## Bronchiolar and Large Alveolar Cell in Pulmonary Phospholipid Metabolism

Abstract. *The nonciliated bronchiolar cells (Clara cells) lining the terminal airways actively secrete a phospholipid. In contrast, the large alveolar epithelial cells (type II, granular pneumonocyte) are active phagocytic cells. It is proposed that the Clara cell is the main source of pulmonary phospholipid production (presumably surfactant) while the large alveolar cell is responsible for its subsequent breakdown.*

The lung has a large metabolic capacity for producing phospholipids (*1*). Presumably these phospholipids line the smaller airways and alveoli with a film capable of markedly reducing surface activity, thus promoting alveolar stability (*2*). As a result of this unique property to reduce surface tension, the material extracted from lungs has been named pulmonary surfactant (*3*).

It is widely accepted that the large alveolar cell is the source of pulmonary surfactant. This fact is based on indirect evidence (*4*) which fails to distinguish between the production of and breakdown of phospholipids. The present study supports the concept that the nonciliated bronchiolar cell [Clara cell (*5*)] is the source of surfactant and that the large alveolar cell is a phagocytic cell responsible for its subsequent clearance from the lung.

The large alveolar cell has been considered a secretory cell with the observation that lipid granules were extruded from the cell (*6*). However, in fixed tissue, it may be difficult to distinguish between the process of secretion and phagocytosis (Fig. 1). This problem was investigated by exposing unanesthetized mice to aerosolized carbon. The large sessile alveolar cells actively phagocytized carbon particles and lipid material from the alveolar space (Fig. 2). At a later stage, carbon particles were observed within osmiophilic lamellar bodies (Fig. 2), clear evidence that the lamellar bodies resulted from the ingestion of lipid material by, and were not a secretory product of, the cell. Acid phosphatase (*7*) was demonstrated at the membrane that lines many of the lamellar bodies, which indicates that these intracellular particles were lysosomes, that is, phagocytic vacuoles containing acid hydrolysates (*8*).

In contrast, the nonciliated bronchiolar cells which line the terminal and respiratory bronchioles, and which are rich in mitochondria and agranular endoplasmic reticulum, are active secretory cells. Secretory droplets appear to form in the Golgi area, to collect at the apex of the cell, and to be extruded into the bronchiolar lumen (Fig. 3). These cells demonstrated no

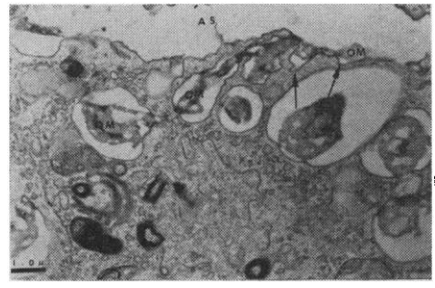


Fig. 1 (left). Large alveolar cell from a mouse exposed to 1 percent carbon monoxide for 12 minutes. Cell appears to be engulfing osmiophilic material (*OM*) with beginning indentation of the cell wall (arrows). However, the distinction between phagocytosis (material entering the cell) and secretion (material leaving the cell) cannot be made from such observations. *AS*, alveolar space.

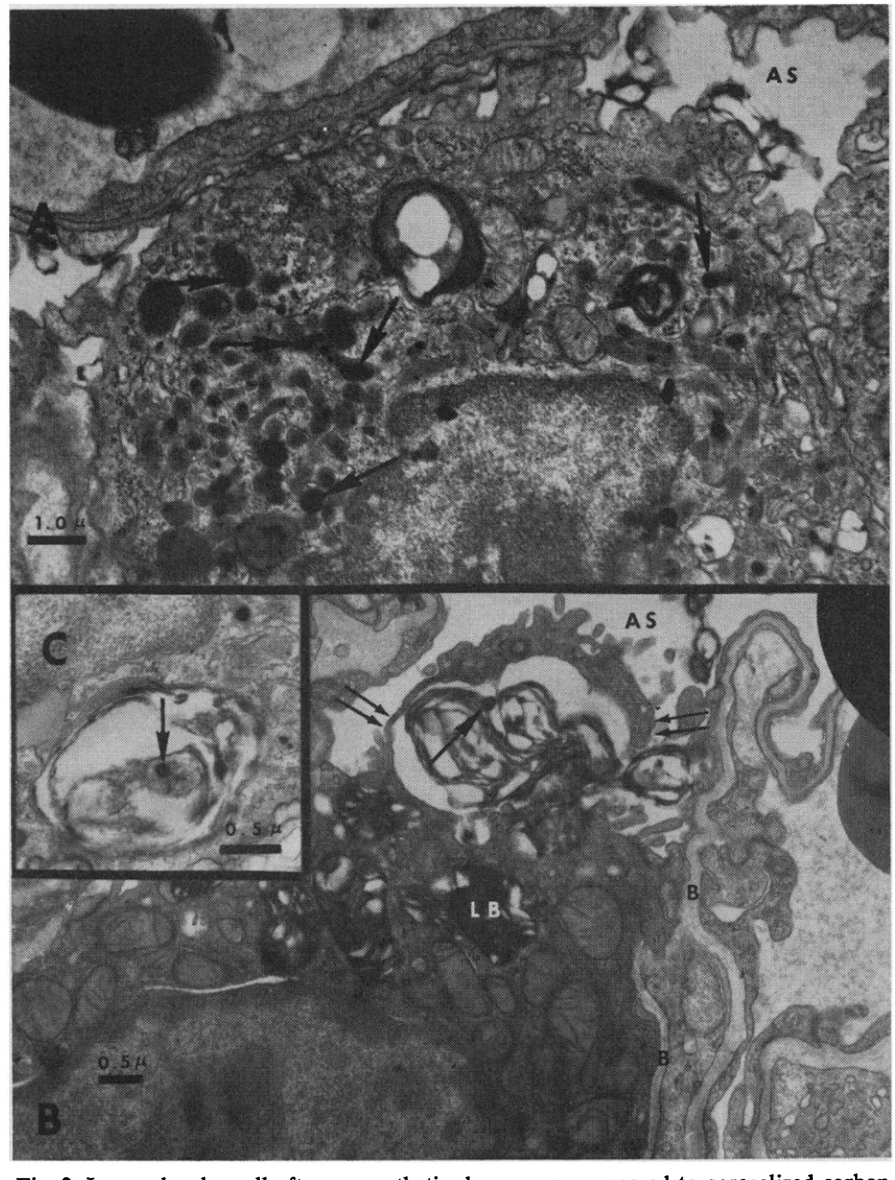


Fig. 2. Large alveolar cell after unanesthetized mouse was exposed to aerosolized carbon for 30 seconds every 5 minutes over a 30-minute period. (A) Carbon particles (arrows) within membrane-limited osmiophilic granules. (B) Attenuated epithelial extension (arrows) enveloping osmiophilic material and carbon particle (arrow). Note normal lamellar bodies (*LB*) and attachment of cell to basement membrane (*B*). (C, inset) Lamellar body with carbon particles inside (arrow). *AS*, alveolar space.

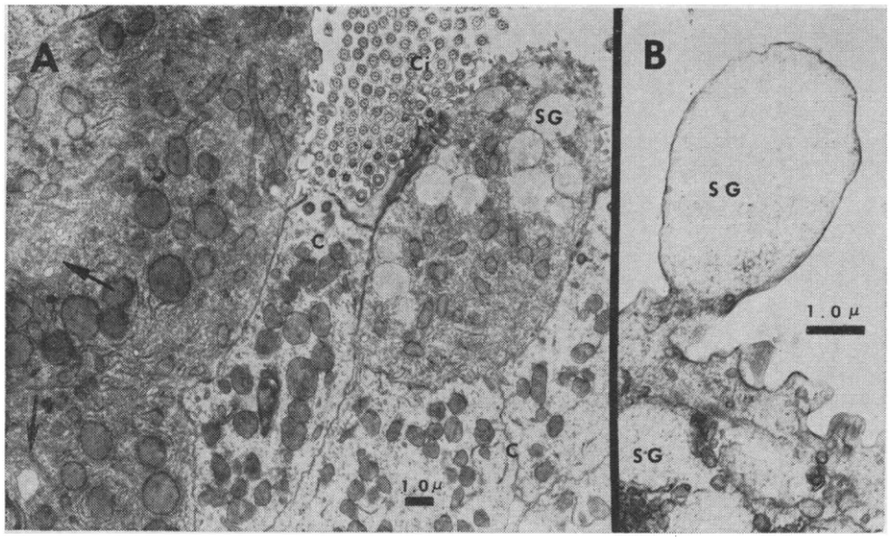


Fig. 3. Terminal bronchiole from normal mouse. (A) Bronchiolar cells at left with well-formed Golgi area and early development of secretion granules (arrows). Bronchiolar cell at right with secretory droplets collecting at apex of cell (*SG*). *C*, ciliated cells; *Ci*, cilia. (B) Extrusion of secretory granule from apex of bronchiolar cell. *SG*, secretory granule.

phagocytic activity. Ciliated cells are present in the terminal bronchiole but disappear in the respiratory bronchiole, well before the alveoli are reached. Thus the major portion of this bronchiolar secretion is not exposed to ciliary activity.

These secretion granules did not stain with periodic acid-Schiff, Alcian blue, or Sudan black, indicating the absence of mucopolysaccharides, acid mucopolysaccharides, and free lipids. However, the granules did stain with Sudan black–acetone, Baker's acid hematin, and silver hydroxylamine in an aqueous solution (Fig. 4A), indicating the presence of a phospholipid (*9*).

Following the injection of tritiated palmitate or acetate intraperitoneally, autoradiographically positive granules (*10*) were observed within 5 minutes at the apex of the Clara cells (Fig. 4B). The presence of positive granules after tissue extraction of free lipids demonstrates the ability of these cells to synthesize phospholipids from fatty acids.

Although pulmonary surfactant has not been completely identified, it has been characterized as a phospholipid (*11*). Thus, until pulmonary surfactant has been more precisely identified, it is only a presumption that the phospholipid produced by the Clara cell is surfactant.

The large alveolar cell was the only other cell which incorporated tritiated palmitate and acetate. Although the possibility that this alveolar cell is also capable of synthesizing phospholipids cannot be excluded, the present study demonstrating the phagocytic activity of this cell suggests that the radioactive material was ingested by the cell as a phospholipid lying free in the alveoli.

Thus it is proposed that the nonciliated bronchiolar cell is the major site of pulmonary phospholipid production (presumably surfactant), while the large alveolar cell is a phagocytic cell responsible for the clearance of lipids as well as other materials from the alveolar area.

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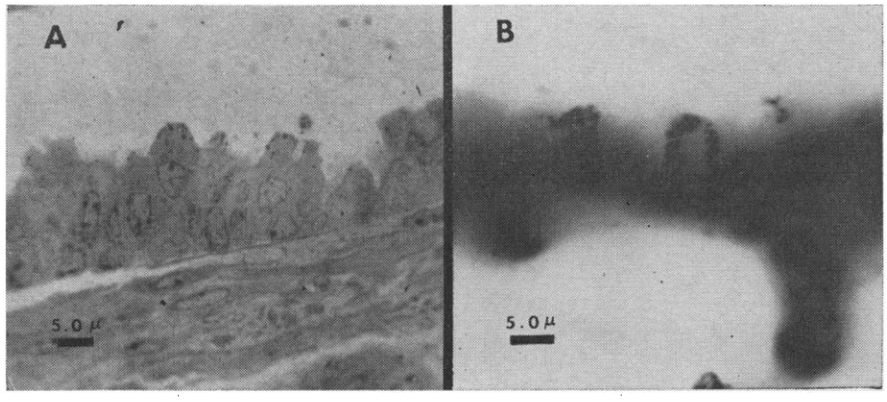


Fig. 4. (A) Nonciliated bronchiolar cells stained with silver-hydroxamate reaction, embedded in Epon and counterstained lightly with Toluidine Blue. Granules at apex of bronchiolar cell stain positive for phospholipid. (B) Autoradiography of terminal bronchus 5 minutes after injection of tritiated palmitate intraperitoneally. Positive granules are at apex of bronchiolar cell.

**References and Notes**

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