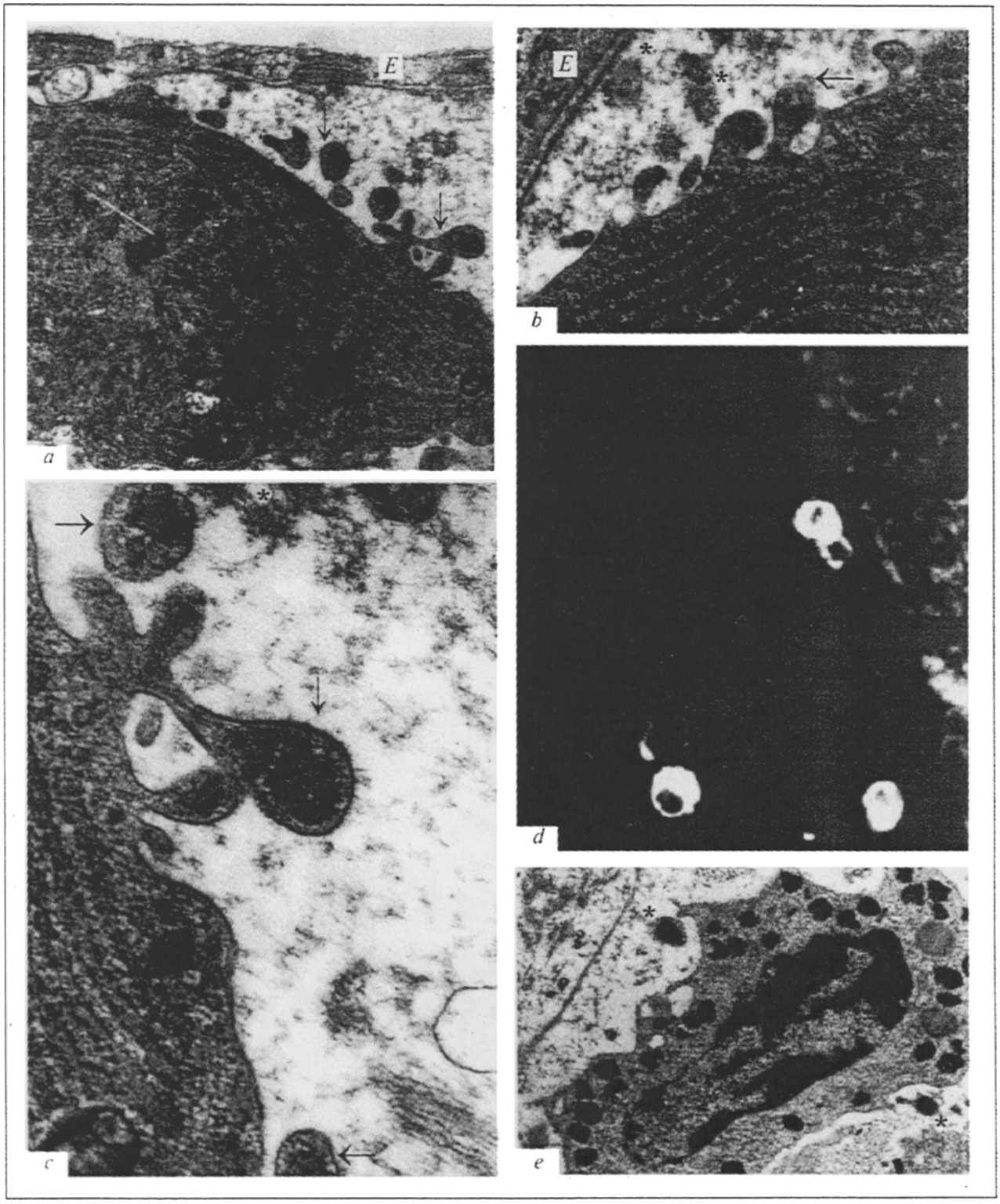

Fig. 1. Atherosclerotic plaques in the aorta of rabbit with experimental atherosclerosis.

a-c) plasma cell that probably synthesizes immunoglobulin; various stages of gemmating cell cytoplasm containing RER are indicated with arrows; asterisk indicates destroyed RER and release of small electron dense granules. *E*) endothelium; Transmission electron microscopy (TEM), ×8500 (*a*), ×12,000 (*b*).

c) fragment of panel *a*: formation of structure resembling a process with a thin "neck" (arrows), ×46,000.

d) B cells actively producing IgG. Coons technique with the use of FITC-conjugated rabbit antihuman IgG (Sigma), ×1000.

e) mast cell inside an atherosclerotic plaque, releasing histamine-like substance by gemmation of cellular cytoplasm with α-granules (indicated with an asterisk). TEM, ×8000.

lease in an atherosclerotic plaque as well as formation of autoimmune complexes *in situ* require further investigations.

REFERENCES

1. S. Clinton and P. Libby, *Arch. Pathol. Lab. Med.*, **116**, 1292-1300 (1992).
2. G. Hansson and S. Stemme, *Atherosclerosis X*, F. Woodford *et al.* (eds.), Elsevier Sci. B.V. (1995), pp. 61-65.
3. W. Hollander, M. A. Colombo, B. Kirkpatrick, and J. Paddock, *Atherosclerosis*, **34**, 391-405 (1979).
4. A. N. Klimov, *Angiologia*, **43**, 95-102 (1991).
5. R. Vlaicu, H. G. Rus, F. Niculescu, and A. Cristea, *Atherosclerosis*, **55**, 35-50 (1985).
6. Q. Xu, G. Oberhuber, M. Gruschwitz, and G. Wick, *Clin. Immunol. Immunopathol.*, **56**, 344-359 (1990).

State of the Myocardium in Rats of a New Hypertensive Strain

M. D. Shmerling, A. R. Antonov, I. M. Korostyshevskaya, A. L. Markel', V. F. Maksimov, E. E. Filyushina, and G. S. Yakobson

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 122, No. 9, pp. 271-273, September, 1996
Original article submitted March 6, 1996

Study of the heart in a new strain of rats with hereditary stress-induced hypertension (NISAG) reveals a complex of structural and functional changes which are analogous to the manifestations of essential hypertension. These changes are shown to be adaptive-compensatory in nature and indicative of limited functional reserves of the hypertrophic myocardium.

Key Words: *arterial hypertension; stress; myocardium; hormones; electrolytes*

The role of emotional stress in the development of hypertensive reactions has been extensively studied [3]. It was hypothesized that hereditary predisposition largely contributes to the etiology and pathogenesis of essential hypertension. However, there are no data on the interaction between the hereditary factor and stress in the realization of potential pathology.

Recently, a new strain of rats with hereditary stress-induced arterial hypertension (NISAG) has been obtained at the Institute of Cytology and Genetics (Siberian Division of the Russian Academy of Sciences) [10]. These rats are characterized by high sensitivity to stress. The information regarding NISAG rats can be found in the literature [2,4,6]; however, no complex morphological and functional studies have been performed.

Our objective was to study structural and functional organization of the myocardium as the target organ in hereditary stress-induced arterial hypertension and to prove the adequacy of this experimental model for studying the role of the relationship between genotype and environment in the etiology and pathogenesis of essential hypertension.

MATERIALS AND METHODS

Experiments were carried out on six 6-month-old male NISAG rats (35th generation) weighing 370± 25 g. Normotensive male Wistar rats of the same age and weight served as the control. Morphological study was performed at the tissue, cellular, and subcellular levels. Cardiomyocytes (CMC) and stroma were studied by histomorphometric analysis [1]. Electron microscopy and stereomorphometry of

Institute of Physiology, Siberian Division of the Russian Academy of Medical Sciences; Institute of Cytology and Genetics, Siberian Division of the Russian Academy of Sciences, Novosibirsk; Novosibirsk Medical Institute

0007-4888/96/0009-0887$15.00