The Ultrastructure and Genesis of Auer Bodies

By James A. Freeman

SINCE THE RECOGNITION of Auer bodies in 1906, the cytochemical, physical and histologic properties of these structures have all been described. With the advent of the electron microscope, these bodies have become amenable to ultrastructural analysis. Correlation of the ultrastructural architecture with previous chemical and physical observations has rendered support to previously proposed theoretical concepts of the nature of Auer bodies. This paper will present electron microscopic evidence to indicate the complex crystalline structure of Auer bodies and will discuss the concepts of their genesis.

Shortly after the detailed description of Auer bodies in "large lymphocytes," their presence in immature white blood cells of leukemias presumed to be lymphocytic was confirmed by Pappenheim, Ottenberg, Isaac and Cobliner and Naegeli. Roth's discovery of Auer bodies in myeloblasts from a patient with subacute miliary tuberculosis and Chosrojeff's studies of Auer rods in immature cells of myelogenous leukemia led the latter to postulate that previous reports had confused myeloblasts and lymphocytes, and the existence of Auer bodies in lymphocytes was deemed doubtful. The demonstration of Auer bodies in the myeloblast was also reported by Ishikawa, who, as previously did Ottenberg, unsuccessfully attempted to transmit the Auer body and the leukemia. Sabrazes and later Aibara found Auer bodies only in myeloblasts. This led Aibara to propose that the presence of Auer bodies was diagnostic of acute myelogenous leukemia.

Sydenstricker and Phinizy observed Auer bodies in acute monocytic leukemia. As a result of Naegeli's earlier work, this leukemia was as yet unrecognized as a true third type of leukemia. This fact plus Aibara's dictum led some investigators to ignore the possible presence of Auer bodies in cells other than those of myelogenous leukemia. Although Inoue is credited with having demonstrated Auer bodies in mature neutrophils, Goodwin had earlier illustrated them in many stages of neutrophilic maturation, and the latter was the first investigator to recognize the reciprocal relationship between the frequency of occurrence of Auer bodies and the cell maturity. Shortly thereafter, Craciuneau, Calalb and Bonciu found Auer bodies in the hemohistioblast.
Despite the varying types of cells in which Auer bodies were demonstrated, the morphologic appearance varied little from one cell type to another. By the time three clinical types of leukemia, namely lymphocytic, myelogenous and monocytic, were recognized, Hawksly had described Auer bodies in the immature monocyte and concomitantly refuted Aibara's dictum. At present it is generally accepted that Auer bodies can occur in both monocytic and myelogenous leukemias.

The first histochemical observation on Auer bodies was made in 1917 by Rosenthal, who demonstrated the positive oxidase reaction of the rods found in cells of myelogenous leukemia. In 1923 Richter revealed the histochemical differentiation among mitochondria, Russel fuschin bodies, azure granules and Auer bodies. He was the earliest investigator to recognize the identity of Auer bodies in both peripheral blood smears and tissue sections. Aibara's dictum that Auer bodies were a pathognomonic sign of myelogenous leukemia was supported by these histochemical studies. Kibler's cytochemical analysis showed Auer bodies to be almost entirely sudanophilic substance, differentiating them from azure granules and Kurloff bodies. Locquin and Bessis, confining their studies to the histochemical structures of the Auer bodies and Charcot crystals, concluded that both are primarily nucleoprotein in nature, and that they are essentially identical in structure. They also showed the similarities of the indexes of refraction of Auer bodies, measuring \( n = 1.459 \) to \( n = 1.461 \), compared to the Charcot crystals with indexes of about \( n = 1.457 \) to \( n = 1.461 \). By spectroscopic analysis these workers demonstrated Auer bodies to have an ultraviolet absorption between 2600 Å (the range of nucleotides) and 2800 Å (the range of cyclic amines). Bessis later accomplished ultracentrifugation separation and ultrasonic fractionation of the Auer bodies from the substance of the leukocyte. No apparent damage could be noted in the fractionated Auer bodies; however, a central lucid core with its long axis in the same direction of the long axis of the rod was notable in the rods after being separated from the substance of the cytoplasm of the leukocyte. Bessis also found that Auer bodies failed to digest in pepsin and trypsin and were insoluble in all solvents in common use. The recent treatise on the histochemical analysis of Auer bodies by Ackerman has shown the chemical composition of these structures to be mucopolysaccharide and ribonucleic acids, with small amounts of lipoid (lecithin?) and acetyl lipid. He observed that visible cellular activity and metabolic changes as well as gradual temperature rises and external trauma failed to damage the Auer rods. In an effort to further elucidate information as to the function of the Auer bodies, Harada repeated the histochemical studies, obtaining essentially the same results as Ackerman. From his chemical data Harada concluded that Auer bodies participated in the protein synthesis of the cell or altered metabolism and/or respiration.

Electron microscopic studies on the ultrastructure of Auer bodies have been limited to date. DiMayorca, Lanzavecchia and LeCoultre pictured the Auer body as a homogeneous, structureless intracytoplasmic rod. More recently, Ito has observed the Auer body to have no capsule, limiting membrane or internal ultrastructure. He gave rise to a new concept of the genesis of
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Auer bodies after finding them consistently located within the swollen sacs of the endoplasmic reticulum. Low and Freeman limited their observations to a morphologic description of previously known Auer body structure.25

Few authors proposed satisfactory theories of the genesis of Auer bodies until 1947, when Quattrin, recalling the similarity among these bodies, azure granules and nuclear fragments, suggested a process of irregular germination or partial segmentation of the nucleoplasm forming these granules.26 However, histologic and cytochemical evidence supporting this theory was conspicuously lacking. Inability to culture or transmit Auer bodies has excluded the possibility of their being an infectious microorganism.3,10 Nakashima’s theory of Auer bodies being pathologic forms of azurophil granulation did not explain the simultaneous presence of both in the same cell,27 and hence has been ill accepted. Noting the histochemical similarities of Auer bodies and cytoplasmic granulation, Ackerman theorized “some alteration must exist in certain leukemic cells, allowing the granules to coalesce into crystal like rods.”16 Ito interpreted the Auer body to be a fused mass of “Auer granules” which were formed from azurophil granules within the endoplasmic reticular system.24 He failed to mention any relationship between these Auer granules and specific cytoplasmic granules. The explanation of Auer body formation by the coalescence of cytoplasmic granulation and the hypothesis proposing their production from azure granulation within the cisternae of the endoplasmic reticulum are presently the most acceptable theories of the nature of Auer bodies.

MATERIALS AND METHODS

Blood samples were obtained from patients with acute leukemias in whose peripheral blood leukocytes Auer bodies were known to be present (reference 25, page 304). Table 1 summarizes the data on these patients. The specimens were withdrawn without stasis (a) in a 10 ml. silicon-coated syringe, fitted with a coated 20 gage needle, and transferred to a siliconized centrifuge tube which had been precooled to 5 to 10 C., or (b) alternately by needle drip directly into a tube coated with a suitable nonwetting agent.28 No anticoagulants, chelating agents or foreign materials were introduced prior to fixation. The cooled sample was centrifuged at 1500 rpm for 15 minutes at 0 C. (R.C.F. 265: International model PR-2, refrigerated, angle head centrifuge) to insure adequate separation of the huffy coat, but without tight packing or rupture of the leukocytes.

The buffy coat was aspirated with a silicon-coated pipette and transferred to a glass tube containing 5 ml. of 1 per cent Veronal buffered (pH ca. 7.40) osmic acid29 which had been precooled to 5 to 10 C. The specimen was fixed in the osmic acid for one-half hour.

Dehydration was accomplished by immersion of the specimen in successive changes of 50, 70, 95 per cent and absolute ethanol, remaining in each for one-half hour. The dehydrated specimen was then placed in three changes of 5 parts n-butyl methacrylate plus 1 part methyl methacrylate catalyzed with 2 per cent, by weight, of 2,4-dichlorobenzoyl peroxide, remaining in each change of monomer for 1 hour.30 Between each successive step of the dehydration and the embedding procedure, the specimen was centrifuged at 500 rpm for 1 to 1 and one-half minutes at room temperature (R.C.F. ca. 385: Clay-Adams safeguard model centrifuge). After centrifugation, the supernatant was decanted, the next fluid added and the tube manually agitated to produce a suspension. The last methacrylate suspension was permitted to settle by gravity in 00 gelatin capsules for one-half to 1 hour to avoid close packing of the cells.

The encapsulated specimens were then polymerized overnight in an oven with dry heat at 47 to 52 C. After polymerization the specimens were sectioned at ca. 1/20 to 1/40 μ with the use of a Porter-Blum ultramicrotome31 fitted with a glass knife.32 The sections were
Table 1.—Summary of Acute Leukemias Exhibiting Auer Bodies

<table>
<thead>
<tr>
<th>Case no.</th>
<th>No. of specimens obtained</th>
<th>Sex, age</th>
<th>Clinical diagnosis*</th>
<th>WBC count (×10⁹/µL)</th>
<th>Peripheral blood picture (%)</th>
<th>% cells with Auer bodies</th>
<th>Therapy prior to obtaining specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>M, 52</td>
<td>myellog., myelogenous, monocyt., monocytic.</td>
<td>287</td>
<td>blasts 65</td>
<td>1–3</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>M, 40</td>
<td>monocyt.</td>
<td>13.5</td>
<td>blasts 83</td>
<td>25</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>F, 53</td>
<td>monocyt.</td>
<td>6.1</td>
<td>blasts 47</td>
<td>8–10</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>F, 53</td>
<td>monocyt.</td>
<td>63</td>
<td>blasts 90</td>
<td>8–10</td>
<td>Blood</td>
</tr>
</tbody>
</table>

*All acute leukemias; myellog., myelogenous; monocyt., monocytic.

examined and photographed without removal of the methacrylate, with the use of RCA EML-1B and RCA EMU-3 electron microscopes. The photographic plates were enlarged to illustration size.

Smears of the buffy coat and direct smears of the peripheral whole blood were stained with Wright's stain for light microscope analysis and photography. Specimens were photographed on Kodak Panatomic-X or Isopan films with a Leitz microscope fitted with a Universal hex shutter, with the use of a Wratten-X green filter. The negatives were photographically enlarged to illustration size.

RESULTS

Light Microscopy

Little can be added to Auer's original detailed light microscope observations of these rodlike structures. Auer bodies are often observed near the nuclear involution or the centrosomal area, but it is not uncommon to find them near the periphery of the cell (figs. 2 and 3). Although they occasionally overlie the nucleus, they are essentially intracytoplasmic structures. Rarely Auer bodies are found free without the cell, usually in the vicinity of a disintegrating leukocyte. Their shape varies from spherical to rectangular, but the rod shape is most common (figs. 2 and 3). With the use of Wright-stained specimens, Auer bodies appear as azurophilic rods, measuring ca. 1 to 6 µ in length and 0.25 to 1.5 µ in breadth. They are not consistently intimately adjacent to or anatomically a part of any of the specific cytoplasmic organoids, such as the Golgi zone or mitochondria. However, they are often found near the Golgi zone. They are usually larger in breadth than the diametric size of the specific granules of leukocytes (ca. 0.15 to 0.3 µ). No constant internal structural architecture or limiting membrane is visible with the limited resolving power of the light microscope.

Electron Microscopy

The frequency of occurrence of Auer bodies varies considerably with the patient, type of leukemia and time at which the specimens are collected during the patient's hospital course (table 1). As many as 25 per cent of the cells of the monocytic leukemia in case 2 contained Auer bodies, while only 1 to 3
Fig. 1.—Diagrammatic representation of the ultrastructure and cytoplasmic relationships of Auer bodies.

a. These structures are intracytoplasmic rods often located near the concavity of the nucleus in the vicinity of the cytocentrum. They occasionally overlie the nucleus.

b. Viewed with the light microscope, the Auer bodies appear to have no limiting membrane or internal ultrastructure. They measure ca. 0.25 to 1.5 μ in breadth and ca. 1 to 6 μ in length.

c. A complex ultrastructural architectural arrangement of laminated plaques is revealed with the electron microscope. Occasionally the planes of cleavage between the plaques are demonstrable. The long axis of the plaques somewhat parallels the long axis of the rod.

d. Fortuitous sectioning through the plane indicated in (c) reveals the homogeneous plaques coalescing to form the typical rodlike crystal. Lucid cores within the coacervate rod are visible in cross section.

per cent of the total number of immature white blood cells in case 1 exhibited these structures. These calculations are based on the percentage of cells containing Auer bodies in the total number of cells seen in the electron microscope. Multiple observations were made on many sections of the same cell as well as on various fields. Since the cells were viewed in thin sections rather than in their entirety, rods may have been present in the cell and not included within the plane of section. Hence, the percentage of cells containing Auer bodies
Fig. 2 (at left).—Wright's stained specimens of monoblasts demonstrate the azurophilic rodlike structure of the Auer bodies (ab). Note the multiple large nucleoli (nu). (× 1700; reduced)

Fig. 3 (at right).—The intracytoplasmic Auer bodies are usually located near the involution of the nucleus. No internal ultrastructure is visible with the limited resolving power of the light microscope. (× 2300; reduced)

in these specimens was probably greater in absolute value than that recorded here.

The same protoplasmic relationships exist as those observed with the light microscope, namely, the Auer bodies being intracytoplasmic structures usually located in the cytoplasm near the concavity of the nucleus and near the cytocentrum (figs. 1, 4 and 5). It is unusual to find Auer bodies intimately associated with any particular cytoplasmic organoid, but occasionally they are found adjacent to the Golgi zone (fig. 8). The association of these two structures, if any, is quite nebulous. The dimensions of the Auer bodies as photographed with the electron microscope conform to the dimensions calculated from light microscope studies, measuring from 0.1 to 2.0 μ in breadth and up to 6 μ in length (figs. 4, 7 and 9). Most commonly they are found to be at the lower limits of the measurements made in light microscope studies. This is possible since the cells are viewed in thin section; the plane of section may not be through the largest diameter of the Auer body, and may often be a cross or tangential section of the rod (figs. 8 and 13). Longitudinal sections show this structure to be a coacervate of laminated plaques forming a rodlike crystalline veneer (fig. 1). Fortuitous sectioning through the same plane as the long axis of the plaque reveals a homogeneous structure of moderate density (fig. 7), but densities may vary from one crystal to another or with the different plaques within the same rod (fig. 8). This coacervate is most often constructed with the long axis of the plaques in the same plane as the long axis of the rod (figs. 6, 7 and 9). It is not unusual to find Auer bodies with a mass of plaques haphazardly arranged in various planes, some being longitudinal and others being tangential. This is not unreasonable, in view of the many shapes assumed by Auer bodies (figs. 6 and 11). If the plaques are wedge-shaped and arranged in various planes, it may give the appearance of a needle-like projection in the center of the rod (fig. 10). Occasionally one of the rods can be found separating along the planes of cleavage, showing the lamellar arrangement of the plaques to best advantage (figs. 6 and 6a). As the plaques are more closely associated, the cleavage planes become somewhat indistinct, but they are still visible on close scrutiny (fig. 12). The formation of an Auer body from irregularly shaped plaques which are not parallel to
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Fig. 4.—Electron micrograph of a monocyte containing an Auer body (ab). This longitudinally sectioned rod measures ca. 5.4 μ in length by 1.0 μ breadth. The large nucleus (n), scanty cytoplasm and large nucleolus (nu) attest to the immaturity of the cell. Mitochondria (m) are present. (x 11,520; reduced)

Fig. 5.—Two Auer bodies (ab) are visible in the cross section in this monoblast. A generous compliment of small oval mitochondria (m) are present. The minute profiles of the endoplasmic reticulum (er) are noted in the cell. Several nucleoli (nu) are seen within the large nucleus (n). (x 11,520; reduced)
Fig. 6.—An Auer body (ab) shown separating along the planes of cleavage is located in the area of the cytocentrum near a small segment of the Golgi zone (gz). Multiple small mitochondria (m) are visible throughout the cell. A small part of the nucleolus (nu) is in the plane of section of the nucleus (n). This cell is an immature monocyte. (× 25,900; reduced)

Fig. 6a (inset).—The laminated architecture of the Auer body can be visualized in the process of being separated along the planes of cleavage (cp). The homogeneous plaques are seen to best advantage. Homogeneous granules (g¹), similar in density to the plaques of the Auer body, are found in the cytoplasm. Occasional small masses of minute granules (g²) are found intimately associated with the rod. However, no morphologic transition from cytoplasmic granules to Auer bodies is unequivocally demonstrable. (× 45,100; reduced)

or in apposition with each other could present as a rod with an apparently lucid core (fig. 13). This electron lucid core could indicate the absence of central structure or dissolution of the contents with preparation, the former being more likely (fig. 1).

There is no constant relationship of Auer bodies to the cisternae and sacs of the endoplasmic reticulum in these preparations. In contrast to Ito's findings, the Auer bodies in these preparations were not found to be located within the endoplasmic reticulum. They were located only in the ground substance of the cytoplasm. In the early immature cell types in which Auer bodies were most
Fig. 7.—Longitudinal sectioning in the same plane as the long axis of the plaques of the Auer body reveals a homogeneous structure of moderate density. Numerous mitochondria (m) are scattered in the cytoplasm. This rod measures 2.4 μ in length by 0.7 μ in breadth. A portion of the nucleus (n) is visible. (× 36,000; reduced)

Fig. 8.—The plaques of the coacervate rod have homogeneous densities; however, densities may vary from one plaque (p₁) to another (p², p³). The Golgi zone (gz) is visible, and its upper extent seems to be intimately adjacent to the Auer body. Mitochondria (m) are present. (× 43,000; reduced)

Fig. 9.—The cleavage plane (cp) of this Auer body separates three distinct plaques (p₁, p², p³). Numerous small granular elements (g) are present in the cytoplasm, and a part of the nucleus is visible. The dimensions of the rod are 3.4 μ in length by 0.8 μ in breadth at its widest margins. (× 25,000; reduced)

Fig. 10.—The needle-like plaque seen in this tangentially sectioned Auer body represents a wedge-shaped plaque (wp) diagonally placed in the rod. The homogeneous granules (g) in the vicinity of the Auer body have a similar density to that of the rod. Cristae mitochondriales are visible in the mitochondria (m). A portion of the nucleus (n) is in the section. (× 42,000; reduced)

frequently present, the system of the endoplasmic reticulum was poorly developed and quantitatively small. The minute amount of reticular element present was in the form of small oval profiles usually measuring less than 0.1 μ diameter. No small granular element could be demonstrated within the
Fig. 11.—Many odd forms can be assumed by Auer bodies. Such is the circumstance in the case of this rod, which has an expansion along its extent, which is the result of two lateral plaques (lp) closely apposed to the central longitudinal plaque (cp). The central plaque is ca. 3.2 μ in length. The lateral plaques expand the breadth to ca. 0.75 μ. The minute profiles of the immature elements of the endoplasmic reticulum (er) are scattered throughout the cell. Nonspecific cytoplasmic granulation (g) and mitochondria (m) are visible. A part of the nucleus (n) with its typical double nuclear membrane is included in the plane of section. This Auer body is located subjacent to the plasma membrane (pm). (Courtesy of Low and Freeman: Electron Mircoscopic Atlas of Normal and Leukemic Human Blood. New York, Blakiston Division, McGraw-Hill Book Co., 1958.) (x 60,600; reduced)

endoplasmic reticulum and no fused granular masses corresponding to Ito’s “Auer granules” could be identified associated with the reticular element. Only rarely could granules conforming to azurophilic granulation be identified with certainty. None of these azurophilic granules could be found within the sacs of the endoplasmic reticulum. The occasionally identifiable fused granular masses within the cytoplasm do not correspond to the morphologic pattern of azure granulation (fig. 6a). Auer bodies could be found adjacent to the profiles of the endoplasmic reticulum. However, this circumstance did not represent itself with enough statistical constancy to define any relationship between the Auer bodies and the reticulum. As the cell matures, the endo-
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Fig. 12.—Close scrutiny of the compacted lamination of plaques of this Auer body reveals a fine cleavage plane (cp) barely visible even with the high resolution of the electron microscope. The lower margin of the rod passes out of the plane of section, so the 2.5 μ length is short of the true longitudinal measurement. (Courtesy of Low and Freeman: Electron Microscopic Atlas of Normal and Leukemic Human Blood. New York, Blakiston Division, McGraw-Hill Book Co., 1958.) (× 85,200; reduced)

plasmic reticular element increases in size and distribution throughout the cell. It increases in quantity to the myelocyte stage, then progressively involutes as further maturation continues (references 25 [page 125] and 33). The frequency of occurrence of Auer bodies, as was previously noted by Goodwin, declines as the cell matures. On noting the large size of the Auer bodies in comparison to the minute size of the profiles of the endoplasmic reticulum, it would seem improbable to find Auer bodies forming within the reticulum.

Many small cytoplasmic granules of unknown genesis are found in the blast cells of the leukemias observed with the electron microscope. Although some of the minute granular-appearing structures viewed with the light microscope are in reality mitochondria, multiple small granular elements measuring less
Fig. 13.—The often visualized apparently lucid central core (lc) of the Auer body is demonstrable in cross section of this rod. Multiple granules (g) are seen in the cytoplasm in addition to the minute ribonucleoprotein granules of Palade (pg), the latter measuring ca. 120 to 150 Å. A part of the nucleus (n) is visible. (x 54,000; reduced)

Fig. 14.—Oblique section of the barrel-shaped fibrillar formation (ff) demonstrates the circular orientation of the fibrils. This formation is an incomplete structural variant of the complex fibrillar whorl. A single fibril measures ca. 75 Å diameter. Branching of the fibrils is evident. (x 28,000; reduced)

than 0.2 μ diameter (below the limits of resolution of the light microscope) exist in these cells (figs. 6a, 10, 11 and 13). The presence of internal ultrastructure and cristae m.tochondriales distinguish the mitochondria from these granules (figs. 7, 11 and 12).28 These granules are scattered throughout the cytoplasm, and occasionally they can be found in close proximity to the Auer bodies (fig. 13). These nonspecific granulations have homogeneous densities similar to the plaques of the Auer bodies. They lack any demonstrable ultrastructure or membranous capsule (fig. 10). Fused granular masses possessing the same ultracytologic characteristics can be demonstrated, although rarely, in juxtaposition with the Auer bodies (fig. 6a). The homogeneous granules of mature neutrophilic leukocytes resemble, in density and form, the plaques of the Auer bodies (fig. 15). However, these granules occasionally exhibit what may be a limiting membrane (fig. 15a).

DISCUSSION

After demonstrating histochemical similarities of Auer bodies and cytoplasmic granulation, Ackerman theorized the nature of the Auer bodies to be a fusion of these granules. Both structures contain relatively high concentrations of mucopolysaccharide, phospholipid, pentosenucleoprotein, and both give a strong peroxidase reaction. With electron-microscopic technics the marked similarities of histologic structure can be analyzed. The homogeneous moderate density of the cytoplasmic granules correlates well with the densities of the individual plaques of the coacervate rod. Fused granular masses can be identified in close proximity to the Auer bodies. Although no certain morphologic transition from cytoplasmic granulation to Auer bodies is clearly demon-
Fig. 15.—Electron micrograph of a mature neutrophil from normal peripheral blood. The portions of the nucleus (n) are the result of sectioning through the multiple lobes. The specific neutrophilic granulations (ng) are evident. Occasional profiles of the endoplasmic reticulum (er) are visible. (x 28,000; reduced)

Fig. 15a (inset).—The neutrophilic granules (ng') are homogeneous structures of moderate density which lack internal ultrastructure. The density is similar to that of the plaques of the Auer bodies. Frequently granules (ng2) are found which exhibit what may be a limiting membrane. (x 57,000; reduced)

strable histologically, the consistent similarities in the ultrastructural organization suggest such a circumstance. These findings tend to support the theory of Auer body formation from the specific cytoplasmic granulation.

Recently granules have been described within the sacs of the endoplasmic reticulum in the exocrine cells of the pancreas.4 However, the system of the endoplasmic reticulum in these cells is highly developed, in contrast to the minute profiles of the reticulum found in immature leukocytes. Granules could not be found within the cisternae and sacs of the endoplasmic reticulum in these immature cells. The occasional demonstration of azurophilic granulation was too random to merit attention. Certainly no granular masses possessing
the characteristics of known azurophilic granules could be found within or without the endoplasmic reticulum. Therefore ultrastructural evidence supporting the concept of Auer body formation from azurophilic granulation within the endoplasmic reticulum system could not be found.

The internal ultrastructure of the rodlike Auer bodies is such that the planes of cleavage of the homogeneous plaques are demonstrable in ultrasonically fractionated preparations as well as in electron-microscopic preparations. It is interesting to note that Bessis’ illustrations of Auer bodies ultrasonically fractionated and ultracentrifugally separated from the protoplasm of the leukocyte show central lucid areas paralleling the long axis of the rods. These lucid areas correspond to the planes of cleavage demonstrable with the electron microscope.

A curious intracytoplasmic “fibrillar formation” was found in blast cells of some acute leukemic cells. The ultrahistology of this complex fibrillar whorl has recently been described, but its significance and genesis, as yet, remain unexplained. The association of the fibrillar formation and Auer bodies is uncertain; however, both of these aberrant structures were often found in the immature leukocytes of monocytic leukemia, although rarely within the same cell. Despite the fact that these structures were well within the limits of resolving power of the light microscope, measuring ca. ½ to 2½ μ oval diameter and ca. ¼ to 1 μ depth, light microscope analysis of Wright-stained peripheral blood smears failed to visualize these structures. The individual fibrillae, averaging 75 A diameter, are probably not closely enough approximated to be resolved with the light microscope, and the area appears to be undifferentiated cytoplasm (fig. 14). A small granular area was found to be enclosed within the whorl of fibrils. Auer bodies were not found within the fibrillar whorl or intimately in contact with the fibrillar formation. Shortly before the description of the fibrillar formation, a “granule-vacuole body” was discovered in cases of acute monocytic and myelogenous leukemias, using light microscope technics. The cytochemical studies on this structure suggested a similarity between the granule-vacuole body, the Auer body and cytoplasmic granulation. Cytochemical studies were not done on the fibrillar formation, but there is evidence indicating that the fibrillar formation and the granule-vacuole body are the same structure. Both were found in the same cell types in the same types of leukemias; both are not visible with alcoholic fixatives such as Wright’s stain. The dimensions of these two structures are essentially within the same range (allowing for spreading distortion on slides, and in vitro swelling in the preparation of smears). The typical whorl-like structure of the fibrillar formation seen with the fine detail of electron microscopy could well appear globular, as do the granule-vacuole bodies seen with the light microscope. The electron microscope reveals that the central portion of the whorl contains a mass of small granules, which could appear as an amorphous single granule viewed with the light microscope. Although the aforementioned evidence represents a surmisal rather than a factual documentation, the structural similarities suggest more than coincidence. Electron-microscopic studies have shown vastly dissimilar structural architecture between the Auer body and the fibrillar formation. If the fibrillar formation and
the granule-vacuole body are the same structure, then the cytochemical similarities between them and the Auer bodies are accidental and probably the result of the construction of different products from similar organic chemical components. Therefore it is concluded that the Auer body and the granule-vacuole body are neither related architecturally nor pathophysiologically.

**SUMMARY**

The light microscopic morphology, chemical composition, ultrasonic fractionation, ultracentrifugal separation and light absorption characteristics of Auer bodies have all been described. However, since the initial observations by John Auer in 1906 and until the advent of electron microscopy, few data have been added to elucidate the structure of these bodies. With the aid of the electron microscope, Auer bodies have been found to be coacervates of laminated, homogeneous, crystalline plaques with the long axis of the plaques in the same plane as the long axis of the rod. The ultracytologic resemblance between Auer bodies and cytoplasmic granulation supports previous histochemical evidence suggesting the genesis of Auer bodies from cytoplasmic granules.

Existing evidence indicates that the newly discovered fibrillar formation and the recently described granule-vacuole body are the same structure. Although histochemical studies show similarities between these structures and Auer bodies, they are architecturally unrelated and probably have distinctly different pathophysiologic significance.

**SUMMARIO IN INTERLINGUA**

Le morphologia lumino-microscopic, le composition chimic, le fractionation ultrasonic, le separation ultracentrifugal, e le caracteristicas lumino-absorptive de corpores de Auer ha omnes essite describite. Tamen, deposit le observationes initial de John Auer in 1906 usque al advento del microscopio electronic, pauc datos ha essite addite al elucidation del structura de iste corpores. Con le adjuta del microscopio electronic, il ha essite trovate que corpores de Auer es coacervatos de laminate, homogenee, crystallin placas, con le axe longe del placas occupante le mesme plano como le axe longe del formation total. Le similitude ultracytologic del corpores de Auer con granulation cytoplasmic corroborara previe observationes chimic que sug-gereva que le genese del corpores de Auer parti ab granulos cytoplasmic.

Le datos currentemente disponibile indica que le movemente discoperite formation fibrillar e le recentemente describite corpore granulo-vacuolar es le mesme structura. Ben que studios histochimic revela similitudes inter iste structuras e le corpores de Auer, illos es architecturalmente differente. Il es probabile que illos ha distinctemente differente significationes pathophysio-

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REFERENCES


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