The Lung in Hemorrhagic Shock

II. Observations on Alveolar and Vascular Ultrastructure

Norman B. Ratliff, MD, James W. Wilson, MD, PhD,
Donald B. Hackel, MD, and Arthur M. Martin, Jr., MD

EXPERIENCE IN VIET NAM has demonstrated the importance of pulmonary damage as a major determinant of survival following hemorrhagic or traumatic shock.[1] However, relatively few studies have been published dealing with the effects of shock on the lung, and the majority of these studies have dealt with functional or with gross and light microscopic alterations (See Ref. 2 for review). The present studies represent an attempt to correlate in vivo observations of the alveoli and microvasculature of the lungs with structural observations of the same lung regions. The techniques employed are microcinematography of the living lung, light microscopic serial sections of the entire lung, and electron microscopic observations on selected areas of the lung.

In the previous paper in this series, the in vivo and light microscopic findings were discussed.[3] This paper is a definition of the ultrastructural alterations observed in the lungs of thoracotomized cats subjected to hemorrhagic shock followed by transfusion.

Methods

The experimental protocol has been described in detail in the first paper in this series.[3] To recapitulate briefly, anesthesia was induced in 15 healthy adult mongrel cats with intraperitoneal sodium pentobarbital, 15 mg/kg body weight, and a right lateral thoracotomy was performed. Through a tracheostomy, the animals were ventilated (Harvard respirator), and the lungs insufflated with a mixture of 95% O_2 and 5% CO_2. Hypotension was then induced in 11 of the cats by the graded withdrawal of blood from a femoral artery so that mean arterial pressure fell slowly from the mean control level of 150 mmHg to the shock level of 60–70 mmHg. The blood pressure was maintained at this level for 2 hr and was stabilized by saline given intravenously as necessary. The animals were not heparinized, but heparin was added to blood as it was withdrawn from the femoral artery.

From the Department of Pathology, Duke University Medical Center, Durham, NC.

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Address for reprint requests: Dr. Norman B. Ratliff, Department of Pathology, Box 3712, Duke University Medical Center, Durham, NC 27706.

This blood was stored in a closed plastic reservior and returned to the animals at the end of the shock period.

With the animals still alive and anesthetized, the lungs were fixed in situ by one of three methods:

1. In 8 shock cats and all 4 control cats, the tracheobronchial tree was filled, through the tracheostomy, with 4% cacodylate buffered gluteraldehyde at room temperature. The infusion pressure was maintained at 10 cm of water. Tissue blocks were removed from the fixed lung with iris scissors, immersed in ice cold cacodylate buffered gluteraldehyde for a total fixation time in gluteraldehyde of 4 hr, and then washed overnight in cacodylate sucrose buffer. The tissue blocks were then cut into cubes (1 mm^3) and postfixed in 1% s-collidine buffered osmium tetroxide for 1 or 2 hr.
2. In 2 shock cats, in addition to the tracheobronchial perfusion with gluteraldehyde, 4% cacodylate buffered gluteraldehyde at room temperature was infused into the pulmonary artery via the right ventricle. The tissue was otherwise processed as above.
3. In 1 shock animal, a cannula was inserted, via the tracheostomy, into the right main stem bronchus. The right lung was then perfused with 1% s-collidine buffered osmium tetroxide for 2 hr.

Some of the tissues from each method of fixation were stained en bloc with uranyl acetate prior to dehydration.[4] All tissues were dehydrated in graded ethanols followed by propylene oxide and were embedded in Epon 812. Sections were cut on a Porter-Blum microtome with a diamond knife. Thick (1μ) sections for light microscopy were stained with toluidine blue. Thin (250–500 Å) sections were stained with uranyl magnesium acetate and lead citrate and were examined and photographed using Hitachi HU-11 or HS-7 electron microscopes. Four cats served as controls and were subjected to all experimental procedures except bleeding.

Results

Fixation

Fine structure was well preserved with both methods of gluteraldehyde fixation. The lungs tended to collapse when cut following the combined arterial and tracheobronchial gluteraldehyde perfusion, but lung architecture was consistently maintained in the expanded state with tracheobronchial gluteraldehyde perfusion alone. The granular pneumocytes were well preserved following osmium fixation, but the other lung elements were not well preserved, and the lung collapsed when cut with poor preservation of pulmonary architecture.

Terminology

There are two types of epithelial cells lining the alveoli. We shall use the term "membranous pneumocytes" to refer to the long, thin (diameter often less than 0.1 μ) lining cells which are sometimes called "Type I" cells.[5] They have relatively sparse cell organelles except in the perinuclear region, and contain numerous cytoplasmic vesicles resembling

the plasmalemmal vesicles of vascular endothelial cells. They are joined to each other by tight junctions (zonulae occludentes) thought to be impermeable to horseradish peroxidase.[6] These cells constitute the principal lining epithelium of the alveoli, but their function has not been clarified. We shall refer to the second type of alveolar lining cells as "granular pneumocytes." These are large cuboidal cells located predominantly within the angles formed by the junction of two or more alveolar septae. They are rich in mitochondria and contain large laminated osmiophilic bodies thought to be surfactant or surfactant precursors.[7] They exist as an integral part of the alveolar lining, and following desquamation, as motile phagocytic cells within the alveolar lumen.[5] They have been variously referred to as, among other names, "Type II" cells, "great alveolar cells," and "alveolar phagocytes."[5]

On morphologic grounds, small arterial vessels in the lung cannot be distinguished with certainty from venous vessels containing a continuous circumferential smooth muscle layer. We shall refer to such vessels simply as "muscular vessels." We shall use the word "capillaries" to mean vessels which have a luminal diameter of less than 10 μ and have no smooth muscle. Vessels with a luminal diameter greater than 10 μ containing either no smooth muscle or only occasional and discontinuous smooth muscle cells we shall call "venules" or "arteriolar precapillaries."

Controls

The control animals were examined carefully for alterations in structure which might have been secondary to the manipulations involved in obtaining the in vivo observations. The only alteration which we observed was minimal subpleural edema in the areas that had been under direct in vivo observation. Presumably, this was secondary to the saline drip which was employed to keep the lung surface moist. Otherwise, the structure by light and electron microscopy appeared completely normal (Fig. 1, 2, and 11).

Shock

The lungs of the shock animals contained extensive alterations in fine structure. The membranous pneumocytes were swollen to a varying degree. The detectable alterations in cell volume ranged from a modest diminution in the density of the cell sap, to severely swollen cells recognizable only as a plasmalemma surrounding an empty space (Fig. 3–5). This swelling was not associated with mitochondrial alterations. Swelling of the matrix compartment of mitochondria became prominent only when the cells were obviously necrotic (Fig. 6). Usually, if one

membranous pneumocyte of an alveolus was swollen, all of the membranous pneumocytes of that alveolus were altered.

Injury to the granular pneumocytes differed from that of the membranous pneumocytes. The granular pneumocytes frequently manifested swelling of the matrix compartment of mitochondria as well as blunting of the surface microvilli (Fig 7). Neither microcrystalline densities nor expansion of the intracristal spaces was observed in the mitochondria of granular pneumocytes, membranous pneumocytes, or endothelial cells.

Alterations of vascular endothelium were most prominent in capillaries, although occasional abnormalities were observed in the endothelial cells of muscular vessels. Venules and arteriolar precapillaries were identified infrequently, and those which were examined appeared uninjured. Variable degrees of swelling of the matrix compartment of mitochondria occurred without other alterations in endothelial cells (Fig 7). In addition, endothelial cells were frequently swollen, with decreased density of the cell sap (Fig 9 and 12). Occasional black laminated inclusions were seen in the endothelial cytoplasm (Fig 9), and plasmalemmal vesicles sometimes appeared more prominent than in the control animals (Fig 12). In contrast to the membranous pneumocytes, frequently one endothelial cell of a capillary was swollen, while the adjacent cells appeared to be uninvolved (Fig 9). In the only 2 animals which did not respond to transfusion, numerous capillary endothelial cells consisted of plasmalemma surrounding a mass of granular unrecognizable debris. Platelet aggregations were observed adhering to the endothelium of muscular vessels and of capillaries, even in the absence of detectable endothelial injury (Fig 13).

The lymphatics were difficult to recognize in the shock animals. This was in sharp contrast to the controls, where the lymphatics were easily identified adjacent to the muscular blood vessels in the interstitium. The recognizable lymphatics in the shock animals were distended. Some of the endothelial cells of these lymphatics were swollen, as were occasional pericytes and fibroblasts (Fig 3).

Separation of the connective tissue elements in the interstitium by electron–lucent spaces was striking and often extensive. These spaces did not contain the electron-dense granularity of plasma proteins or the finer granularity of the normal interstitial ground substance. The separation of connective tissue was diffuse, but did not take the form of subendothelial or subepithelial blebs. The location of this disruption of the interstitium was specific, occurring between the muscle layer and the adventitia of muscular vessels situated at the junction of two or more alveolar septa (Fig 7, 8, and 10).

Disruption of the interstitium was present in every shock animal examined, and the predictability of its location and occurrence suggests that both arterial vessels and veins were involved. Separation of connective tissue elements often extended into the contiguous thin alveolar septa for a variable distance, but never into the thinnest portion of the air-blood barrier, which consists of a membranous pneumocyte, a capillary endothelial cell, and a basement membrane. Furthermore, breaks in the alveolar lining were not seen. Interstitial disruption frequently occurred in association with swelling of the adjacent membranous pneumocytes and endothelial cells. However, it was also observed in the absence of injury to the adjacent cells, with the exception of modest swelling of the matrix compartment of endothelial cell mitochondria.

Discussion

Injury to the membranous pneumocytes of the lung of the extent and severity which we have observed has not been previously reported in association with shock, or with other forms of injury that involve alterations in vascular permeability.[8,9,10] Similar alterations have been reported in naturally occurring and artificially induced "bovine emphysema,"[11] following exposure to 15% CO_2,[12] secondary to alloxan poisoning,[13] and as a late event in the development of pulmonary oxygen toxicity.[14] However, we observed swelling of the membranous pneumocytes without alteration in the contiguous subjacent endothelium and interstitium; this has heretofore been reported only in bovine emphysema [11] and following exposure to 15% CO_2.[12] Animals breathing 15% CO_2 developed swelling of the membranous pneumocytes of the lung only during the phase of respiratory acidosis, and not when the acidosis was compensated.[12] It is possible that these three disparate conditions, hemorrhagic shock, CO_2 inhalation, and bovine emphysema, have the common link of alterations in acid-base balance. It would appear then that the extensive swelling of the membranous pneumocytes may be a reaction to a somewhat specific but as yet undefined type of injury in which disturbances in acid-base balance possibly are an important feature. The effects of injury to these cells on the movement of fluid into and out of the alveoli are not known, but swelling of the membranous pneumocytes would increase the diffusion path traversed by gases between alveolar air and blood.

In contrast, the alterations in vascular endothelial cells are probably a nonspecific manifestation of cell injury, since similar alterations have been reported as being secondary to bacterial, chemical, and physical injury.[8,10,12-20]

Alterations in the morphology of the granular pneumocytes following hemorrhagic shock may be related to the impaired surfactant activity reported to occur 18–72 hr postshock in nonheparinized dogs.[21] In conflict with this hypothesis is a recent report of injury to the granular pneumocytes in heparinized shock dogs without postshock alteration of surfactant activity.[22] The conflicting results obtained in these two studies may have been due to the use of heparin in one,[22] but not in the other.[21] Platelet agglutinations, which we observed, are known to occur in the pulmonary vascular bed secondary to shock,[20,23] and to adhere to even minimally injured endothelium;[24] the agglutinations can be prevented by prior heparinization of the experimental animal.[20] These facts suggest that platelet agglutinations may interfere with the recovery of the granular pneumocytes following shock.

The connective tissue elements of the interstitium were separated by clear spaces lacking the electron–dense granularity characteristic of a protein-rich fluid. This observation leads us to suggest that the interstitial edema fluid is predominately a transudate rather than an exudate. This concept is strengthened by the fact that we did not see widened intercellular spaces between endothelial cells or denuded vascular basement membranes, one or both of which would be expected in conjunction with an exudate.[15,17] The in vivo observations indicate that at least part of the separation of interstitial elements was secondary to gas in the interstitium.[3] Unfortunately, the preservation and identification of gas in fixed and embedded tissue is currently at a technical impasse, and we cannot distinguish between electron-lucent fluid and gas.

The lymphatics are located in the interstitium in the areas which were disrupted. This disruption plus lymphatic distension may have accounted for the difficulty in recognizing lymphatics in the shock animals.

The first alteration noted in the in vivo studies of shock animals was an increasing wall-to-lumen ratio in precapillary arterioles, frequently followed by a slowing and cessation of blood flow in the alveolar rings supplied by these vessels. Furthermore, the slowing and cessation of flow was temporally related to the later appearance of bubbles of gas in the interstitium.[3] The increased precapillary arteriolar wall-to-lumen ratio observed in vivo may correspond to fine structural separation of the adventitia from the smooth muscle of vessels whose location and structure are consistent with that of precapillary arterioles.

From the standpoint of pressure-flow relationships, the blood vessels

in the lung fall into 2 distinct groups: alveolar vessels (capillaries) which bulge into the alveoli and are exposed to the intra-alveolar pressure, and extra-alveolar (muscular) vessels which are surrounded by the connective tissue of the interstitium and are exposed to the interstitial pressure.[25-28] The relative negative interstitial pressure surrounding the extra-alveolar vessels plays an important role in maintaining the patency of these vessels and in promoting blood flow through them.[25-28] However, this relative negative pressure makes the interstitium particularly vulnerable to the accumulation of fluid but not to gas. Edema in this region would increase the interstitial pressure with the probable result being partial or complete loss of patency of the extra-alveolar vessels with subsequent slowing or cessation of blood flow through them. As blood flow slows, the gas partial pressure gradient from alveolar lumen to blood will become less, and, if the alveolus is ventilated, the gas in blood will approach equilibrium with the alveolar gas. Thus, the driving force for gas transfer and the inherent unsaturation of the interstitium will decrease. The system will then approach a state of phase equilibrium fulfilling Hills's thermodynamic conditions for random nucleation of the gas phase in tissues.[29,30] Once gas nuclei are established, formation of visible bubbles will depend on growth of the nuclei by acquiring gas from solution in the adjacent tissue, and their subsequent coalescence. When small bubbles coalesce, one would predict from thermodynamic principles that the bubbles would continue to enlarge unless impeded by some external force.[29,30] In the normal interstitium, the close approximation of connective tissue components would exert an external mechnical force against the enlargement of bubbles. In an edematous interstitium, the connective tissue elements are separated, creating a potential space for bubble enlargement. Thus, increasing interstitial pressure should facilitate the accumulation of gas in the interstitium.

As a result of their lower intraluminal pressure, flow through the veins would cease prior to arterial closure in the face of rising interstitial pressure. The effects of this would be similar to the effects of active venous constriction, and could account for the pulmonary congestion noted after transfusion.[2,3]

Consideration of the nature and extent of the alterations in fine structure, together with the sequence of events observed in vivo,[3] leads us to conclude that the precapillary arteriole and its enveloping interstitium is a strategic site of injury in the pathogenesis of the pulmonary damage which occurs secondary to hemorrhagic shock.

Summary

We have studied the alterations in the ultrastructure of feline lungs following hemorrhagic shock and transfusion, and have correlated our findings with in vivo observations on the microvasculature and alveoli of these same animals. Injury to the membranous pneumocytes of the lungs is a previously unreported but prominent feature of shock. Alterations in granular pneumocytes and vascular endothelium, platelet agglutinations, and derangement of the architecture of lymphatics are all present in the lung following shock. The most consistent alteration in shock is extensive interstitial edema around muscular blood vessels. We have suggested, on the basis of the sequence of events observed in vivo and the alterations in fine structure, that the precapillary arterioles and their surrounding interstitium are key sites of injury in the development of the pulmonary damage observed secondary to hemorrhagic shock.

References

1. EISEMAN B: Introduction to conference. *J Trauma 8:* 649–650, 1968.
2. SEALY WC: The lung in hemorrhagic shock. *J Trauma 8:*774–781, 1968.
3. WILSON JW, RATLIFF NB, HACKEL DB: The lung in hemorrhagic shock I. *In vivo* observations of pulmonary microcirculation in cats. *Amer J Path 58,* 337–351, 1970.
4. FARQUHAR MG, PALADE GE: Cell junctions in amphibian skin. *J Cell Biol 26:*263–291, 1965.
5. BERTALANFFY FD: On the nomenclature of the cellular elements in respiratory tissue. *Amer Rev Resp Dis 91:*605–609, 1965.
6. SCHNEEBERGER-KEELEY EE, KARNOVSKY MJ: The ultrastructural basis of alveolar-capillary membrane permeability to peroxidase used as a tracer. *J Cell Biol 37:*781–793, 1968.
7. BENSCH K, SCHAEFER K AVERY ME: Granular pneumocytes: Electron microscopic evidence of their exocrinic function. *Science 145:*1318–1319, 1964.
8. FINEGOLD MJ: Interstitial plumonary edema; an electron microscopic study of the pathology of staphylococcal enterotoxemia in Rhesus monkeys. *Lab Invest 16:*912–924, 1967.
9. FINEGOLD MJ: Pneumonic plague; an electron microscopic study. *Amer J Path 54:*167–185, 1969.
10. TEPLITZ C: The ultrastructural basis for pulmonary pathophysiology following trauma. *J Trauma 8:*700–712, 1968.
11. EPLING GP, GIDDINGS FP, KILMINSTER AE, DUNHAM D, STRINGER JM: The sequence of alveolar wall damage in emphysema—an electron microscopic study. *Anat Rec 163:*182, 1969.
12. SCHAEFER KE, AVERY ME, BENSCH K: Time course of changes in surface tension and morphology of alveolar epithelial cells in CO_2 induced hyaline membrane disease. *J Clin Invest 43:*2080–2093, 1964.

13. COTTRELL TS, LEVINE OR, SENIOR RM, WIENER J, SPIRO D, FISHMAN AP: Electron microscopic alterations at the alveolar level in pulmonary edema. *Circ Res 21*:783–797, 1967.

14. KISTLER GS, CALDWELL PRB, WEIBEL ER: Development of fine structural damage to alveolar and capillary lining cells in oxygen-poisoned rat lungs. *J Cell Biol 32*:605–628, 1967.

15. COTRAN RS: The delayed and prolonged vascular leakage in inflammation. II. An electron microscopic study of the vascular response after thermal injury. *Amer J Path 46*:589–620, 1965.

16. COTRAN RS: Delayed and prolonged vascular leakage in inflammation III. Immediate and delayed vascular reactions in skeletal muscle. *Exp Molec Path 6*:143–155, 1967.

17. COTRAN RS: Studies on inflammation. Ultrastructure of the prolonged vascular response induced by clostridium oedematiens toxin. *Lab Invest 17*:39–60, 1967.

18. BERDJIS CC, VICK JA: Endotoxin and traumatic shock. *JAMA 204*:191–194, 1968.

19. LEROY EP, LIEBNER EJ, JENSIK RJ: The ultrastructure of canine alveoli after supervoltage irradiation of the thorax. *Lab Invest 15*:1544–1558, 1966.

20. GOODMAN JR, LIM RC JR, BLAISDELL FW, HALL AD, THOMAS AN: Pulmonary microembolism in experimental shock. *Amer J Path 52*:391–400, 1968.

21. HENRY JN, MCARDLE AH, BOUNOUS G, HAMPSON, LG, SCOTT HJ, GUARD FN: The effect of experimental hemorrhagic shock on pulmonary alveolar surfactant. *J Trauma 7*:691–726, 1967.

22. BARKETT VM, COALSON JJ, GREENFIELD LJ: Early effects of hemorrhagic shock on surface tension properties and ultrastructure of canine lungs. *Bull Johns Hopkins Hosp 124*:87–94, 1969.

23. ROBB HJ: The role of micro-embolism in the production of irreversible shock. *Ann Surg 158*:685–692, 1963.

24. ASHFORD TP, FREIDMAN DG: Platelet aggregation at sites of minimal endothelial injury. *Amer J Path 53*:599–607, 1968.

25. HOWELL JBL, PERMUTT S, PROCTOR DF, RILEY RL: Effects of inflation of the lung on different parts of pulmonary vascular bed. *J Appl Physiol 16*:71–76, 1961.

26. PERMUTT S: Effect of interstitial pressure of the lung on pulmonary circulation. *Med Thorac 22*:118–131, 1965.

27. WEST JB, DOLLERY CT, HEARD BE: Increased pulmonary vascular resistance in the dependent zone of the isolated dog lung caused by perivascular edema. *Circ Res 17*:191–206, 1965.

28. WEST JB: "Aspects of the Pulmonary Microcirculation." In *Microcirculation as Related to Shock*. Shepro, D., and Fulton, G. P., Eds. Acad Press, New York, 1968.

29. HILLS BA: *A Thermodynamic and Kinetic Approach to Decompression Sickness*. Libraries Board of South Australia, Adelaide, 1966.

30. HILLS BA, LEMESSURIER DH: Unsaturation in living tissue relative to the pressure and composition of inhaled gas and its significance in decompression theory. *Clin Sci 36*:185–195, 1969.

Legends for Figures

Key: A Alveolar air space
B Blood vessel lumen
I Interstitium
M Mitochondria
E Erythrocyte

Fixation and staining: All illustrations are micrographs of lungs fixed by perfusing the tracheobronchial tree with 4% cacodylate buffered gluteraldehyde and postfixed in 1% s-collidine buffered osmium tetroxide. Sections for electron microscopy were stained with uranyl magnesium acetate and lead citrate. Sections for light microscopy were stained with toluidine blue.

Fig 1. *(upper)* Control. Capillary protrudes into alveolus from thick septum. Endothelial cells of capillary and membranous pneumocytes lining alveolus share common basement membrane. Membranous pneumocytes and endothelial cells are thin and have electron-dense cytoplasm. Collagen fibers in thick septum beneath capillary are densely packed. × 18,500.

Fig 2. *(lower)* Control. Interstitium at vascular branching point. Two capillaries are evident. Note fine electron-dense granularity of normal interstitial ground substance. × 18,500.

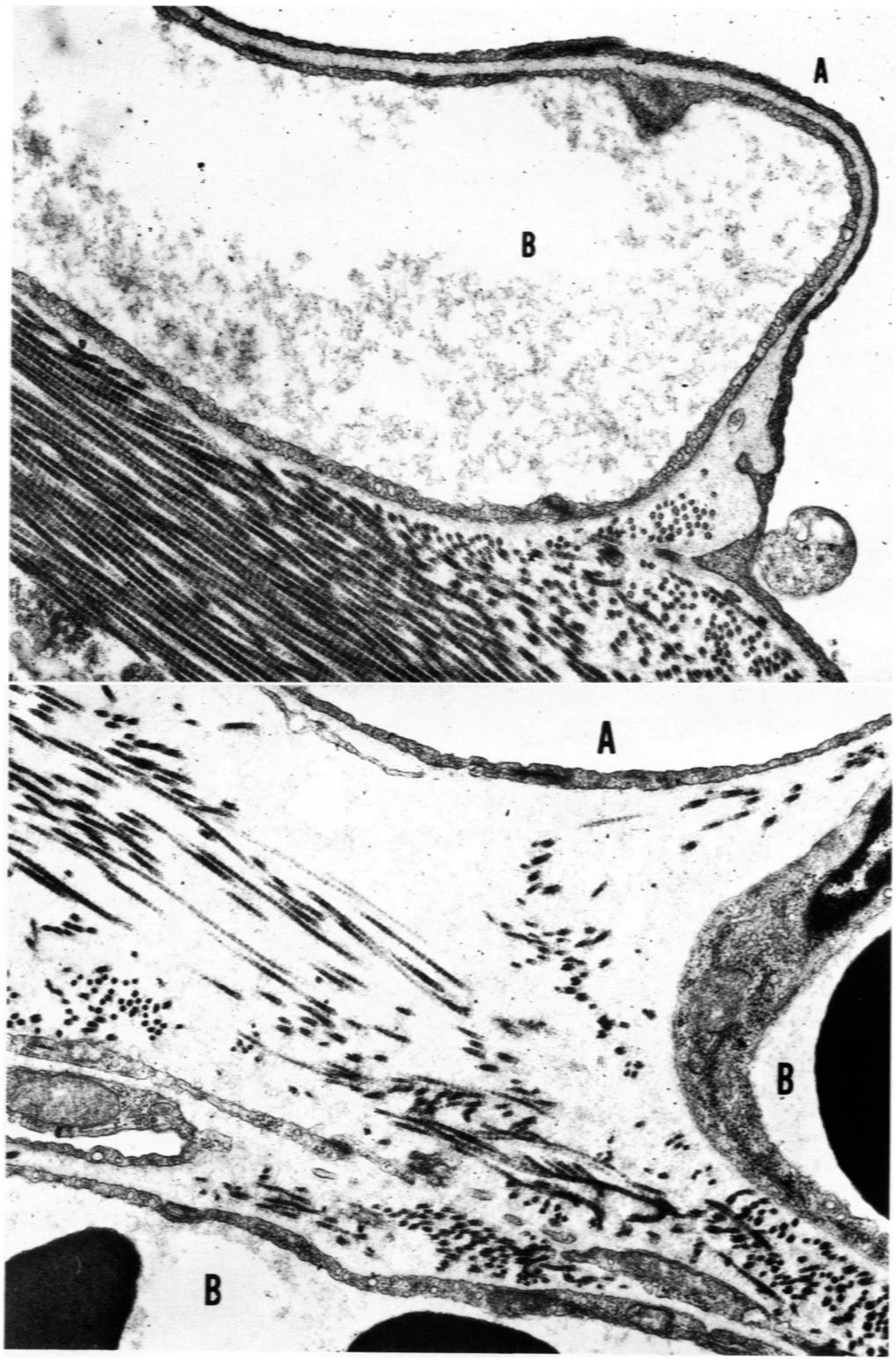
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Fig 3. *(upper)* Shock. Swollen membranous pneumocytes. Cell diameter is increased, with decrease in density of cytoplasm. Similar changes are evident in portion of fibroblast in interstitium on left side of picture. Tip of granular pneumocyte is adjacent to membranous pneumocyte in alveolar air space on right side of picture. Interstitium beneath membranous pneumocyte is disrupted, with elastic tissue surrounded by electron lucent space. × 47,725.

Fig 4. *(lower)* Shock. Swollen membranous pneumocyte situated at tip of thin alveolar septum. Plasmalemmal vesicles are apparent near basal and alveolar plasmalemma. Otherwise, cytoplasm is empty with exception of mitochondrion which appears to be uninjured. × 40,180.

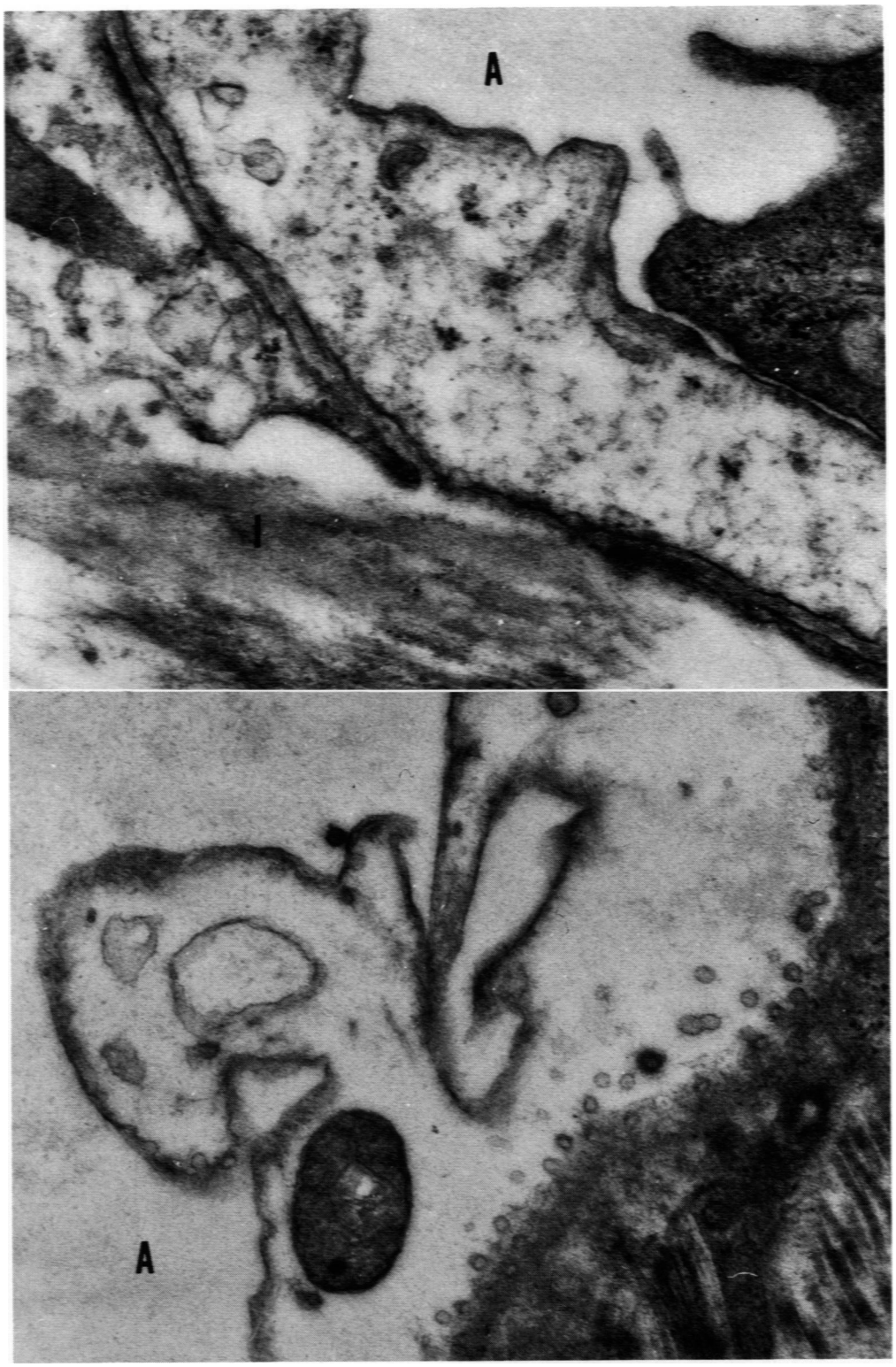
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Fig 5. *(upper)* Shock. Thin alveolar septum with alveolar air spaces on both sides. One of the membranous pneumocytes is severely swollen. In contrast, the other membranous pneumocytes appear normal, an unusual occurrence. × 11,100.

Fig 6. *(lower)* Shock. Necrosis of membranous pneumocytes. Cell volume is increased. Cytoplasm contains membrane profiles and granular debris. The only recognizable cell organelles are mitochondria with severe matrix swelling and absence of normal cristae. × 20,780.

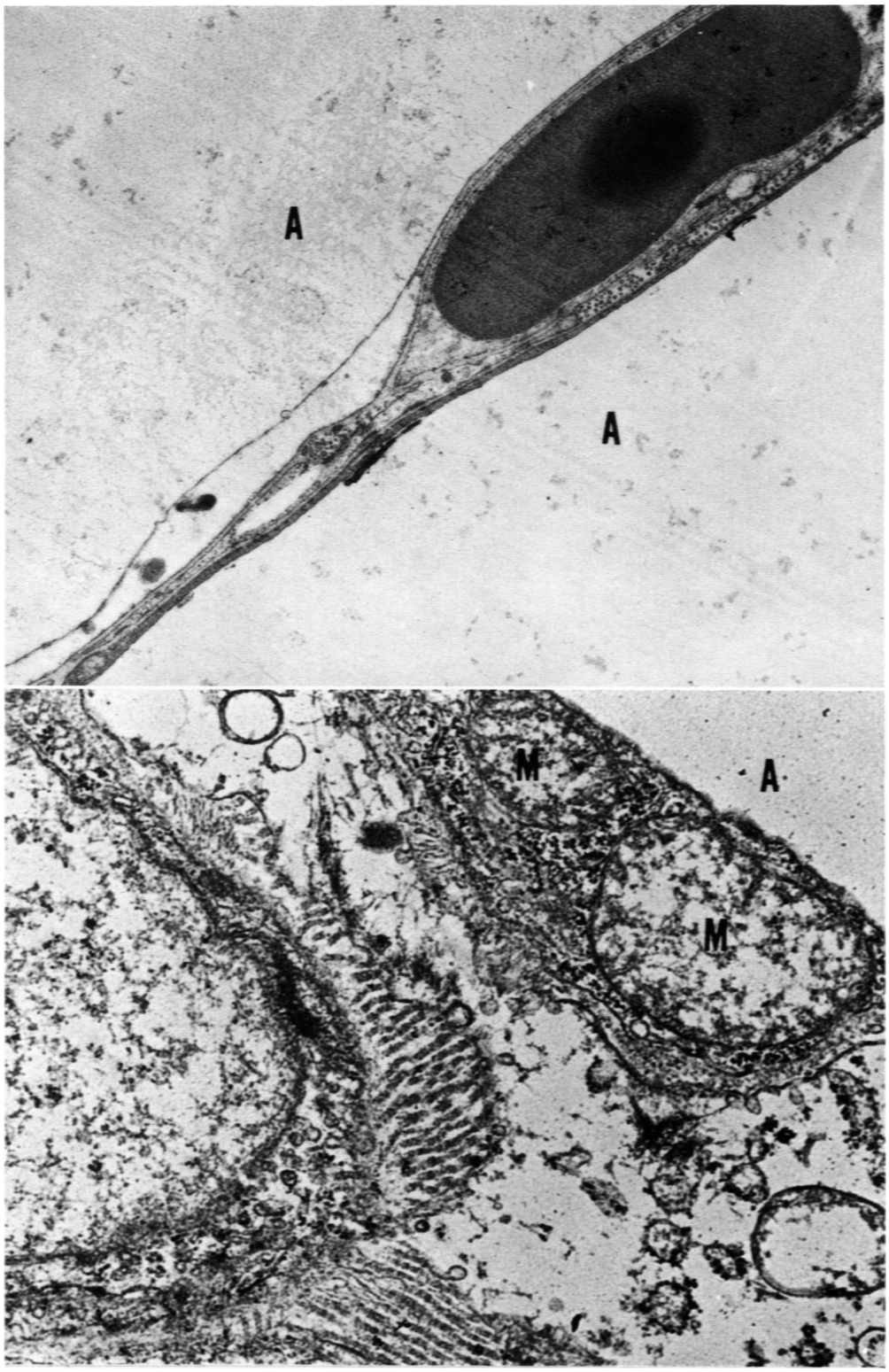
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Fig 7. *(upper)* Shock. Disruption of interstitium around muscular blood vessel. Muscle layers appear intact, but connective tissue elements of interstitium are separated by electron-lucent space. Matrix compartment of mitochondrion in endothelial cell of muscular vessel is severely swollen, with absence of normal cristae. Adjacent alveolus contains granular pneumocyte. Matrix compartment of mitochondrion in this cell is swollen, but cristae are still recognizable. Membranous pneumocyte lining alveolus is somewhat swollen (compare with Fig 1). Cells lying free in interstitium could be either fibroblasts or lymphatic endothelial cells. They are not swollen, and are situated where lymphatics were consistently seen in control cats. × 13,830.

Fig 8. *(lower)* Shock. Disruption of interstitium around muscular blood vessel, more severe than that in Fig 7. Interstitial elements are widely separated by clear space, but none of the cells (endothelial, membranous pneumocytes, smooth muscle, and interstitial) are altered. × 11,260.

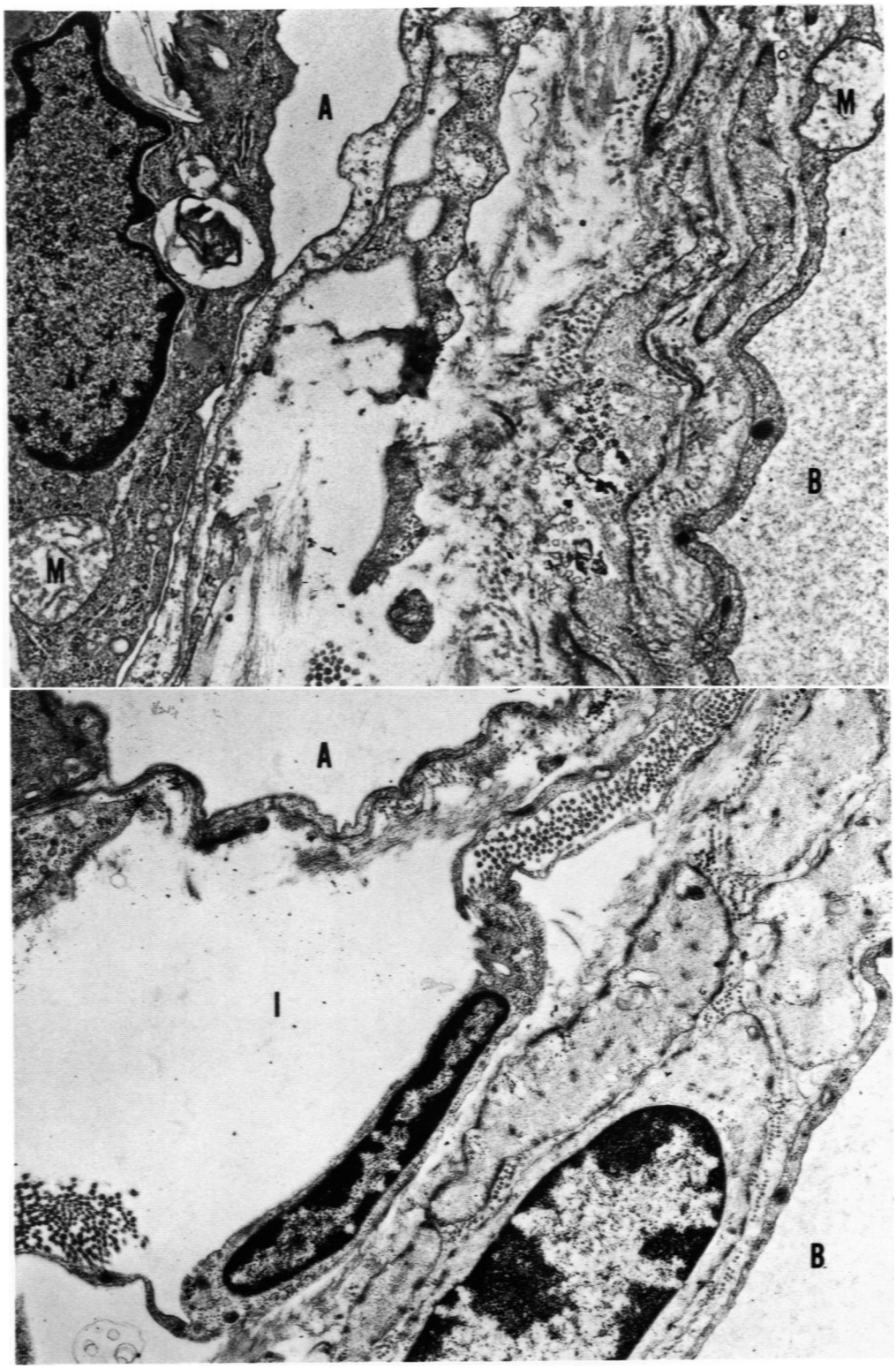
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Fig 9. *(left)* Shock. Capillary endothelial cells. On left-hand side of picture is alveolar air space bounded by membranous pneumocyte. Directly beneath basement membrane of pneumocyte are portions of two interstitial cells, probably pericytes. On right-hand side of picture is capillary lumen lined by endothelial cells. Endothelial cell at top of picture is swollen and cell sap is pale. This cell contains two prominent osmiophilic structures reminiscent of myelin figures. There is an apparent loss of continuity of luminal plasmalemma overlying osmiophilic structures. Adjacent endothelial cell (bottom of picture) appears completely normal. × 44,650.

Fig 10. *(upper right)* Shock. Disruption of interstitium around muscular vessel at septal branching point. Vessel, which is devoid of erythrocytes, is probably an arteriole. Note extension of disruption into adjacent thin septums. Compare with Fig 11. Light microscopy. × 400.

Fig 11. *(lower right)* Control. Normal muscular vessel, filled with erythrocytes, at septal branching point. Compare with Fig 10. Light microscopy. × 400.

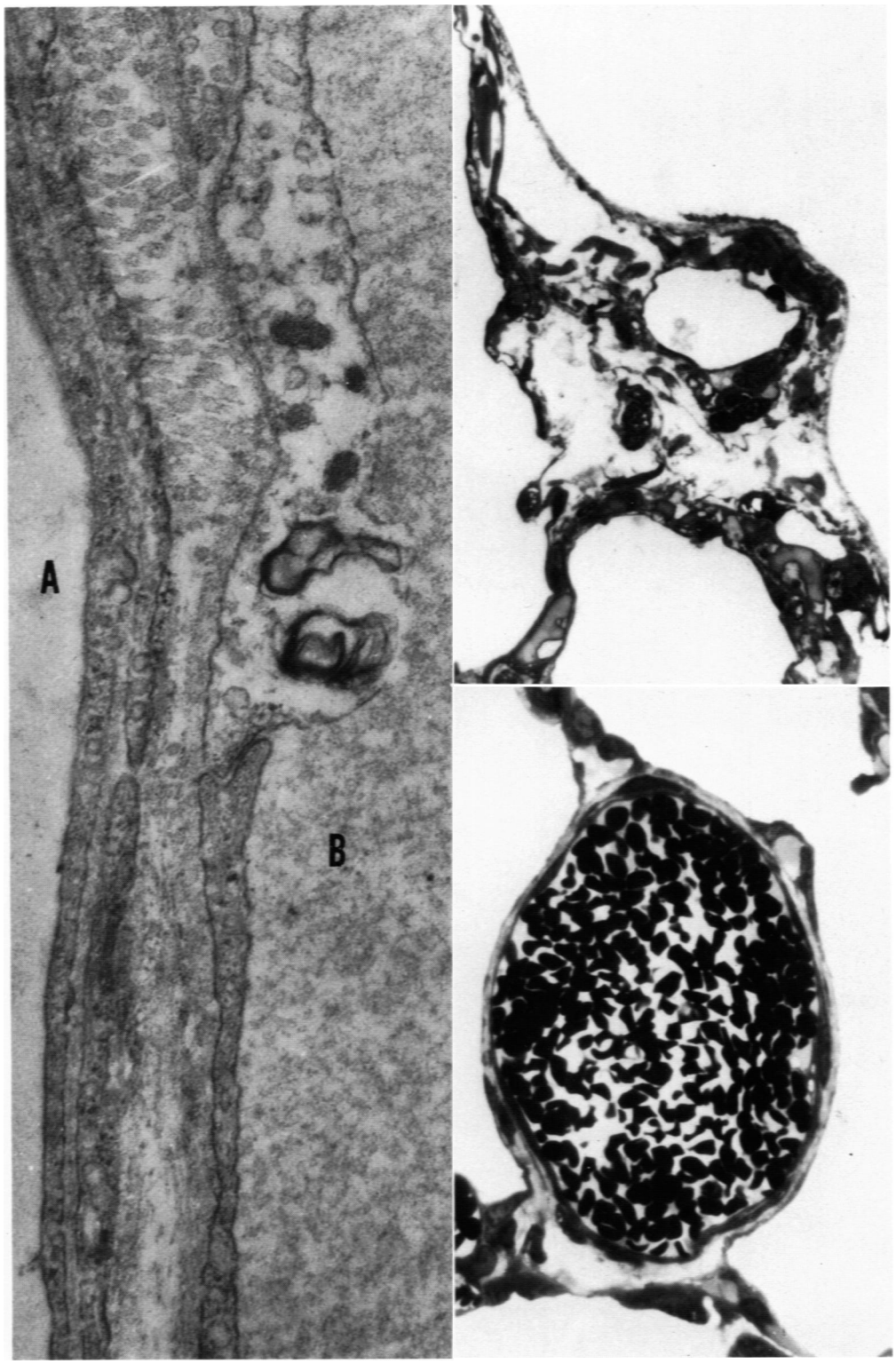
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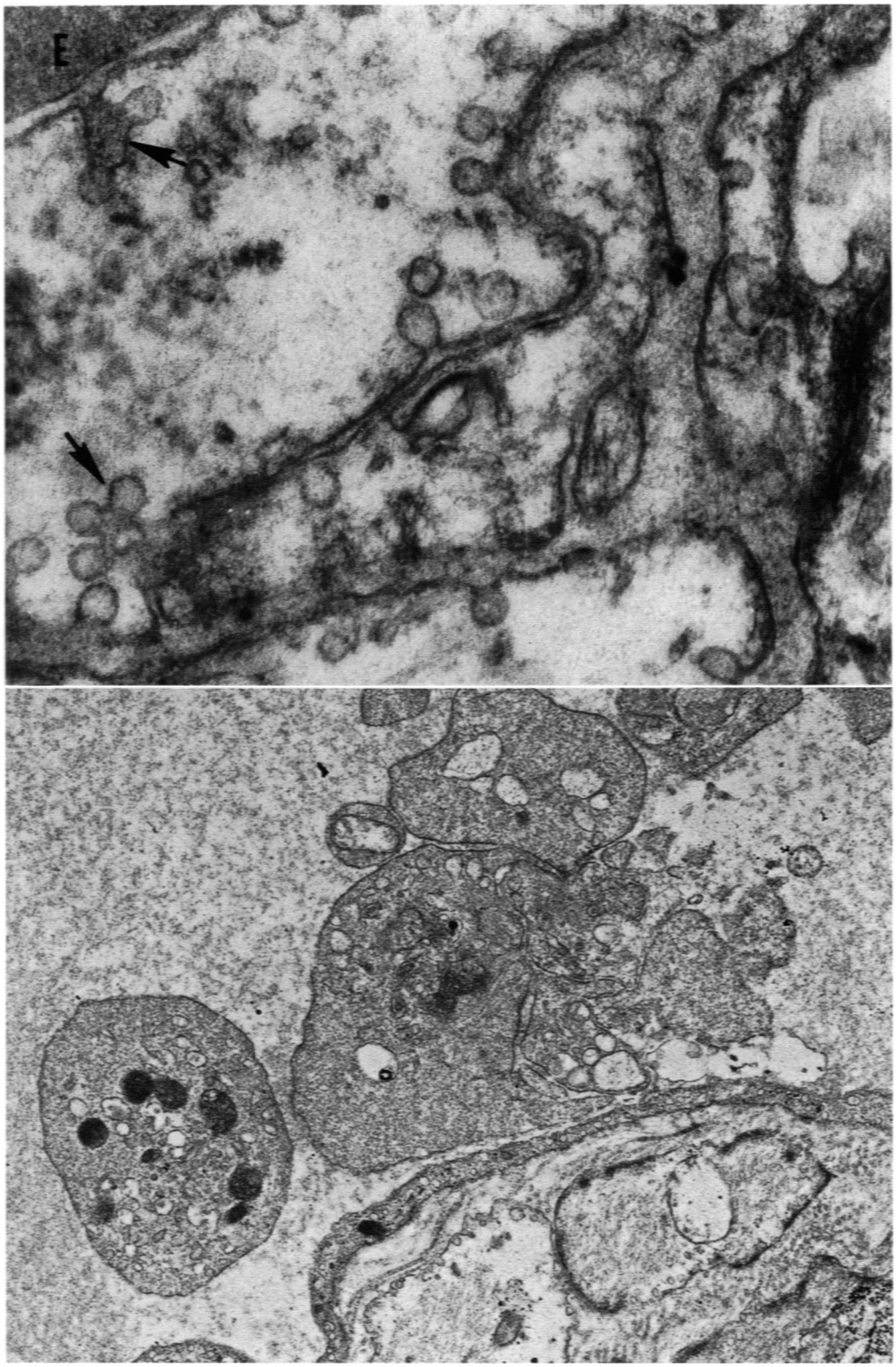
Fig 12. *(upper)* Shock. Swollen capillary endothelial cell. Density of cell sap is decreased. Plasmalemma is intact. Two of the plasmalemmal vesicles have an unusually complex structure *(arrow)*. × 69,840.

Fig 13. *(lower)* Shock. Platelets adherent to endothelium of muscular blood vessel. Endothelium appears normal, but adherent platelets are degranulated. Platelet floating free in vascular lumen contains normal granules. × 16,600.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