Effects of Antimicrotubular Agents on the Fine Structure of the Golgi Complex in Embryonic Chick Osteoblasts*

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Summary. Embryonic chick frontal bones were cultured in the presence of colchicine or vinblastine and subsequently examined by transmission electron microscopy. In control cultures the osteoblasts showed a large Golgi complex consisting of dictyosomes arranged in a well-defined juxtanuclear area. Microtubules were particularly numerous within this Golgi area although they could be observed throughout the cytoplasm. Colchicine and vinblastine caused the disappearance of cytoplasmic microtubules, while bundles of 10 nm diameter filaments appeared more frequently. In addition, cell polarity was lost and the Golgi complex became disorganized, with the dictyosomes randomly dispersed in the cytoplasm and showing a decreased number of cisternae and an increased number of vacuoles, the latter generally lacking stainable material. Increased number of autophagosomes were also noted.

These findings indicate that microtubules function in the organization of the Golgi complex in osteoblasts. In view of the well documented role of this organelle system in collagen secretion it is suggested that previously observed secretory disturbances produced by antimicrotubular drugs may be due to a defective transfer of material to the dictyosomes and/or a defect in the packaging and transport of such material away from them.

Key words: Osteoblasts (Chick embryo) – Golgi complex – Microtubules – Colchicine – Electron microscopy.

It is well established that the Golgi complex is functionally important in secretory cells (Palade, 1975; Hand and Oliver, 1977). During recent years, increasing interest...
has also been paid to the role of cytoplasmic microtubules in the secretory process. Antimicrotubular agents like colchicine and vinblastine have been found to inhibit secretion from endocrine gland cells (Lacy, 1975; Chu et al., 1977), exocrine gland cells (Redman et al., 1975; Seybold et al., 1975; Williams and Lee, 1976; Patzelt et al., 1977) and connective tissue cells (Ehrlich et al., 1974; Lohmander et al., 1976).

In their study on embryonic chick cranial bone, Ehrlich et al. (1974) found colchicine to inhibit procollagen secretion and conversion to collagen as well as collagen synthesis. Cells exposed to colchicine showed an increased number of Golgi-associated vesicles and vacuoles. On the basis of these findings it was suggested that disruption of microtubules interferes with the translocation of Golgi-derived vesicles, leading to accumulation of secretory material in the Golgi complex and, secondarily, inhibition of synthesis. Vinblastine was also found to inhibit secretion of procollagen and its conversion to collagen. In addition this drug was reported to depress general protein synthesis and to cause striking morphological changes in the endoplasmic reticulum, complicating the interpretation of its effects.

Studies in our laboratory on cultured chondrocytes have shown that colchicine and vinblastine cause characteristic alterations in the Golgi complex (Moskalewski et al., 1975; Thyberg et al., 1977b). These include dispersion of the dictyosomes (stacks of cisternae) throughout the cytoplasm, morphological transformation of many dictyosomes and clustering of lysosomes close to some of them, and appearance of increased numbers of autophagosomes. The endoplasmic reticulum is, however, apparently unaffected by either drug. Similar observations have been made in other cell types (Moskalewski et al., 1976; Thyberg and Hinek, 1977; Thyberg et al., 1977a). These findings suggest that the effects of antimicrotubular drugs on secretion could be due, at least partly, to a role of microtubules in the organization and function of the Golgi complex.

Previous fine structural studies concerning the effects of antimicrotubular drugs on bone cells have largely concentrated on changes related to secretory vacuoles (Ehrlich et al., 1974; Scherft and Heersche, 1975), and it is not clear whether a general disorganization of the Golgi complex, as described above, occurs in these cells. The object of the present study therefore was to reinvestigate the morphological effects of colchicine and vinblastine in cultures of embryonic bone and to compare them with those occurring in chondrocyte cultures. The results show that osteoblasts are affected in the same way as chondrocytes by antimicrotubular drugs, supporting the idea of a function for microtubules in the organization of the Golgi complex.

Materials and Methods

Tissue and Cell Culture

Frontal bones were dissected from 17 day old chick embryos (White leghorn). Each bone was divided into 4 parts. These were then cultured in Falcon organ culture dishes, supported by a metal grid covered by a piece of lens paper. Medium F-12 (Ham, 1965; Gibco Bio-Cult) was used, supplemented with 10% fetal calf serum (Gibco Bio-Cult), 0.3% tryptose phosphate broth (Difco), 50 µg/ml of L-ascorbic acid, 150 units/ml of benzylpenicillin and 150 µg/ml of streptomycin sulfate. Colchicine (Merck) and