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A Human Tubular Array Plasma Cell

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Summary. A human plasma cell is described which is distinct with both the light and electron microscope. With indirect immunofluorescence its cytoplasm is immunoglobulin-associated and the ultrastructure is characterized by tubular arrays of endoplasmic reticulum similar to those described in a number of diseases. Hypotheses regarding these tubular structures are reviewed.

Key words: Plasma cell – Tubular arrays – Endoplasmic reticulum.

Introduction

A group of structures, often referred to as tubular arrays, tubuloreticular structures, undulating tubules, paramyxovirus-like particles and other terms, have been described in a wide variety of human disease and experimental conditions. These include tumors, autoimmune disorders, lymphoid proliferations and infections. This report describes the morphology of a human lymphoreticular adenopathy in which is found an immunoglobulin-producing cell, discernible with light microscopy, the cytoplasm of which is filled with tubular structures.

Clinical Data

A 75-year-old female presented with a rapidly enlarging left cervical mass 7 cm in diameter noted three weeks before, associated with undocumented recent weight loss. Abnormal laboratory studies included T_4 index 0.1, increased ^{75}Se uptake in the cervical mass, increased ^{131}I uptake in the left lobe and decreased ^{131}I uptake in the right lobe of the thyroid, lymphopenia (306/5000 WBC/mm^3), and thrombocytopenia (75,000/mm^3). Other investigations, including serum protein electrophoresis, were within normal. Uncomplicated operative removal of the left lobe and part of the

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right lobe of the thyroid, the cervical mass, and adjacent lymph nodes was performed and the diagnosis of Hashimoto's thyroiditis and immunoblastic lymphadenopathy (see below) was made. She was placed on oral thyroxine. A post-operative bone marrow aspiration and biopsy showed slight myeloid and megakaryocyte hyperplasia and siderosis, but no abnormal cells. Four months later the mass began to recur and she was given 3000 rads of Cobalt 60 over three weeks over the ipsilateral supraclavicular and upper mediastinal nodes. At that time serum antithyroid, anti-smooth muscle, and anti-mitochondria antibody were negative, and slightly enlarged para-aortic lymph nodes were visualized by lymphangiography. There has been no recurrence in the ensuing year.

Material and Methods

The surgical specimen comprised two parts: pale, greyish-white, firm thyroid, and lymph node tissue which consisted of a $10 \times 9 \times 5$ cm firm, white mass enclosed in a small amount of fat. Both parts were fixed in 10% formalin and embedded in paraffin, and separate 1×1 mm pieces of lymph nodes were also fixed in 3% glutaraldehyde, washed in 0.1 M sodium cacodylate, postfixed in 1% osmium tetroxide, placed in graded alcohol, then propylene oxide, embedded in Epon, cut with a diamond knife, mounted on copper grids and stained with uranyl acetate and lead citrate and examined with the electron microscope.

Light Microscopy. The thyroid showed Hashimoto's disease. The normal architecture of the lymph node was obliterated by a polymorphous cell population with abundant vascularization and intercellular reticulin positive eosinophilic material (Fig. 1). The cells consisted of immunoblasts with large nuclei, prominent nucleoli, and a small amount of amphophilic cytoplasm, plasmacytoid

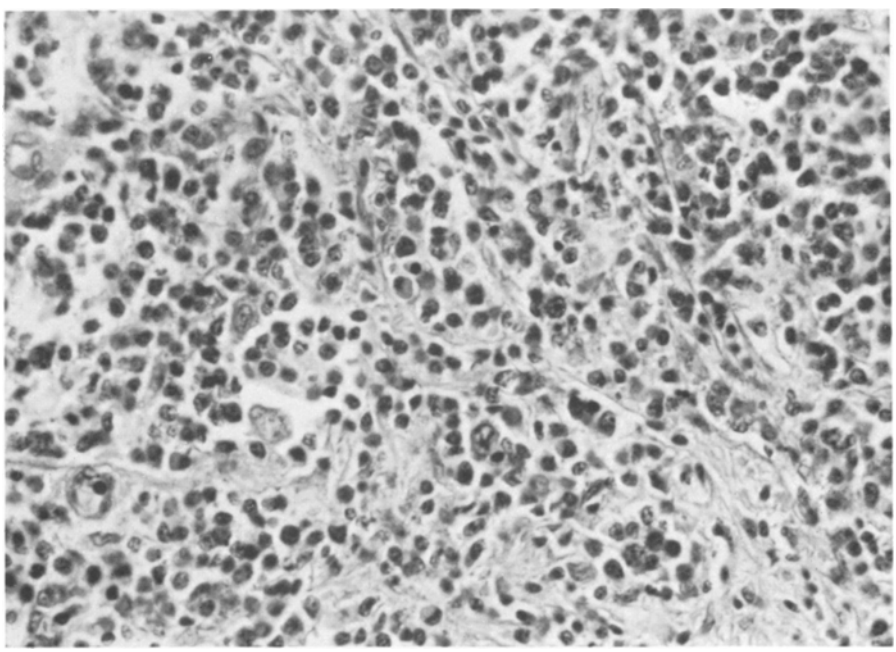


Fig. 1. Lymph node, showing immunoblastic proliferation, plasmacytoid lymphocytes, eosinophilic extracellular substance, arborizing vessels and occasional tubular array plasma cell. (H. and E, $\times 370$)

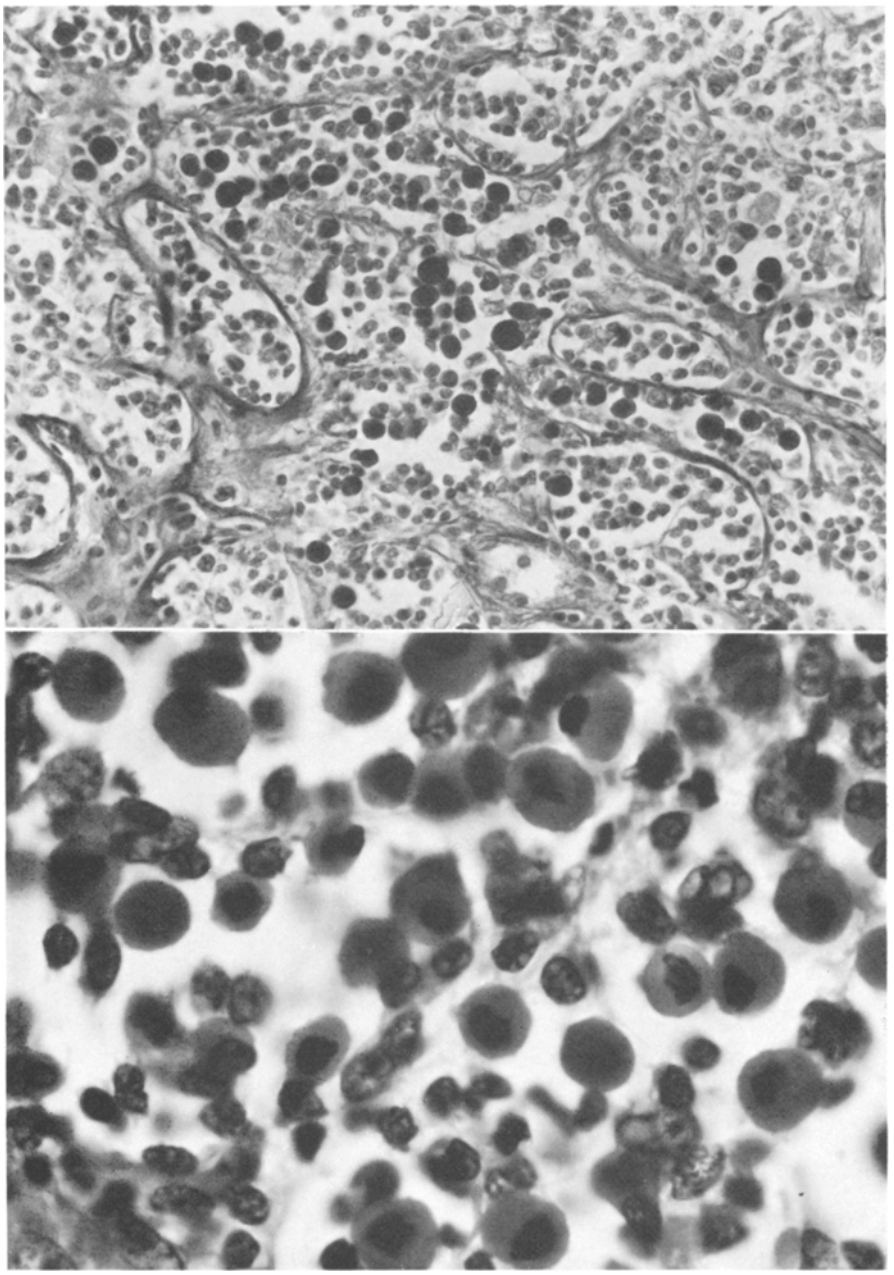


Fig. 2. Cluster of tubular array plasma cells (PAS, ×370). b) Higher magnification. (PAS, ×1000)

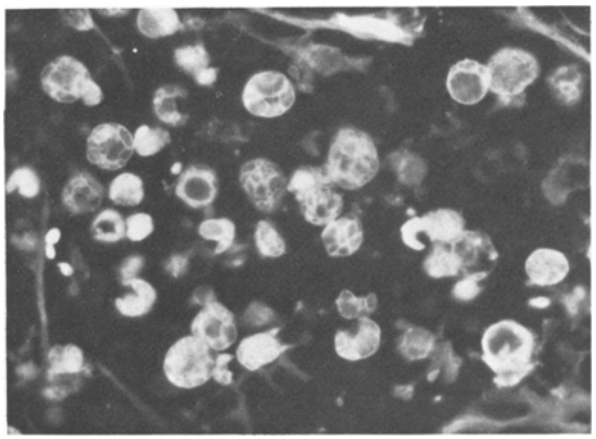


Fig. 3. Positive indirect immunofluorescence of tubular array cell, showing IgM. (× 500)

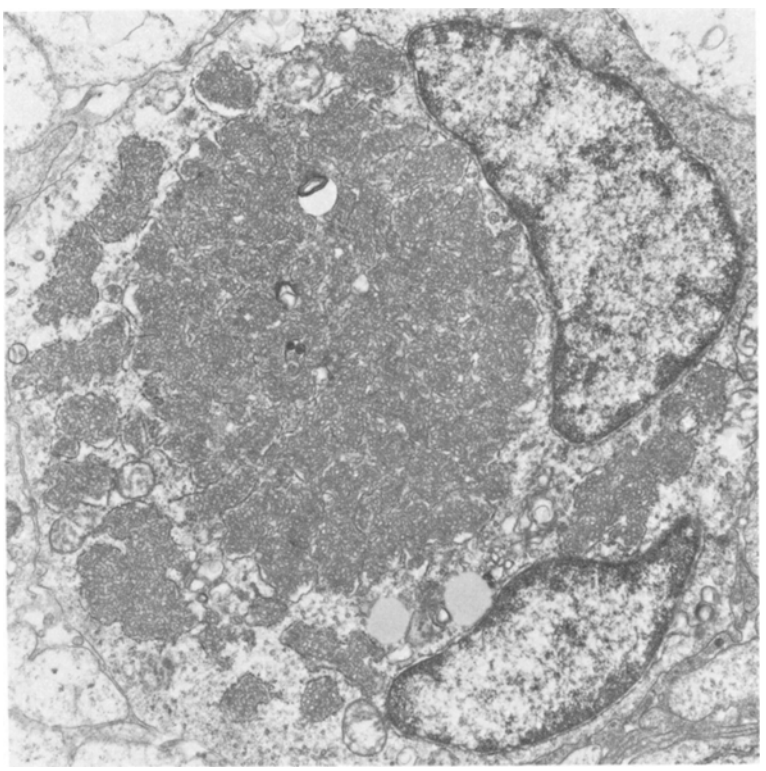
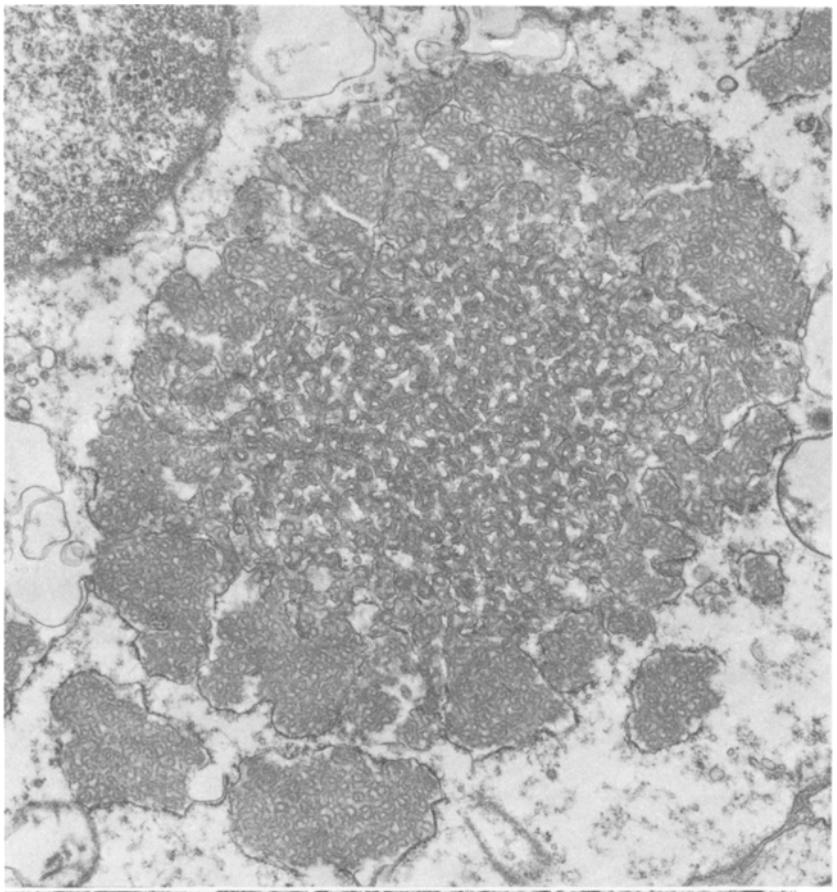


Fig. 4. Overall view of tubular array cell showing dense clumps of tubular material, Golgi apparatus, swollen mitochondria and two nuclei. (× 10,000)



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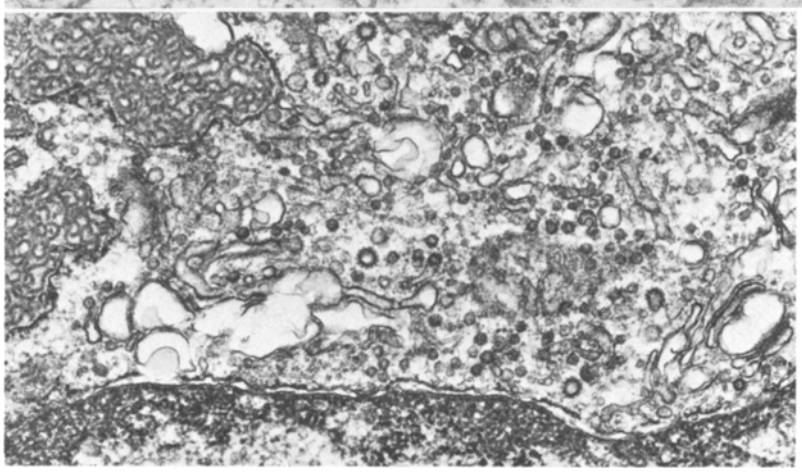

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Fig. 5. Aggregate of tubules and dilated cisternae of the endoplasmic reticulum. (× 18,000)

Fig. 6. Intracisternal material in relation to ribosomes, Golgi complex, microtubules and coated vesicles. (× 33,000)

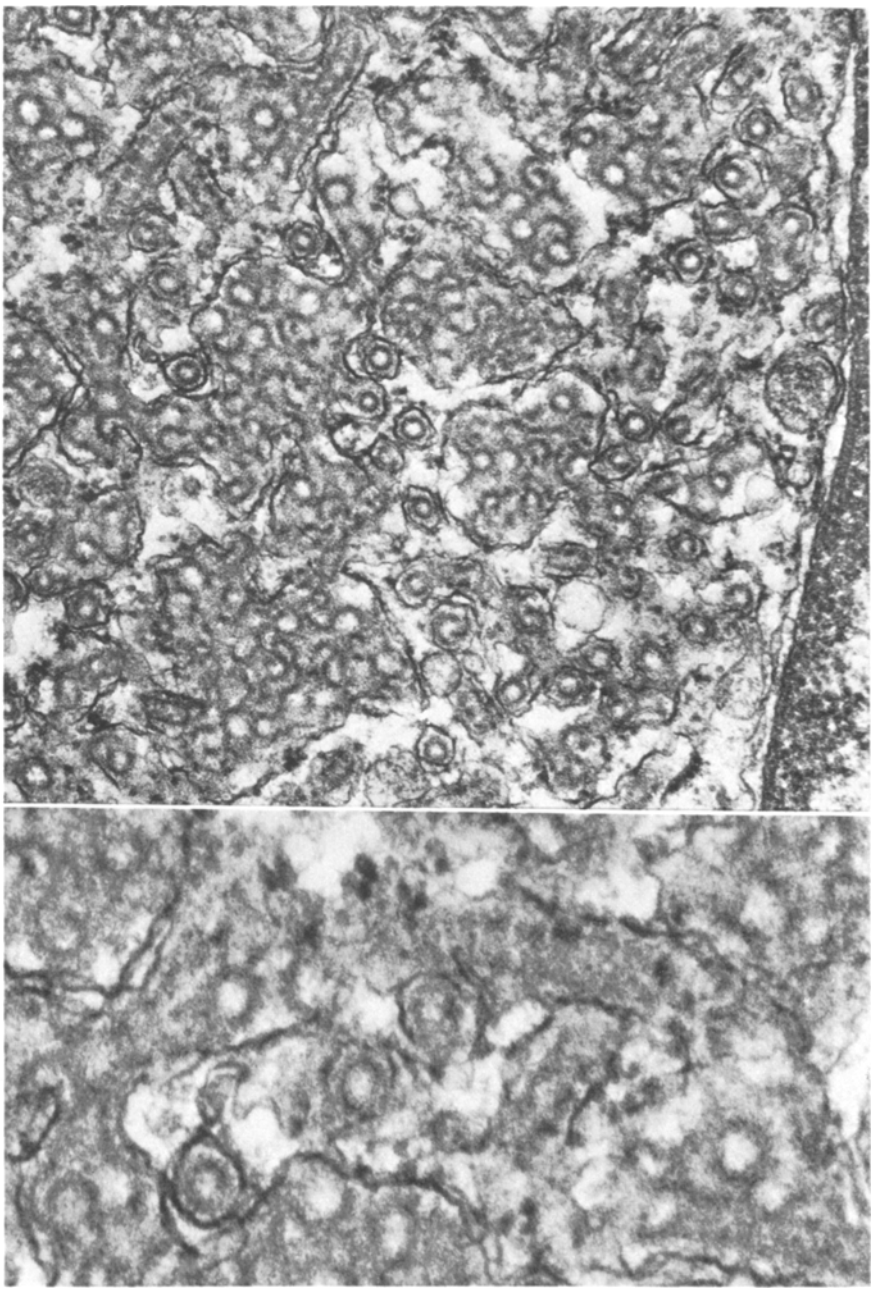

Fig. 7. Helical arrays within tubules; longitudinal and cross-sectional profiles. ($\times 60{,}000$)

Fig. 8. Higher magnification showing subunit structure. ($\times 90{,}000$)

lymphocytes, and many collections of round, distended, strongly PAS-positive cells scattered among the other cells, sometimes found in large clusters around vessels (Fig. 2). The latter cell was strongly eosinophilic, PAS positive, moderately pyroninophilic, mildly positive with Luxol Fast Blue, and negative with Sudan Black and Alcian Blue stains. With indirect immunofluorescence (rabbit antihuman-immunoglobulin and fluoresceinated sheep antirabbit-immunoglobulin, Huang et al., 1977), the cells were found to fluoresce strongly (IgM, IgG, IgA, Kappa and Lambda chains) especially around the edges of intracellular lobules (several per cell) (Fig. 3). The diagnosis of immunoblastic lymphadenopathy was made (Frizzera and Moran, 1974; Lukes and Tindle, 1975).

Electron Microscopy. The cytoplasm of the cell contains undulating, interweaving tubular formations and distended cisternae of endoplasmic reticulum, with few other organelles (Fig. 4). Within cisternae of the rough endoplasmic reticulum circular and horseshoe profiles, and occasional helical profiles are seen. At higher magnifications sub-units of the tubular structures are identified (Figs. 7, 8), revealing helical tubular material within tubules. The diameter of the inner material (Fig. 8), when measured in cross-section profile, is 280 to 320 Å. Tubular aggregates with granulated borders are also found adjacent to cytoplasmic regions with Golgi complex, microtubules, and coated vesicles (Fig. 6).

Discussion

Tubular cytoplasmic structures have been discribed frequently (reviewed by Uzman et al., 1971; Schaff et al., 1972; Kistler and Groscurth, 1973; Hruban et al., 1976) and have been called "tubular arrays", "tubular networks", "crystalline aggregates", "virus-like inclusions", "reticular network", "undulating tubules", "crystalline arrays", "filamentous tubular structures", "tubular inclusions", "tubuloreticular structures", "tubular aggregates", "glomiform inclusions", and other terms. These structures have been noted in systemic lupus erythematosus (endothelium of kidney and skin, lymphocytes of blood and lymph node, lung, muscle, pancreas, salivary gland), dermatomyositis (endothelium, macrophages, fibroblasts of skin and muscle), rheumatoid arthritis (leukocytes, synovium), Sjögren's syndrome (endothelium), Henoch-Schönlein purpura, Goodpasture's syndrome, Reye's syndrome, idiopathic thrombocytopenic purpura, scleroderma, sickle cell anemia, various glomerulopathies (endothelium), Hodgkin's disease, astrocytomas, pituitary adenomas, sarcomas (fibro-, osteo-, lipo-, rhabdo-), Burkitt's lymphoma (African and American), staphylococcal enterotoxinemia, mumps (peripheral mononuclear cells), and Coxsackie B encephalomyocarditis (endothelium in heart), for example (see above reviews). They have been seen in tissue culture of normal human lymphoid cells, normal human adult and fetal spleen and thymus, lymphocytes from patients with SLE, human lymphoid cells treated with 5 bromodeoxyuridine, Burkitt's lymphoma, histiocytic lymphoma, carcinoma of cervix (spleen culture), myeloproliferative disorder (spleen), buffy coat culture from leukemia (ALL, AML, CML), infectious mononucleosis, hepatitis, multiple myeloma, Chediak-Higashi syndrome, cancer of pancreas and colon, melanoma, and virus infected cells. Examples in non-human tissue include endothelial (rabbit herpes encephalitis, pig poliomyelitis, equine arteritis, canine hepatitis, monkey AML, mink aleutian nephropathy, normal canine prostate) mononuclear cells (rabbit herpes, monkey AML, poliomyelitis), Kupffer cells (monkey AML), astrocytes (pig poliomye-

litis), tumors (dog, monkey; sarcoma), cotton plants (egg zygote and embryo) (Schaff et al., 1972, 1973; Pothier et al., 1973).

Proposed interpretations for the structures include that they are viral nucleocapsid (paramyxovirus), an atypical infectious agent, or an incomplete form of latent virus (Chou, 1968; Kawano et al., 1969; Györkey et al., 1969, 1971; Grausz et al., 1970; Jenson et al., 1971); phagocytosed cellular material (Hurd et al., 1969); extranuclear DNA (Landolt et al., 1976); specialized membrane amplification (Schaff et al., 1973) altered cellular replicative activity (Baringer and Swoveland, 1972); or structurally modified endoplasmic reticulum (Chandra, 1968; Jenson et al., 1971; Uzman et al., 1971; Schaff et al., 1972, 1973; Baringer and Swoveland, 1972; Hruban et al., 1976).

The reported tubular structures have been found to measure in the range of 200 to 350 Å in diameter with slightly greater measurements obtained with cross-sectional as compared to longitudinal estimates of diameter. They are usually present in small quantities in the cytoplasm, and their presence or absence has not been correlated with any light microscopic criteria. Reviews (see above) have pointed out that the structures range from loosely-interwoven tubules to densely-packed, highly-ordered patterns. Some of these structures are probably not equivalent, and different from those reported here. Discrepancies in measurements from different reports may reflect technical factors or biologic variability (functional variation).

In electron microscopic descriptions (Bessis, 1961; Sorenson, 1964; Maldonado and Brown, 1966; Fisher and Zawadzki, 1970; Suzuki et al., 1970), the Russell body and other plasma cells show no tubular endoplasmic reticulum structures; the content of the Russell body is finely granular or amorphous material within granular cisternae. In this cell, a block in intracellular transport may precede the accumulation of the tubular material, i.e. the tubules may represent an abnormal product which cannot pass normally through the cytological pathways or there may be increased amounts of product synthesized, or abnormalities in concentration, storage, or discharge (Palade, 1975). The location of the tubular material within the cisternae suggests an abnormality of the zone of condensation where translocation to the Golgi complex occurs.

An hypothesis that has not been advanced regarding the tubular structures is that they could represent dysplastic organelles caused by derepression (dedifferentiation). This is brought to mind by the occurrence of tubular arrays in white blood elements and endothelium (cells of related embryogenesis) and tumors (cells with abnormal DNA), and the fact that the present cell is found in a premalignant condition (a dysplastic cell).

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