optimal situation conditioning the highest radioresistance can be understood as a preponderance of the favorable effects of intermittent fasting over the simultaneously acting unfavorable influences, e.g. stress due to a reduced caloric intake after a long period of fasting.

The type of metabolism in which the energy potential of a system is restored, in particular on account of the free energy of lipids, generally characterizes processes of long-term adaptation to stress effects[8]. The results presented may therefore be discussed especially from the point of view of the role of lipid metabolism. This consideration is supported by some earlier experimental results. Increased radiation resistance of mice exhibiting RQ-values greater than 1.0 before irradiation was demonstrated, and the importance of higher fat energy stores and of the subsequent sparing of proteins during the postirradiation catabolic reaction was considered[9]. Analogous mechanisms may participate in the radioprotective action of long-term acclimatization of animals to cold[10]. A greater body mass due to higher storage of fat was observed in mice selected for higher radioresistance[11]. The possible active role of some components of lipid metabolism in the regulation of cell populations, and/or of their radiosensitivity cannot be neglected. It was shown that increasing the content of fat reserve substances in yeast cells decreased their radiosensitivity[12]. Further, lipogenesis as well as lipid composition of the bone marrow are altered in medullary hemopoiesis changes, and causal relationships between these functions are suggested[13,14]. It is of course possible that some other metabolic or enzyme pathways, independent of fat metabolism, which facilitate the repair or recovery processes in the irradiated organism, may be involved in the radioprotective effects of the intermittent food intake.

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Clara cell surface of the rat: scanning and transmission electron microscopic study[1]

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Summary. In normal young rats, groups of Clara cells in the bronchioles showed the formation of many cytoplasmic blebs on their cytoplasmic domes. Detached blebs rested on the bronchiolar epithelial cells. The scanning (SEM) and transmission electron microscope (TEM) studies suggest localized changes of Clara cell surface activities by increased formation of cytoplasmic blebs which may represent the apocrine type of secretion.

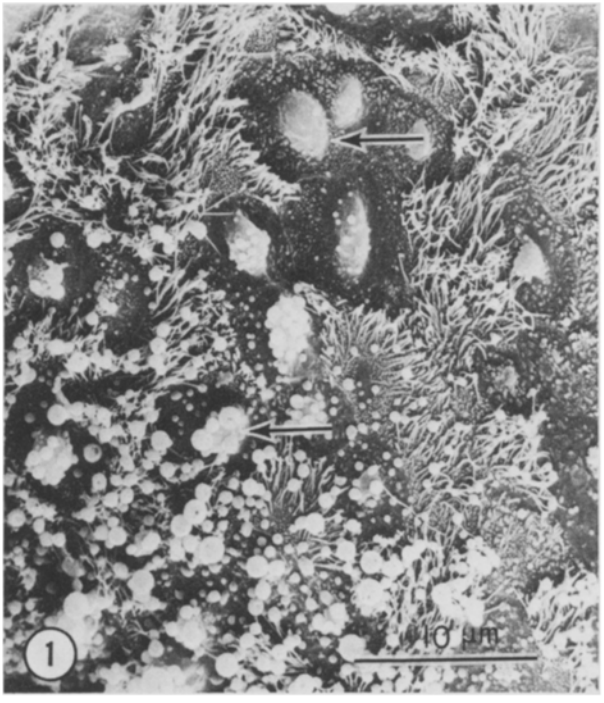
Clara cells are unique non-ciliated epithelial cells located in the bronchioles of many mammals. Their histochemical and ultrastructural characteristics indicate that these are secretory cells. Investigators were divided concerning their mode of secretion. Clara[2] who first described these cells in detail favored the mechanism of apocrine secretion, or decapitation of the apical cytoplasm. This mechanism was supported by more recent papers dealing with normal animals by Etherton et al.[3,4], and experimental animals exposed to hypoxia by Smith et al.[5] and Heath et al.[6,7], or treated with naphthalene by Mahvi et al.[8]. On the other hand, based on TEM and freeze fracture studies, Wang et al.[9], Kuhn et al.[10], Yoneda[11] and Yoneda and Birk[12] suggested the process of exocytosis or merocrine type of secretion, and Niden[13], Stinson and Loosli[14] and Pack et al.[15] illustrated that both apocrine and merocrine types probably occurred. The present report will show that in limited areas of the normal rat bronchioles, hyperactive Clara cells appear to undergo apocrine secretion or decapitation.

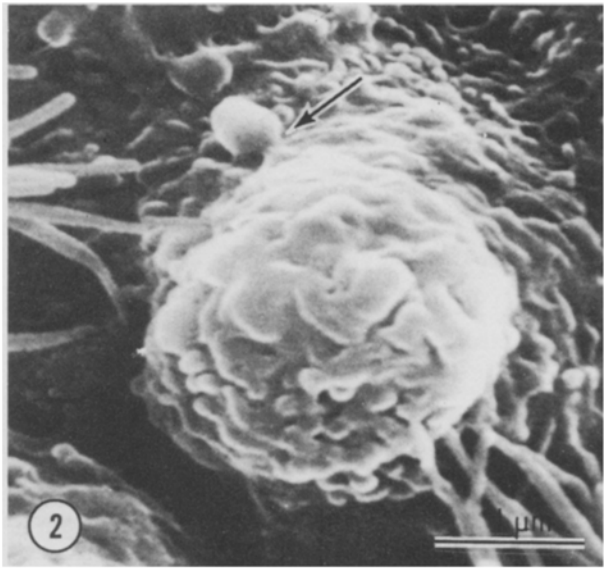
45 Sprague-Dawley rats at various ages from neonates to adults were used. Each animal was anesthetized with ether, the trachea was exposed, and the chest was opened to allow the lungs to collapse. 2% glutaraldehyde in 0.1 M phosphate buffer (pH 7.2, 480 mosm) was then injected slowly into the lungs through the trachea until the lungs filled the chest cavity. The entire lung was removed and placed in glutaraldehyde solution for at least 1 h. Each lobe of the lung was then cut along the long axis of the major airways to expose bronchiolar surfaces. The lung slices were then critical point dried and gold coated and observed in a JEOL JSM-35 SEM. Selected SEM specimens were reprocessed according to the methods of Hung et al.[16] for TEM observations. The specimens were placed in absolute alcohol, processed for embedding in araldite[17], thin sectioned, stained and observed in a JEOL 100S TEM. Some of the glutaraldehyde fixed lungs were processed for paraffin embedding and the sections stained with hematoxylin and eosin for light microscopy.

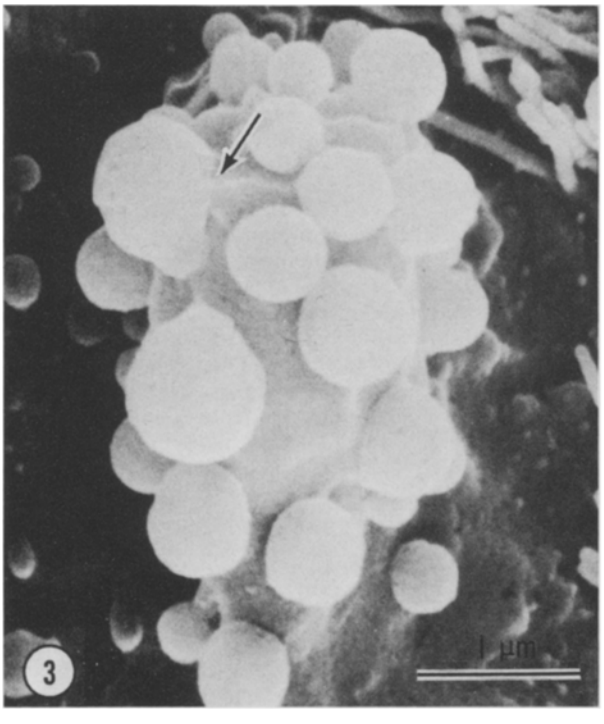
The light and electron microscope observations showed that the bronchioles were covered by the ciliated and Clara cells (figs 1 and 6). All Clara cells had characteristic cytoplasmic domes which sometimes showed surface convolution and microvilli (fig. 2). Occasionally, small cytoplasmic blebs projected from these cells (fig. 2). In 2 31-day-old rats, among the regular epithelium were small loci of apparently hyperactive Clara cells (fig. 1), which were covered by various amount of cytoplasmic blebs on their protruded domes (figs 1 and 2). The blebs were spherical and of random sizes (fig. 3) and were attached to the cell through a narrow cytoplasmic neck (fig. 4). In these specific loci, many detached blebs were seen to rest on the Clara or

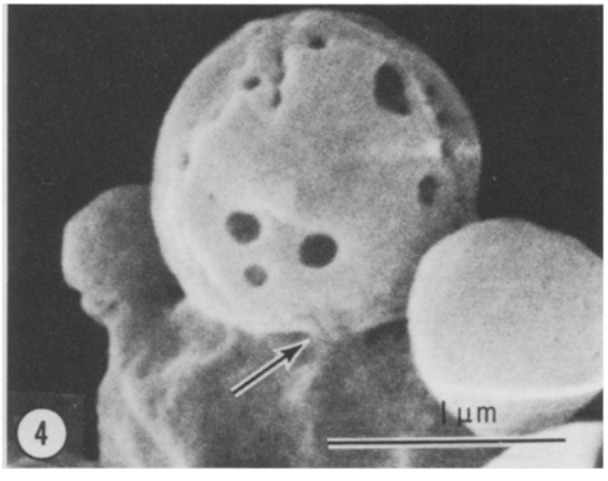
ciliated cells (fig. 5). Some of these blebs showed numerous small openings on their surfaces (fig. 4). TEM observations of the areas previously viewed by SEM showed projections of the cytoplasmic blebs from the lumenal surfaces of the Clara cells (figs 6 and 7). The blebs contained mostly dense cytoplasmic matrix including many ribosomal particles and other cell organelles (figs 6 and 7).

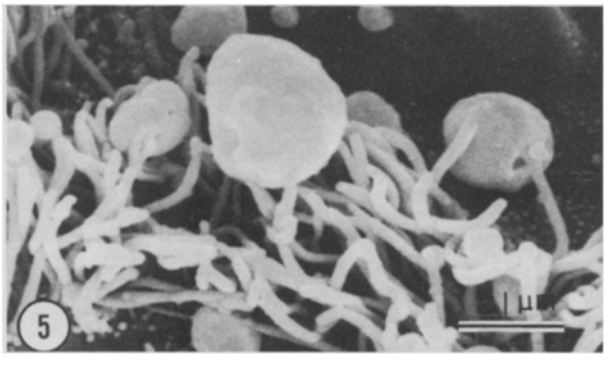
The present SEM observations indicate that Clara cells in specific loci of the rat lungs can develop many cytoplasmic blebs on their lumenal surfaces, and these blebs can become detached and rest on the bronchiolar epithelial cells. These blebs specifically occur on some Clara cells only and are not generalized throughout the entire lung. Therefore, it is unlikely that these blebs are artifacts.



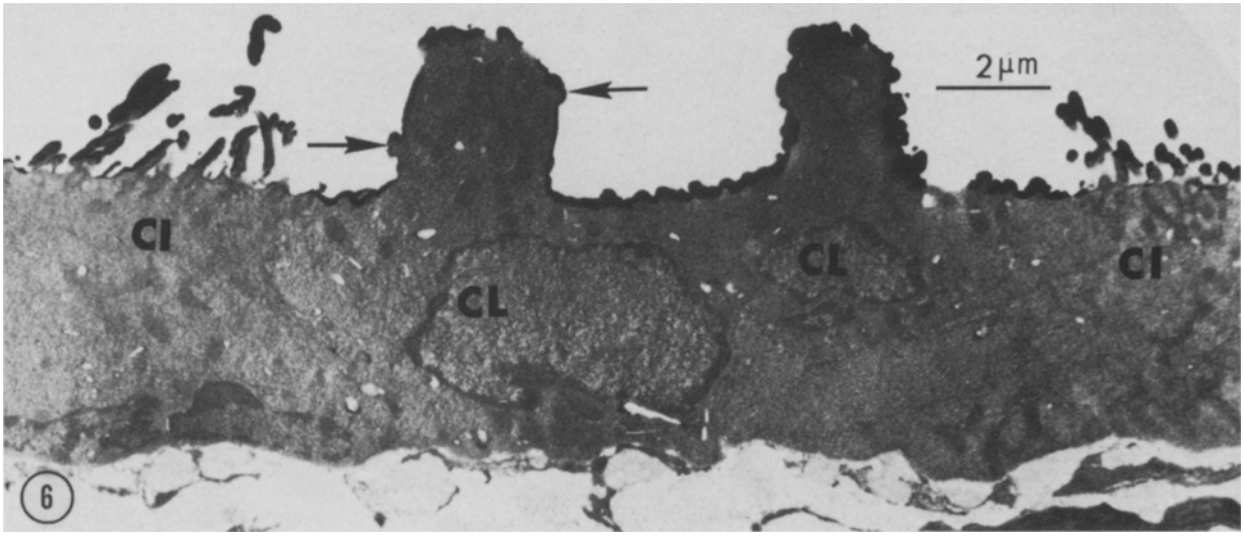


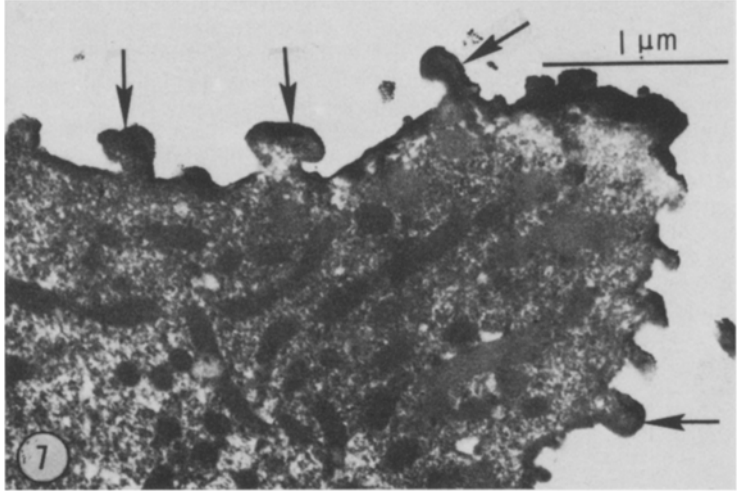






Figures 1–5. These are SEM photomicrographs. Fig. 1. This area of bronchiole shows ciliated cells and Clara cells with different surface activities. The Clara cells in the upper part of the figure (upper arrow) have very few surface blebs, while other Clara cells (lower arrow) have many blebs. Note that many free blebs rest on the ciliated cells in the lower portion of this figure. Fig. 2. The majority of the Clara cells have irregular surface convolutions but with only occasional cytoplasmic blebs (arrow). Fig. 3. This is a higher magnification of the cytoplasmic dome of a hyperactive Clara cell with many attached blebs. Fig. 4. This bleb is connected to the cytoplasm (arrow) and has many oval openings on its surface. Fig. 5. The detached cytoplasmic blebs are scattered on the surface of the cilia.





Figures 6 and 7. These are TEM photographs derived from the SEM specimens. The cells illustrated in these figures are adjacent to the cells shown under SEM. Fig. 6. Two Clara cells (CL) with characteristic cytoplasmic domes and two ciliated cells (CI) are seen. The Clara cells have small blebs (arrows) on their surfaces. Fig. 7. Higher magnification of the surface blebs (arrows) which are connected to the surface of the cytoplasmic dome.

Furthermore, the correlated TEM studies confirmed the well fixed Clara cells with cytoplasmic blebs similar in sizes and locations to those seen under SEM. The blebing process involves the loss of a small amount of cytoplasm and organelles and not the extrusion of the entire cytoplasmic dome. However, the contents of the blebs are very similar to those previously described in a massive loss of cytoplasm due to total decapitation[3,5–8,15]. Because only a portion of the cytoplasm is released into the bronchiolar lumen, we believe that this is a process of apocrine secretion. It is interesting to note that vitamin E-deficient rats exposed to ozone[18] produced similar cytoplasmic blebs.

The fate of the cytoplasmic blebs is not known. It is possible, as suggested by Smith et al.[5] that they undergo dissolution and their identification becomes difficult. Based on our findings of the porous profiles of the blebs it is also possible that their contents are slowly released through the small openings. In view of the localized nature of the occurrence of the blebs, we agree with Mahvi et al.[8] that in times of stress, the Clara cells may respond by undergoing decapitation or apocrine secretion. Although the exact stimuli for the formation of the blebs shown in the present study is not known, our results indicate that alterations of the surface activities of the Clara cells can be a very selective phenomenon.

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