Giant-Cell Centrioles

Abstract. *The giant cell of osteoclastic origin and the giant cell produced in response to foreign bodies are characterized by multiple nuclei. Electron microscopy of these multinucleated cells reveals a special centrosphere in the osteoclast, which is not typical of other types of giant cells.*

Multinucleated giant cells are readily found in areas of bone resorption and in granulomatous tissue that forms in reaction to foreign bodies. The multinucleated cells of bone are osteoclasts, which rapidly increase in number after stimulation of the tissue by administration of parathormone, pressure, vitamin A, and so forth (*1*). Multinucleated granuloma giant cells are readily produced in tissue into which a foreign material such as talc has been introduced.

Two ways have been suggested by which production of these cells is accomplished. First, uninucleated precursor cells could fuse, producing a multinucleated giant cell. This concept of formation is currently in favor (*2*, *3*). Second, there could be repeated nuclear divisions, mitotic or amitotic, in the precursor cells, without simultaneous cytoplasmic cleavage. Although there are a few reports of mitosis in osteoclasts (*4*), dividing cells are infrequently found and have not been observed often enough to account for the large number of cells that appear within 24 hours after an osteoclastic stimulus. Mitoses have been observed infrequently in other giant cells studied in vitro. We have studied rat bone, human bone, a human giant-cell (osteoclastoma) bone tumor, and giant-cell granulomas to further evaluate the fine structure and possible mechanism of formation of giant cells.

Electron micrographs of these tissues revealed multinucleated giant cells

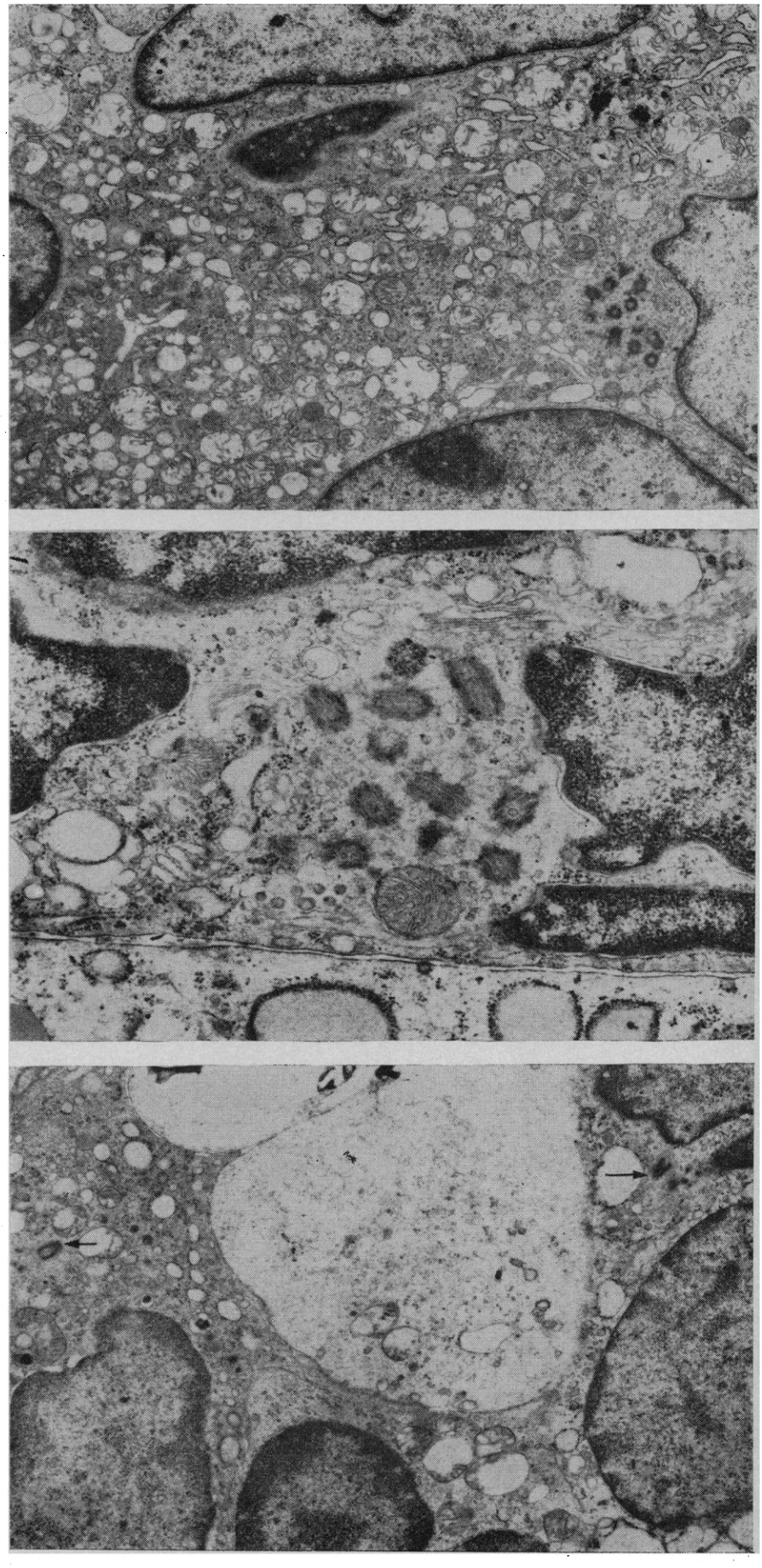

Fig. 1 (top). Osteoclast from normal bone. A giant centrosphere containing 13 centrioles is visible in this plane (× 9000). Fig. 2 (middle). Osteoclast from normal bone. A giant centrosphere which contained nine pairs of centrioles and nine nuclei. Parts of four nuclei and ten centrioles are visible in this plane (× 60,000). Fig. 3 (bottom). Giant cell from granuloma induced by *Cryptococcus neoformans*. Two centrioles (arrows) are present in this plane. Centrioles are present at opposite ends of the cell. No giant centrosphere is present (× 10,000).

containing large numbers of mitochondria and vesicles typical of osteoclasts and other giant cells. For electron microscopy the tissues were fixed in paraformaldehyde buffered with collidine and osmic acid, and embedded in epon (*5*).

In one osteoclast was a centrosphere containing seven pairs of centrioles (Fig. 1). The number of pairs corresponded to the number of nuclei in the cell. We examined serial sections of giant cells from rat bone, a human aneurysmal bone cyst, a human osteoclastoma, and several human granulomas to determine if this property of a common centrosphere was characteristic of all giant cells. The granulomas were selected because we felt they would offer a technical advantage since they have a greater number of giant cells per unit of tissue. Since they are not mineralized, difficulties in serial sectioning were reduced. Eleven osteoclasts were sectioned for electron microscopy. Each of the 11 cells had a single centrosphere containing centriole pairs corresponding to the number of nuclei. The largest centrosphere contained nine centriole pairs (Fig. 2). In this cell, as in others, the centrosphere was so large that not all of the centrioles could be identified in any one ultrathin section. We reconstructed the centrosphere by comparing the position and number of centrioles seen in successive sections. To better determine the number of nuclei and the position of the centrosphere, we examined stained epon thin sections (1 μ) with the light microscope before making ultrathin sections (80 mμ) of the same cells for study with the electron microscope. With this technique, giant cells could be readily located. Serial sections of cells identified in this manner either contained a centrosphere, the ratio of nuclei to centrioles being 1 : 2, or contained no centrosphere or centrioles. In the latter case, we presumed that the centrosphere was lost in the original sectioning process. Serial sectioning of the smaller giant cells made determination of the ratio of nuclei to centrioles much simpler.

Examination of the osteoclastoma revealed several "osteoclasts." However, serial sections of these cells revealed centrioles scattered in the cytoplasm. No giant centrosphere could be detected. Similarly, the giant granuloma cell also did not have any special arrangement of centrioles. In all granulomas examined centrioles were found (Fig. 3), but no special centrosphere was present. Apparently, the special arrangement of the centrosphere is a unique feature of the normal osteoclast and is not a feature common to all multinucleated cells.

The organization of centrioles within one centrosphere in the osteoclast could be the result of incorporation of centriole pairs from mononucleated cells, after they fuse, and subsequent inclusion into a common centrosphere. The single centrosphere may be related to the need for regulating cell cleavage in a cell with a large ratio of cell volume to cell surface. However, granuloma cells with a comparable ratio did not have this arrangement. It is possible, but unlikely, that this arrangement represents a mechanism for the production of multiple nuclei from one mitotic configuration. Autoradiographic studies of bone after the administration of tritiated thymidine (*6*) have indicated that some labeled nuclei occur in osteoclasts. This finding was interpreted by the author as evidence that multinucleated cells are formed by fusion. Studies of giant cells with electron microscopy (*3*) have provided supportive evidence for the fusion mechanism although mitotic figures within forming giant cells have also been observed (*3*), indicating that both mitosis without cell cleavage and fusion of preexistent cells occur. The difference between osteoclasts and other giant cells, with respect to the arrangement of the centrosphere, may be related to the ultimate fate of the cell. Giant cells often are subject to disintegration and to removal by other phagocytes. In the case of the osteoclast, there is some suggestion that this cell dissociates into uninucleated cells and reenters an osteo-progenitor pool (*6*, *7*). If this idea is proved correct, the arrangement of the centrioles into a common body would facilitate the orderly cleavage of this giant cell into subunits with a full complement of cell parts.

Centrioles have long been recognized as structures that have a special role in the process of cell division. They are related to the formation of the division spindle and to formation of continuous tubules of the midbody, the site of cell cleavage. The observation of a peculiar centriole configuration in osteoclasts, which is not generally characteristic of other giant cells, suggests that a special mechanism for formation and cleavage of these cells may be involved.

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Muscle-Spindle Histochemistry

Abstract. *Reduced nicotinamide adenine dinucleotide tatrazolium reductase is abundant in cat intrafusal muscle fibers, whereas in the toad its activity is equal to that in extrafusal fibers. Spindles of both species contain little fat. In sections stained for adenosine triphosphatase bound to myofibrils, two types of intrafusal muscle fibers appear in spindles of both the cat and toad.*

In recent years great interest has been focused on a possible correlation between muscle histochemistry and physiology. Much physiological (*1*) and morphological (*2*) information has been presented favoring the existence of two types of intrafusal muscle fibers. However, only a few histochemical investigations on muscle spindles have been published, and only one of them deals with those generally used in spindle physiology. As demonstrated by the histochemical tests for various oxidative enzymes (*3*), phosphorylase (*4*) and myoglobin (*5*), there are three types of intrafusal muscle